1. Br J Hosp Med (Lond). 2024 Jul 30;85(7):1-13. doi: 10.12968/hmed.2024.0114.

Impact of mechanical barrier damage and interleukin-17 on symptoms in patients

with post-infectious irritable bowel syndrome.

Zhao J(1), Dai Y(2), Tian J(1), Lei L(1), Zhou X(1).

Author information:

(1)Department of Gastroenterology, The First Affiliated Hospital of Chongqing

Medical University, Chongqing, China.

(2)Department of Gastroenterology, People's Hospital of Longchang, Longchang,

Sichuan, China.

Aims/Background The pathogenesis of irritable bowel syndrome encompasses various

factors, including abnormal gastrointestinal motility, heightened visceral

sensitivity, dysfunction in the brain-gut axis, psychological influences, and

disturbances in the intestinal flora. These factors manifest primarily as

persistent or intermittent abdominal pain, diarrhoea, alterations in bowel

habits, or changes in stool characteristics. In our investigation, we delve into

the repercussions of mechanical barrier damage and immune dysfunction on

symptoms among patients with post-infectious irritable bowel syndrome. Methods

This study recruited a total of 20 healthy controls and 49 patients diagnosed

with irritable bowel syndrome. Among the irritable bowel syndrome patients, we

categorised them into two groups based on the ROME IV diagnostic criteria: the

post-infectious irritable bowel syndrome group (n=23) and the

non-post-infectious irritable bowel syndrome group (n=26). To compare clinical

features, we utilised the Gastrointestinal Symptom Rating Scale, Self-Rating

Depression Scale, and Self-Rating Anxiety Scale. Furthermore, we employed

various techniques including haematoxylin and eosin (HE) staining, electron

microscopy, Enzyme-linked Immunosorbent Assay, and flow cytometry to assess

changes in immune cells, immune factors, inflammatory biomarkers, and intestinal

barrier function. Results Under haematoxylin and eosin staining, post-infectious

irritable bowel syndrome patients demonstrated increased neutrophils and plasma

cells compared to the control group. Additionally, electron microscopy revealed

ultrastructural changes such as the widening of the epithelial cell gap in the

intestinal mucosa among post-infectious irritable bowel syndrome patients.

Comparatively, the Gastrointestinal Symptom Rating Scale, Self-Rating Anxiety

Scale, and Self-Rating Depression Scale scores were significantly elevated in

the post-infectious irritable bowel syndrome group in contrast to both the

control group and the non- post-infectious irritable bowel syndrome group (p <

0.05). Moreover, post-infectious irritable bowel syndrome patients exhibited a

notably higher neutrophil-to-lymphocyte ratio compared to the control group (p <

0.05). Furthermore, the levels of interleukin-17 (IL-17) were elevated in

post-infectious irritable bowel syndrome patients compared to the control group

(p < 0.05). Additionally, the post-infectious irritable bowel syndrome group

displayed a higher percentage of T helper 17 (Th17) cells compared to both the

control and non-post-infectious irritable bowel syndrome groups (p < 0.05).

Conclusion Acute gastrointestinal infection can disrupt the balance of

intestinal flora, leading to dysbiosis. This dysbiosis can trigger the release

of pro-inflammatory factors, including interleukin-17, which contributes to the

impairment of the intestinal mucosal barrier. Consequently, this sets the stage

for the development of long-lasting, mild chronic intestinal inflammation,

ultimately culminating in the onset of post-infectious irritable bowel syndrome.

Furthermore, within the framework of the gut-brain axis interaction, anxiety and

depression may exacerbate intestinal inflammation in post-infectious irritable

bowel syndrome patients. This interaction can perpetuate and prolong clinical

symptoms in individuals with post-infectious irritable bowel syndrome, further

complicating the management of the condition.

DOI: 10.12968/hmed.2024.0114

PMID: 39078895 [Indexed for MEDLINE]

2. World J Gastroenterol. 2018 Jan 7;24(1):46-57. doi: 10.3748/wjg.v24.i1.46.

Increased intestinal mucosal leptin levels in patients with diarrhea-predominant

irritable bowel syndrome.

Liu DR(1), Xu XJ(2), Yao SK(3).

Author information:

(1)Graduate School, Peking Union Medical College and Chinese Academy of Medical

Sciences, Beijing 100730, China.

(2)Department of Gastroenterology, First Hospital of Shanxi Medical University,

Taiyuan 030001, Shanxi Province, China.

(3)Department of Gastroenterology, China-Japan Friendship Hospital, Beijing

100029, China. shukunyao@126.com.

AIM: To measure the leptin levels in patients with diarrhea-predominant

irritable bowel syndrome (IBS-D) and analyze the relationship of leptin with

clinical features, visceral sensitivity, mast cells, and nerve fibers.

METHODS: Forty-two patients with IBS-D fulfilling the Rome III criteria and 20

age- and sex-matched healthy controls underwent clinical and psychological

evaluations using validated questionnaires (including IBS Symptom Severity

Scale, IBS-specific Quality of Life, Hamilton Anxiety Scale, and Hamilton

Depression Scale), along with colonoscopy, colonic mucosal biopsy, and visceral

sensitivity testing. Serum leptin levels were assayed using enzyme-linked

immunosorbent assay. Mucosal leptin expression and localization were evaluated

using immunohistochemistry and immunofluorescence. Mucosal leptin mRNA levels

were quantified using quantitative real-time reverse transcription polymerase

chain reaction. Mast cell counts and activation rates were investigated by

toluidine blue staining. Correlation analyses between these parameters were

performed.

RESULTS: There were no statistically significant differences in age, gender, or

body mass index between the IBS-D group and the control group. The median IBS

Symptom Severity Scale score in the IBS-D group was 225.0 (range, 100-475).

IBS-D patients had significantly increased anxiety [IBS-D: median, 6.5;

interquartile range (IQR), 3.3; control: median, 2.0; IQR, 2.0; P < 0.001] and

depression (IBS-D: median, 7.0; IQR, 3.0; control: median, 3.0; IQR, 2.0; P <

0.001) scores. IBS-D patients had significantly lower first sensation threshold

(IBS-D: median, 50.6; IQR, 25.9; control: median, 80.5; IQR, 18.6; P < 0.001),

defecation sensation threshold (IBS-D: median, 91.5; IQR, 29.3; control: median,

155.0; IQR, 21.1; P < 0.001) and maximum tolerable threshold (IBS-D: median,

163.2; IQR, 71.2; control: median, 226.2; IQR, 39.3; P < 0.001). Mucosal leptin

expression, as reflected by integrated optical density (IBS-D: median, 4424.71;

IQR, 4533.63; control: median, 933.65; IQR, 888.10; P < 0.001), leptin mRNA

expression (IBS-D: median, 1.1226; IQR, 1.6351; control: median, 0.8947; IQR,

0.4595; P = 0.009), and mast cell activation rate (IBS-D: median, 71.2%; IQR,

12.9%; control group: median, 59.4%; IQR, 18.88%; P < 0.001) were significantly

increased in IBS-D patients. The colocalization of leptin and leptin receptors

was observed on mast cells and PGP9.5-positive nerve fibers in the intestinal

mucosa. Also, leptin expression was positively correlated with anxiety,

depression, and the mast cell activation rate, but negatively correlated with

the defecation sensation threshold and the maximum tolerance threshold during

visceral sensitivity testing (adjusted P < 0.0038).

CONCLUSION: Increased levels of mucosal leptin may interact with mast cells and

the nervous system to contribute to the pathogenesis of IBS-D.

DOI: 10.3748/wjg.v24.i1.46

PMCID: PMC5757124

PMID: 29358881 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: All authors have

no conflict of interest related to this manuscript.

3. Clin Gastroenterol Hepatol. 2025 Feb;23(2):371-373.e1. doi:

10.1016/j.cgh.2024.08.019. Epub 2024 Aug 30.

Missed Opportunity to Triage Patients With Irritable Bowel Syndrome to

Multidisciplinary Therapy.

Tetali B(1), Chey WD(2), Menees SB(3).

Author information:

(1)Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan.

(2)Division of Gastroenterology and Hepatology, University of Michigan, Ann

Arbor, Michigan.

(3)Division of Gastroenterology and Hepatology, University of Michigan, Ann

Arbor, Michigan; Veterans Affairs Ann Arbor Healthcare System, Ann Arbor,

Michigan. Electronic address: sbartnik@med.umich.edu.

DOI: 10.1016/j.cgh.2024.08.019

PMID: 39209195

4. United European Gastroenterol J. 2024 Oct;12(8):1145. doi: 10.1002/ueg2.12681.

Epub 2024 Sep 26.

Translational evaluation of Gelsectan庐 effects on gut barrier dysfunction and

visceral pain in animal models and irritable bowel syndrome with diarrhea.

Lucca LC(1), Brusamarello NP(1), Fornari F(1).

Author information:

(1)School of Medicine, University of Passo Fundo, Passo Fundo, Brazil.

DOI: 10.1002/ueg2.12681

PMCID: PMC11485293

PMID: 39324606

5. J Clin Med. 2022 Jul 22;11(15):4269. doi: 10.3390/jcm11154269.

Abdominal Pain in Inflammatory Bowel Diseases: A Clinical Challenge.

Wils P(1), Caron B(2)(3), D'Amico F(4)(5), Danese S(4), Peyrin-Biroulet L(2)(3).

Author information:

(1)Department of Gastroenterology, Claude Huriez Hospital, University of Lille,

F-59000 Lille, France.

(2)Department of Gastroenterology, University of Lorraine, CHRU-Nancy, F-54000

Nancy, France.

(3)Department of Gastroenterology, University of Lorraine, Inserm, NGERE,

F-54000 Nancy, France.

(4)Gastroenterology and Endoscopy, IRCCS Ospedale San Raffaele, 20132 Milan,

Italy.

(5)Department of Biomedical Sciences, Humanitas University, 20090 Milan, Italy.

Up to 60% of inflammatory bowel disease (IBD) patients experience abdominal pain

in their lifetime regardless of disease activity. Pain negatively affects

different areas of daily life and particularly impacts the quality of life of

IBD patients. This review provides a comprehensive overview of the

multifactorial etiology implicated in the chronic abdominal pain of IBD patients

including peripheral sensitization by inflammation, coexistent irritable bowel

syndrome, visceral hypersensitivity, alteration of the brain-gut axis, and the

multiple factors contributing to pain persistence. Despite the optimal

management of intestinal inflammation, chronic abdominal pain can persist, and

pharmacological and non-pharmacological approaches are necessary. Integrating

psychological support in care models in IBD could decrease disease burden and

health care costs. Consequently, a multidisciplinary approach similar to that

used for other chronic pain conditions should be recommended.

DOI: 10.3390/jcm11154269

PMCID: PMC9331632

PMID: 35893357

Conflict of interest statement: P.W. declares no conflict of interest. B.C.

declares no conflict of interest. F.D. declares no conflict of interest. S.D.

has served as a speaker, consultant, and advisory board member for

Schering-Plough, AbbVie, Actelion, Alphawasserman, AstraZeneca, Cellerix, Cosmo

Pharmaceuticals, Ferring, Genentech, Grunenthal, Johnson and Johnson, Millenium

Takeda, MSD, Nikkiso Europe GmbH, Novo Nordisk, Nycomed, Pfizer, Pharmacosmos,

UCB Pharma, and Vifor. L.P.-B. declares personal fees from Galapagos, AbbVie,

Janssen, Genentech, Ferring, Tillots, Celltrion, Takeda, Pfizer, Index

Pharmaceuticals, Sandoz, Celgene, Biogen, Samsung Bioepis, Inotrem, Allergan,

MSD, Roche, Arena, Gilead, Amgen, BMS, Vifor, Norgine, Mylan, Lilly, Fresenius

Kabi, OSE Immunotherapeutics, Enthera, Theravance, Pandion Therapeutics,

Gossamer Bio, Viatris, Thermo Fisher; grants from Abbvie, MSD, Takeda, and

Fresenius Kabi; stock options: CTMA.

6. Gastroenterol Hepatol Bed Bench. 2024;17(3):288-296. doi:

10.22037/ghfbb.v17i3.2920.

Comparing the effectiveness of online individualized transdiagnostic treatment

with acceptance and commitment therapy on medication adherence, gastrointestinal

symptoms and perceived stress of patients with irritable bowel syndrome.

Shahkaram H(1), Sadeghi A(2), Masjedi Arani A(1), Bakhtiari M(1), Kianimoghadam

AS(1).

Author information:

(1)Department of Clinical Psychology, School of Medicine, Shahid Beheshti

University of Medical Sciences, Tehran, Iran.

(2)Gastroenterology and Liver Diseases Research Center, Research Institute for

Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical

Sciences, Tehran, Iran.

AIM: This study aimed to investigate whether transdiagnostic treatment as well

as acceptance and commitment therapy (ACT) could improve treatment adherence and

alleviate gastrointestinal symptoms plus perceived stress in patients suffering

from irritable bowel syndrome.

BACKGROUND: Research has shown that people with chronic diseases often have

negative attitudes toward medications, especially when they also have

psychiatric disorders. This, along with the complex dosing requirements and

inadequate knowledge about medication adherence among irritable bowel syndrome

patients, can affect the treatment efficacy.

METHODS: A randomized clinical trial was conducted using a pre-test-post-test

design. The statistical population included patients with irritable bowel

syndrome referring to Taleghani Hospital in Tehran between winter 2021 and

spring 2022. Convenience sampling was used to select 30 individuals, with 15

people assigned to each group. Two types of psychotherapy were provided online

and individually to the participants. The desired treatments were given to the

transdiagnostic treatment and ACT groups in eight weekly sessions of 45-60

minutes.

RESULTS: There was no significant difference between the transdiagnostic

treatment pre-test and ACT regarding perceived stress, medication adherence, and

gastrointestinal symptoms (P>0.05). There was no significant difference either

between the transdiagnostic treatment and ACT post-test. However, there was a

significant difference between the pre-test and post-test phases of ACT

regarding adherence, gastrointestinal symptoms, plus perceived stress (P<0.05)

and transdiagnostic treatment regarding gastrointestinal symptoms (P<0.05).

CONCLUSION: Specialists may use transdiagnostic treatment and ACT as effective

psychological treatments to alleviate gastrointestinal symptoms and perceived

stress, thereby increasing treatment adherence in patients with irritable bowel

syndrome.

漏 2024, Gastroenterology and Hepatology From Bed to Bench (GHFBB).

DOI: 10.22037/ghfbb.v17i3.2920

PMCID: PMC11413384

PMID: 39308538

Conflict of interest statement: The authors declare that they have no competing

interests.

7. World J Gastroenterol. 2024 Jun 7;30(21):2744-2747. doi:

10.3748/wjg.v30.i21.2744.

Unresolved conundrum of the role of physical activity in inflammatory bowel

disease: What next?

Ananthakrishnan N(1).

Author information:

(1)Department of Surgery, Sri Balaji Vidyapeeth, Pondicherry 607402, India.

n.ananthk@gmail.com.

There is considerable controversy on the role of physical activity in irritable

bowel disease (IBD) since published reports are conflicting. It is well known

that there is known relapse with specific treatment in IBD. This, in addition to

onset of extraintestinal symptoms creates a need to think of alternate

approaches. In this context, the current article describes the need of a

multi-institutional study with standard protocol of physical activity for

documenting its effect on both the primary disease and the extra alimentary

manifestations. This paper also points out the possibility of using adjuvant

complementary medicine such as yoga, whose effects have been documented in other

diseases like irritable bowel syndrome. A third approach could be to focus on

the intestinal dysbiosis in IBD and concentrate on research on restoring the

microbial flora to normal, to see whether the extra-intestinal symptoms are

alleviated.

漏The Author(s) 2024. Published by Baishideng Publishing Group Inc. All rights

reserved.

DOI: 10.3748/wjg.v30.i21.2744

PMCID: PMC11185299

PMID: 38899327 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: All the authors

report no relevant conflicts of interest for this article.

8. Clin Exp Med. 2024 Sep 28;24(1):232. doi: 10.1007/s10238-024-01496-9.

Intestinal permeability disturbances: causes, diseases and therapy.

Macura B(1), Kiecka A(2), Szczepanik M(2).

Author information:

(1)Faculty of Health Sciences, Institute of Physiotherapy, Chair of Biomedical

Sciences, Jagiellonian University Medical College, Kopernika 7a, 31-034, Krak贸w,

Poland. barbara.macura@uj.edu.pl.

(2)Faculty of Health Sciences, Institute of Physiotherapy, Chair of Biomedical

Sciences, Jagiellonian University Medical College, Kopernika 7a, 31-034, Krak贸w,

Poland.

Nowadays, a pathological increase in the permeability of the intestinal barrier

(the so-called leaky gut) is increasingly being diagnosed. This condition can be

caused by various factors, mainly from the external environment. Damage to the

intestinal barrier entails a number of adverse phenomena: dysbiosis,

translocation of microorganisms deep into the intestinal tissue, immune

response, development of chronic inflammation. These phenomena can ultimately

lead to a vicious cycle that promotes the development of inflammation and

further damage to the barrier. Activated immune cells in mucosal tissues with

broken barriers can migrate to other organs and negatively affect their

functioning. Damaged intestinal barrier can facilitate the development of local

diseases such as irritable bowel disease, inflammatory bowel disease or celiac

disease, but also the development of systemic inflammatory diseases such as

rheumatoid arthritis, ankylosing spondylitis, hepatitis, and lupus

erythematosus, neurodegenerative or psychiatric conditions, or metabolic

diseases such as diabetes or obesity. However, it must be emphasized that the

causal links between a leaky gut barrier and the onset of certain diseases often

remain unclear and require in-depth research. In light of recent research, it

becomes crucial to prevent damage to the intestinal barrier, as well as to

develop therapies for the barrier when it is damaged. This paper presents the

current state of knowledge on the causes, health consequences and attempts to

treat excessive permeability of the intestinal barrier.

漏 2024. The Author(s).

DOI: 10.1007/s10238-024-01496-9

PMCID: PMC11438725

PMID: 39340718 [Indexed for MEDLINE]

Conflict of interest statement: The authors declare no competing interests.

9. PLoS One. 2021 Jun 11;16(6):e0252930. doi: 10.1371/journal.pone.0252930.

eCollection 2021.

Disruption of the pro-inflammatory, anti-inflammatory cytokines and tight

junction proteins expression, associated with changes of the composition of the

gut microbiota in patients with irritable bowel syndrome.

Ivashkin V(1), Poluektov Y(2), Kogan E(1), Shifrin O(1), Sheptulin A(1),

Kovaleva A(1), Kurbatova A(1), Krasnov G(2), Poluektova E(1).

Author information:

(1)I.M. Sechenov First Moscow State Medical University (Sechenov University),

Moscow, Russian Federation.

(2)Engelhardt Institute of Molecular Biology, Russian Academy of Sciences,

Moscow, Russia.

BACKGROUND: Irritable bowel syndrome (IBS) is a pathologic condition

characterized by changes in gut microbiome composition, low-grade inflammation,

and disruption of intestinal wall permeability. The interaction between the gut

microbiome and the disease manifestation remains unclear. The changing of tight

junction proteins and cytokines expression throughout the gastrointestinal tract

in IBS patients has not been studied yet.

AIM OF THE STUDY: To assess the changes of gut microbiome composition, tight

junction proteins, and cytokines expression of intestinal mucosa from the

duodenum to the distal part of the colon in IBS patients and healthy volunteers.

METHODS: In 31 IBS patients (16 patients with IBS-D; 15 patients with IBS-C) and

10 healthy volunteers the expression of CLD-2, CLD-3, CLD-5, IL-2, IL-10, and

TNF-伪 in mucosal biopsy specimens was determined by morphological and

immune-histochemical methods. The qualitative and quantitative composition of

the intestinal microbiota was assessed based on 16S rRNA gene sequencing in both

groups of patients.

RESULTS: The expression of IL-2 and TNF-伪 was significantly increased in IBS

patients compared with the controls (p<0.001), with a gradual increase from the

duodenum to the sigmoid colon. The expression of IL-10, CLD-3, and CLD-5 in

mucosal biopsy specimens of these patients was lower than in the control group

(p<0.001). Increased ratios of Bacteroidetes and decreased ratios of Firmicutes

were noted in IBS patients compared to healthy volunteers (p<0.05).

CONCLUSION: IBS patients have impaired gut permeability and persisting low-grade

inflammation throughout the gastrointestinal tract. Changes in the gut

microbiota may support or exacerbate these changes.

DOI: 10.1371/journal.pone.0252930

PMCID: PMC8195381

PMID: 34115808 [Indexed for MEDLINE]

Conflict of interest statement: The authors have declared that no competing

interests exist.

10. World J Gastroenterol. 2022 Sep 7;28(33):4861-4874. doi:

10.3748/wjg.v28.i33.4861.

Are bowel symptoms and psychosocial features different in irritable bowel

syndrome patients with abdominal discomfort compared to abdominal pain?

Fang XC(1), Fan WJ(2)(3), Drossman DD(4)(5)(6), Han SM(7), Ke MY(2).

Author information:

(1)Department of Gastroenterology, Peking Union Medical College Hospital,

Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing

100730, China. fangxiucai2@aliyun.com.

(2)Department of Gastroenterology, Peking Union Medical College Hospital,

Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing

100730, China.

(3)Department of Gastroenterology, Tongji Hospital, Tongji Medical College,

Huazhong University of Science & Technology, Wuhan 430030, Hubei Province,

China.

(4)Center of Functional GI and Motility Disorders, University of North Carolina,

Chapel Hill, NC 27517, United States.

(5)Center for Education and Practice of Biopsychosocial Care, Drossman

Gastroenterology, Durham, NC 27713, United States.

(6)Rome Foundation, Rome Foundation, Raleigh, NC 27614, United States.

(7)Department of Epidemiology and Statistics, Institute of Basic Medical

Sciences, Chinese Academy of Medical Sciences & School of Basic Medicine, Peking

Union Medical College, Beijing 100005, China.

BACKGROUND: The Rome IV criteria eliminated abdominal discomfort for irritable

bowel syndrome (IBS), which was previously included in Rome III. There are

questions as to whether IBS patients with abdominal discomfort (seen in Rome III

but not Rome IV) are different from those with abdominal pain (Rome IV).

AIM: To compare bowel symptoms and psychosocial features in IBS patients

diagnosed with Rome III criteria with abdominal discomfort, abdominal pain, and

pain & discomfort.

METHODS: We studied IBS patients meeting Rome III criteria. We administered the

IBS symptom questionnaire, psychological status, and IBS quality of life.

Patients were classified according to the predominant abdominal symptom

associated with defecation into an only pain group, only discomfort group, and

pain & discomfort group. We compared bowel symptoms, extraintestinal symptoms,

IBS quality of life, psychological status and healthcare-seeking behaviors, and

efficacy among the three groups. Finally, we tested risk factors for symptom

reporting in IBS patients.

RESULTS: Of the 367 Rome III IBS patients enrolled, 33.8% (124 cases) failed to

meet Rome IV criteria for an IBS diagnosis. There were no meaningful differences

between the pain group (n = 233) and the discomfort group (n = 83) for the

following: (1) Frequency of defecatory abdominal pain or discomfort; (2) Bowel

habits; (3) Coexisting extragastrointestinal pain; (4) Comorbid anxiety and

depression; and (5) IBS quality of life scores except more patients in the

discomfort group reported mild symptom than the pain group (22.9% vs 9.0%).

There is a significant tendency for patients to report their defecatory and

non-defecatory abdominal symptom as pain alone, or discomfort alone, or pain &

discomfort (all P < 0.001).

CONCLUSION: IBS patients with abdominal discomfort have similar bowel symptoms

and psychosocial features to those with abdominal pain. IBS symptoms manifesting

abdominal pain or discomfort may primarily be due to different sensation and

reporting experience.

漏The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights

reserved.

DOI: 10.3748/wjg.v28.i33.4861

PMCID: PMC9476853

PMID: 36156921 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: There are no

conflicts of interest to report.

11. Ter Arkh. 2022 Feb 15;94(2):180-187. doi: 10.26442/00403660.2022.02.201368.

[The effectiveness of a probiotic containing Bifidobacterium longum BB-46 and

Enterococcus faecium ENCfa-68 in the treatment of post-infectious irritable

bowel syndrome. Prospective randomized comparative study].

[Article in Russian; Abstract available in Russian from the publisher]

Yakovenko EP(1), Strokova TV(1), Ivanov AN(1), Iakovenko AV(1), Gioeva IZ(2),

Aldiyarova MA(3).

Author information:

(1)Pirogov Russian National Research Medical University.

(2)North Ossetian State Medical Academy.

(3)Kazakh-Russian Medical University.

BACKGROUND: In the treatment of post-infectious irritable bowel syndrome

(PI-IBS), the leading role belongs to the normalization of the composition of

the intestinal microbiome, the disturbances of which are associated with

previous intestinal infections.

AIM: To study the effectiveness of the drug Bifiform in the treatment of PI-IBS.

MATERIALS AND METHODS: An open, prospective, comparative, randomized study

included 62 patients with PI-IBS. The diagnosis was confirmed by the results of

clinical, laboratory and endoscopic examination of the intestine and met the

diagnostic criteria for IBS of the Rome Consensus IV. The patients were

randomized into 2 groups depending on the therapy. The patients of the main

group received an antispasmodic drug (mebeverin 200 mg 2 times a day or

trimebutin 200 mg 3 times a day for 4 weeks), an antibiotic (rifaximin 400 mg 3

times a day or nifuroxazide 400 mg 2 once a day for 1 week), a drug that

normalizes the consistency of feces (dioctahedral smectite or macrogol 4000) and

Bifiform 2 capsules 2 times a day for 2 weeks. For patients of control group

similar therapy was performed without the Bifiform. Evaluation of the

effectiveness of treatment was carried out at the end of the course of therapy

and 6 months after its termination.

RESULTS: All included patients with PI-IBS had abdominal pain, flatulence and

tenderness to palpation along the bowel, most of them had diarrhea. Disorders of

the intestinal microbiota were detected in 77.4% of patients, while excessive

bacterial growth in the small intestine occurred in 72.6%, disorders of the

colon microbiocenosis with the presence of opportunistic bacteria in 62.9% of

patients. A significant part of the patients had a combination of small and

large intestinal dysbiosis. Histological examination of the colon mucosa showed

signs of low degree of inflammation activity in all patients. The moderate

increase in the level of fecal calprotectin was found in 62.2% of patients with

colonic dysbiosis. The majority of patients in the main group showed a

pronounced positive dynamics of clinical manifestations of the disease,

restoration of the normal composition of the intestinal microbiota and

normalization of the content of fecal calprotectin at the end of the course

therapy. The good result was observed much more often in the main group at the

end of the course of treatment and 6 months after its termination.

CONCLUSION: The inclusion of Bifiform in the complex therapy of PI-IBS

significantly increases its effectiveness both in arresting the clinical

manifestations of the disease, and in restoring the normal composition of the

intestinal microbiome and reducing the inflammatory process in the intestinal

mucosa. In the majority of patients receiving Bifiform, the remission of the

disease achieved at the end of the course of treatment and persisted even 6

months after its termination.

Publisher: 袨斜芯褋薪芯胁邪薪懈械. 袙 谢械褔械薪懈懈 锌芯褋褌懈薪褎械泻褑懈芯薪薪芯谐芯 褋懈薪写褉芯屑邪 褉邪蟹写褉邪卸械薪薪芯谐芯

泻懈褕械褔薪懈泻邪 (袩袠-小袪袣) 胁械写褍褖邪褟 褉芯谢褜 锌褉懈薪邪写谢械卸懈褌 薪芯褉屑邪谢懈蟹邪褑懈懈 褋芯褋褌邪胁邪 泻懈褕械褔薪芯谐芯

屑懈泻褉芯斜懈芯屑邪, 薪邪褉褍褕械薪懈褟 泻芯褌芯褉芯谐芯 邪褋褋芯褑懈懈褉芯胁邪薪褘 褋 锌械褉械薪械褋械薪薪褘屑懈 泻懈褕械褔薪褘屑懈

懈薪褎械泻褑懈褟屑懈. 笑械谢褜. 袠蟹褍褔懈褌褜 褝褎褎械泻褌懈胁薪芯褋褌褜 锌褉械锌邪褉邪褌邪 袘懈褎懈褎芯褉屑 胁 谢械褔械薪懈懈 袩袠-小袪袣.

袦邪褌械褉懈邪谢褘 懈 屑械褌芯写褘. 袙 芯褌泻褉褘褌芯械 锌褉芯褋锌械泻褌懈胁薪芯械 褋褉邪胁薪懈褌械谢褜薪芯械 褉邪薪写芯屑懈蟹懈褉芯胁邪薪薪芯械

懈褋褋谢械写芯胁邪薪懈械 斜褘谢懈 胁泻谢褞褔械薪褘 62 锌邪褑懈械薪褌邪 褋 袩袠-小袪袣. 袛懈邪谐薪芯蟹 锌芯写褌胁械褉卸写械薪

褉械蟹褍谢褜褌邪褌邪屑懈 泻谢懈薪懈褔械褋泻芯谐芯, 谢邪斜芯褉邪褌芯褉薪芯谐芯 懈 褝薪写芯褋泻芯锌懈褔械褋泻芯谐芯 懈褋褋谢械写芯胁邪薪懈泄

泻懈褕械褔薪懈泻邪 懈 褋芯芯褌胁械褌褋褌胁芯胁邪谢 写懈邪谐薪芯褋褌懈褔械褋泻懈屑 泻褉懈褌械褉懈褟屑 小袪袣 袪懈屑褋泻芯谐芯 泻芯薪褋械薪褋褍褋邪 IV.

袙 蟹邪胁懈褋懈屑芯褋褌懈 芯褌 锌褉芯胁芯写懈屑芯泄 褌械褉邪锌懈懈 锌邪褑懈械薪褌褘 斜褘谢懈 褉邪薪写芯屑懈蟹懈褉芯胁邪薪褘 胁 2 谐褉褍锌锌褘.

袩邪褑懈械薪褌褘 芯褋薪芯胁薪芯泄 谐褉褍锌锌褘 锌芯谢褍褔邪谢懈 褋锌邪蟹屑芯谢懈褌懈泻 (屑械斜械胁械褉懈薪 200 屑谐 2 褉邪蟹邪 胁 写械薪褜

懈谢懈 褌褉懈屑械斜褍褌懈薪 200 屑谐 3 褉邪蟹邪 胁 写械薪褜 4 薪械写), 邪薪褌懈斜懈芯褌懈泻 (褉懈褎邪泻褋懈屑懈薪 400 屑谐 3 褉邪蟹邪

胁 写械薪褜 懈谢懈 薪懈褎褍褉芯泻褋邪蟹懈写 400 屑谐 2 褉邪蟹邪 胁 写械薪褜 1 薪械写), 锌褉械锌邪褉邪褌 写谢褟 薪芯褉屑邪谢懈蟹邪褑懈懈

泻芯薪褋懈褋褌械薪褑懈懈 泻邪谢邪 (写懈芯泻褌邪褝写褉懈褔械褋泻懈泄 褋屑械泻褌懈褌 懈谢懈 屑邪泻褉芯谐芯谢 4000) 懈 袘懈褎懈褎芯褉屑 锌芯 2

泻邪锌褋褍谢褘 2 褉邪蟹邪 胁 写械薪褜 2 薪械写. 袩邪褑懈械薪褌邪屑 泻芯薪褌褉芯谢褜薪芯泄 谐褉褍锌锌褘 锌褉芯胁芯写懈谢邪褋褜

邪薪邪谢芯谐懈褔薪邪褟 褌械褉邪锌懈褟 斜械蟹 胁泻谢褞褔械薪懈褟 锌褉械锌邪褉邪褌邪 袘懈褎懈褎芯褉屑. 袨褑械薪泻邪 褝褎褎械泻褌懈胁薪芯褋褌懈

谢械褔械薪懈褟 胁褘锌芯谢薪褟谢邪褋褜 锌芯褋谢械 芯泻芯薪褔邪薪懈褟 泻褍褉褋芯胁芯泄 褌械褉邪锌懈懈 懈 褔械褉械蟹 6 屑械褋 锌芯褋谢械 械械

蟹邪胁械褉褕械薪懈褟. 袪械蟹褍谢褜褌邪褌褘. 校 胁褋械褏 胁泻谢褞褔械薪薪褘褏 胁 懈褋褋谢械写芯胁邪薪懈械 锌邪褑懈械薪褌芯胁 褋 袩袠-小袪袣

懈屑械谢懈褋褜 邪斜写芯屑懈薪邪谢褜薪褘械 斜芯谢懈, 屑械褌械芯褉懈蟹屑 懈 斜芯谢械蟹薪械薪薪芯褋褌褜 锌褉懈 锌邪谢褜锌邪褑懈懈 锌芯 褏芯写褍

泻懈褕械褔薪懈泻邪, 褍 斜芯谢褜褕懈薪褋褌胁邪 写懈邪褉械褟. 袧邪褉褍褕械薪懈褟 泻懈褕械褔薪芯泄 屑懈泻褉芯斜懈芯褌褘 胁褘褟胁谢械薪褘 褍 77,4%

斜芯谢褜薪褘褏, 锌褉懈 褝褌芯屑 懈蟹斜褘褌芯褔薪褘泄 斜邪泻褌械褉懈邪谢褜薪褘泄 褉芯褋褌 胁 褌芯薪泻芯泄 泻懈褕泻械 懈屑械谢 屑械褋褌芯 褍

72,6%, 薪邪褉褍褕械薪懈褟 褌芯谢褋褌芯泻懈褕械褔薪芯谐芯 屑懈泻褉芯斜懈芯褑械薪芯蟹邪 褋 薪邪谢懈褔懈械屑 褍褋谢芯胁薪芯-锌邪褌芯谐械薪薪褘褏

斜邪泻褌械褉懈泄 褍 62,9%. 校 蟹薪邪褔懈褌械谢褜薪芯泄 褔邪褋褌懈 斜芯谢褜薪褘褏 薪邪斜谢褞写邪谢芯褋褜 褋芯褔械褌邪薪懈械 褌芯薪泻芯- 懈

褌芯谢褋褌芯泻懈褕械褔薪芯谐芯 写懈褋斜邪泻褌械褉懈芯蟹邪. 袩褉懈 谐懈褋褌芯谢芯谐懈褔械褋泻芯屑 懈褋褋谢械写芯胁邪薪懈懈 褋谢懈蟹懈褋褌芯泄

芯斜芯谢芯褔泻懈 褌芯谢褋褌芯泄 泻懈褕泻懈 褍 胁褋械褏 芯斜薪邪褉褍卸械薪褘 锌褉懈蟹薪邪泻懈 胁芯褋锌邪谢械薪懈褟 薪懈蟹泻芯泄 褋褌械锌械薪懈

邪泻褌懈胁薪芯褋褌懈. 校 62,2% 锌邪褑懈械薪褌芯胁 褋 褌芯谢褋褌芯泻懈褕械褔薪褘屑 写懈褋斜邪泻褌械褉懈芯蟹芯屑 懈屑械谢芯褋褜 褍屑械褉械薪薪芯械

锌芯胁褘褕械薪懈械 褍褉芯胁薪褟 褎械泻邪谢褜薪芯谐芯 泻邪谢褜锌褉芯褌械泻褌懈薪邪. 袣 芯泻芯薪褔邪薪懈褞 泻褍褉褋芯胁芯泄 褌械褉邪锌懈懈 胁

芯褋薪芯胁薪芯泄 谐褉褍锌锌械, 锌芯谢褍褔邪胁褕械泄 袘懈褎懈褎芯褉屑, 褍 斜芯谢褜褕懈薪褋褌胁邪 芯褌屑械褔械薪褘 胁褘褉邪卸械薪薪邪褟

锌芯谢芯卸懈褌械谢褜薪邪褟 写懈薪邪屑懈泻邪 泻谢懈薪懈褔械褋泻懈褏 锌褉芯褟胁谢械薪懈泄 蟹邪斜芯谢械胁邪薪懈褟, 胁芯褋褋褌邪薪芯胁谢械薪懈械

薪芯褉屑邪谢褜薪芯谐芯 褋芯褋褌邪胁邪 泻懈褕械褔薪芯泄 屑懈泻褉芯斜懈芯褌褘 懈 薪芯褉屑邪谢懈蟹邪褑懈褟 褋芯写械褉卸邪薪懈褟 褎械泻邪谢褜薪芯谐芯

泻邪谢褜锌褉芯褌械泻褌懈薪邪. 袣 芯泻芯薪褔邪薪懈褞 泻褍褉褋芯胁芯谐芯 谢械褔械薪懈褟 懈 褔械褉械蟹 6 屑械褋 锌芯褋谢械 械谐芯

锌褉械泻褉邪褖械薪懈褟 褏芯褉芯褕懈泄 褉械蟹褍谢褜褌邪褌 蟹薪邪褔懈褌械谢褜薪芯 褔邪褖械 薪邪斜谢褞写邪谢褋褟 褍 斜芯谢褜薪褘褏, 锌芯谢褍褔邪胁褕懈褏

袘懈褎懈褎芯褉屑. 袟邪泻谢褞褔械薪懈械. 袙泻谢褞褔械薪懈械 胁 泻芯屑锌谢械泻褋薪褍褞 褌械褉邪锌懈褞 袩袠-小袪袣 谢械泻邪褉褋褌胁械薪薪芯谐芯

锌褉械锌邪褉邪褌邪 袘懈褎懈褎芯褉屑 褋褍褖械褋褌胁械薪薪芯 锌芯胁褘褕邪械褌 械械 褝褎褎械泻褌懈胁薪芯褋褌褜 泻邪泻 胁 泻褍锌懈褉芯胁邪薪懈懈

泻谢懈薪懈褔械褋泻懈褏 锌褉芯褟胁谢械薪懈泄 蟹邪斜芯谢械胁邪薪懈褟, 褌邪泻 懈 胁 胁芯褋褋褌邪薪芯胁谢械薪懈懈 薪芯褉屑邪谢褜薪芯谐芯 褋芯褋褌邪胁邪

泻懈褕械褔薪芯谐芯 屑懈泻褉芯斜懈芯屑邪 懈 褋薪懈卸械薪懈懈 胁芯褋锌邪谢懈褌械谢褜薪芯谐芯 锌褉芯褑械褋褋邪 胁 褋谢懈蟹懈褋褌芯泄 芯斜芯谢芯褔泻械

泻懈褕械褔薪懈泻邪. 校 斜芯谢褜褕懈薪褋褌胁邪 锌邪褑懈械薪褌芯胁, 锌芯谢褍褔邪胁褕懈褏 袘懈褎懈褎芯褉屑, 写芯褋褌懈谐薪褍褌邪褟 泻 芯泻芯薪褔邪薪懈褞

泻褍褉褋芯胁芯谐芯 谢械褔械薪懈褟 褉械屑懈褋褋懈褟 蟹邪斜芯谢械胁邪薪懈褟 褋芯褏褉邪薪褟谢邪褋褜 懈 褔械褉械蟹 6 屑械褋 锌芯褋谢械 械谐芯

芯泻芯薪褔邪薪懈褟.

DOI: 10.26442/00403660.2022.02.201368

PMID: 36286741 [Indexed for MEDLINE]

12. World J Gastroenterol. 2019 Aug 7;25(29):3956-3971. doi:

10.3748/wjg.v25.i29.3956.

Berberine prevents stress-induced gut inflammation and visceral hypersensitivity

and reduces intestinal motility in rats.

Yu ZC(1), Cen YX(2), Wu BH(1), Wei C(1), Xiong F(1), Li DF(1), Liu TT(1), Luo

MH(1), Guo LL(1), Li YX(1), Wang LS(1), Wang JY(3), Yao J(4).

Author information:

(1)Department of Gastroenterology, Jinan University of Second Clinical Medical

Sciences, Shenzhen Municipal People's Hospital, Shenzhen 518020, Guangdong

Province, China.

(2)Department of Gastroenterology, Foshan Gaoming Affiliated Hospital of

Guangdong Medical University, Foshan 528500, Guangdong Province, China.

(3)Department of General Surgery, Shenzhen Children's Hospital, Shenzhen 518026,

Guangdong Province, China.

(4)Department of Gastroenterology, Jinan University of Second Clinical Medical

Sciences, Shenzhen Municipal People's Hospital, Shenzhen 518020, Guangdong

Province, China. yj\_1108@126.com.

BACKGROUND: Irritable bowel syndrome (IBS) is a common chronic non-organic

disease of the digestive system. Berberine (BBR) has been used to treat patients

with IBS, but the underlying therapeutic mechanism is little understood. We

believe that BBR achieves its therapeutic effect on IBS by preventing stress

intestinal inflammation and visceral hypersensitivity and reducing bowel

motility.

AIM: To test the hypothesis that BBR achieves its therapeutic effect on IBS by

preventing subclinical inflammation of the intestinal mucosa and reducing

visceral hypersensitivity and intestinal motility.

METHODS: IBS was induced in rats via water avoidance stress (WAS). qRT-PCR and

histological analyses were used to evaluate the levels of cytokines and mucosal

inflammation, respectively. Modified ELISA and qRT-PCR were used to evaluate the

nuclear factor kappa-B (NF-魏B) signal transduction pathway. Colorectal

distention test, gastrointestinal transit measurement, Western blot, and qRT-PCR

were used to analyze visceral sensitivity, intestinal motility, the expression

of C-kit (marker of Cajal mesenchymal cells), and the expression of brain

derived neurotrophic factor (BDNF) and its receptor TrkB.

RESULTS: WAS led to mucosal inflammation, visceral hyperalgesia, and high

intestinal motility. Oral administration of BBR inhibited the NF-魏B signal

transduction pathway, reduced the expression of pro-inflammatory cytokines

[interleukin (IL)-1尾, IL-6, interferon-纬, and tumor necrosis factor-伪], promoted

the expression of anti-inflammatory cytokines (IL-10 and transforming growth

factor-尾), and improved the terminal ileum tissue inflammation. BBR inhibited

the expression of BDNF, TrkB, and C-kit in IBS rats, leading to the reduction of

intestinal motility and visceral hypersensitivity. The therapeutic effect of BBR

at a high dose (100 mg/kg) was superior to than that of the low-dose (25 mg/kg)

group.

CONCLUSION: BBR reduces intestinal mucosal inflammation by inhibiting the

intestinal NF-魏B signal pathway in the IBS rats. BBR reduces the expression of

BDNF, its receptor TrkB, and C-kit. BBR also reduces intestinal motility and

visceral sensitivity to achieve its therapeutic effect on IBS.

DOI: 10.3748/wjg.v25.i29.3956

PMCID: PMC6689801

PMID: 31413530 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: The authors of

this manuscript have no conflicts of interest to disclose.

13. Int J Mol Sci. 2018 Nov 16;19(11):3619. doi: 10.3390/ijms19113619.

Intestinal Microbiome in Irritable Bowel Syndrome before and after Gut-Directed

Hypnotherapy.

Peter J(1), Fournier C(2), Keip B(3), Rittershaus N(4), Stephanou-Rieser N(5),

Durdevic M(6), Dejaco C(7), Michalski M(8), Moser G(9).

Author information:

(1)Division of Gastroenterology and Hepatology, Department of Internal Medicine

III, Medical University of Vienna, 1090 Wien, Austria.

johannes.peter@meduniwien.ac.at.

(2)Division of Gastroenterology and Hepatology, Department of Internal Medicine

III, Medical University of Vienna, 1090 Wien, Austria. camille.4nier@gmail.com.

(3)Division of Gastroenterology and Hepatology, Department of Internal Medicine

III, Medical University of Vienna, 1090 Wien, Austria.

bettina.keip@meduniwien.ac.at.

(4)Division of Gastroenterology and Hepatology, Department of Internal Medicine

III, Medical University of Vienna, 1090 Wien, Austria.

ninarittershaus@gmail.com.

(5)Division of Gastroenterology and Hepatology, Department of Internal Medicine

III, Medical University of Vienna, 1090 Wien, Austria.

nicola.stephanou@hotmail.com.

(6)Center of Medical Research, Medical University Graz, 8036 Graz, Austria.

marija.durdevic@medunigraz.at.

(7)Division of Gastroenterology and Hepatology, Department of Internal Medicine

III, Medical University of Vienna, 1090 Wien, Austria.

clemens.dejaco@meduniwien.ac.at.

(8)Division of Gastroenterology and Hepatology, Department of Internal Medicine

III, Medical University of Vienna, 1090 Wien, Austria.

maria.michalski@medway.at.

(9)Division of Gastroenterology and Hepatology, Department of Internal Medicine

III, Medical University of Vienna, 1090 Wien, Austria.

gabriele.moser@meduniwien.ac.at.

Irritable bowel syndrome (IBS) is a disorder with brain-gut-microbiome

alterations. Gut-directed hypnotherapy (GHT) has been shown to improve quality

of life and symptoms in IBS. This therapy targets psychological coping, central

nervous processing and brain-gut interaction. Studies have also demonstrated

effects of hypnosis on intestinal transit and the mucosal immune system. So far,

no study has examined the effect of GHT on the intestinal microbiome. This study

aimed at examining microbial composition, IBS symptoms, and psychological

distress before and after GHT.

METHODS: Fecal samples were collected from 38 IBS patients (Rome-III criteria,

mean age 44 years, 27 female, 11 male, 22 diarrhea-dominant, 12 alternating-type

and 4 constipation-dominant IBS) before and after 10 weekly group sessions of

GHT. Assessments in psychological (perceived stress, PSQ; psychological

distress, HADS-D; quality of life, visual analogue scales) and IBS

symptom-related variables (IBS severity, IBS-SSS; single symptoms, visual

analogue scales) were performed with validated questionnaires. Fecal samples

underwent microbial 16S rRNA analyses (regions V1鈦?2).

RESULTS: Microbial alpha diversity was stable before and after GHT (chao1 2591 卤

548 vs. 2581 卤 539, p = 0.92). No significant differences were found in relative

bacterial abundances but trends of reduced abundance of Lachnospiraceae 32.18

(4.14鈦?39.89) Median (Q1鈦籕3) vs. 28.11 (22.85; 35.55) and Firmicutes:

Bacteroidetes ratio after GHT were observable. Significant reductions in symptom

severity (323 (266鈦?371) vs. 264 (191鈦?331), p = 0.001) and psychological distress

17.0 (12.6鈦?21.8) vs. 12.0 (8.3鈦?18.0), p = 0.001, and increased well-being were

found after GHT. Adequate relief after therapy was reported by 32 (84%)

patients.

CONCLUSION: Reductions in IBS symptoms and psychological burden were observed

after gut-directed hypnotherapy, but only small changes were found in intestinal

microbiota composition. The findings suggest that hypnosis may act by central

nervous impact and other factors largely independent from microbiota composition

modulating the brain-gut axis, possibly alterations in vagus nerve functioning

and microbiota metabolism.

DOI: 10.3390/ijms19113619

PMCID: PMC6274728

PMID: 30453528 [Indexed for MEDLINE]

Conflict of interest statement: The authors declare having no conflict of

interest. Unrelated to this study, Johannes Peter has received travel expenses

from Yakult. Gabriele Moser has been on the Advisory Boards of Allergan and

Almirall, she has received grants to the Medical University of Vienna by AbbVie,

Vifor, Almirall, Merck, Falk, Yakult, Sanova, Danone, and she has been on the

speakers bureaus for Falk, Peri Consulting, Henrich Communication, Milton

Erickson Institut Austria, Wirtschaftskammer Austria, and Gebro. She has

received payments for development of educational presentations by 脛rztekammer

Austria and travel expenses by Gebro and Falk. The funders had no role in the

design of the study; in the collection, analyses, or interpretation of data; in

the writing of the manuscript, and in the decision to publish the results.

14. Turk J Gastroenterol. 2022 May;33(5):397-405. doi: 10.5152/tjg.2022.21311.

Rome IV Criteria-Defined Irritable Bowel Syndrome in Atopic Patients and the

Effect of Anxiety and Depression: A Case-Control Study.

Emre E(1), Tazegul G(2), Ak谋n M(3).

Author information:

(1)Allergology, and Immunology Specialist, Hatay State Hospital, Hatay, Turkey.

(2)Internal Medicine Specialist, Ankara Polatl谋 Duatepe State Hospital, Ankara,

Turkey.

(3)Department of Internal Medicine, Gastroenterology Division, Akdeniz

University Faculty of Medicine, Antalya, Turkey.

BACKGROUND: Numerous studies report an increased prevalence of irritable bowel

syndrome in patients with atopic diseases such as allergic rhinitis, allergic

asthma, and chronic urticaria. Both disease groups have a higher incidence of

psychological disorders. In this study, we aimed to examine the relationship of

irritable bowel syndrome with the presence and severity of allergic diseases and

accom- panying anxiety and depression.

METHODS: One hundred sixty-two patients (56 with AR, 34 with AA, and 72 with CU)

and 43 healthy volunteers were included in the study. Demographic and clinical

data, along with disease duration and severity, was analyzed. Irritable bowel

syndrome was diagnosed using Rome IV criteria. Hospital Anxiety and Depression

Scale was used to evaluate anxiety and depression. All statistical analyses were

performed using Statistic Program for Social Sciences 23.0.

RESULTS: Irritable bowel syndrome prevalence in the control group was 9.3% and

56% in atopic patients (P < .0001). Hospital Anxiety and Depression Scale

anxiety scores of 11 and above increased the odds of IBS approximately 14 times,

and independently, the presence of allergic disease increased the odds 10 times.

In the allergic patient subgroup, Hospital Anxiety and Depression Scale anxiety

scores of 11 and above increased the risk of irritable bowel syndrome

approximately 18 times.

CONCLUSION: In this first study using Rome IV criteria to examine the

relationship of irritable bowel syndrome, allergic diseases, and anxiety and

depression, irritable bowel syndrome was more frequent in allergic patients,

especially in patients with anxiety. Awareness of a disease cluster where these

3 disease groups intersect will guide clinicians from different disciplines

involved in patients' treatment and follow-up.

DOI: 10.5152/tjg.2022.21311

PMCID: PMC11158317

PMID: 35678797 [Indexed for MEDLINE]

15. World J Gastroenterol. 2019 Sep 28;25(36):5469-5482. doi:

10.3748/wjg.v25.i36.5469.

Clostridium butyricum alleviates intestinal low-grade inflammation in

TNBS-induced irritable bowel syndrome in mice by regulating functional status of

lamina propria dendritic cells.

Zhao Q(1), Yang WR(2), Wang XH(3), Li GQ(3), Xu LQ(1), Cui X(1), Liu Y(4), Zuo

XL(5).

Author information:

(1)Department of Gastroenterology, Qilu Hospital, Shandong University, Jinan

250012, Shandong Province, China.

(2)Department of Clinical Nutrition, Taian City Central Hospital, Taian 271000,

Shandong Province, China.

(3)Department of Gastroenterology, Taian City Central Hospital, Taian 271000,

Shandong Province, China.

(4)Department of Medicine, Beijing 316 Hospital, Beijing 100093, China.

(5)Department of Gastroenterology, Qilu Hospital, Shandong University, Jinan

250012, Shandong Province, China. zuoxiuli\_s@163.com.

BACKGROUND: Irritable bowel syndrome (IBS) is one of the most common functional

gas-troenterological diseases characterized by abnormal visceral sensitivity and

low-grade inflammation. The role of Clostridium butyricum (C. butyricum) in

reducing intestinal low-grade inflammation via immune pathways has been well

defined. However, the detailed mechanisms of the effects of C. butyricum on

intestinal mucosal immunity, especially on immune cells of the lamina propria,

remain unclear. Dendritic cells (DCs), which are important immune cells, secrete

proinflammatory cytokines (IL-1尾, IL-6, and others) and express T cell

immuno-globulin and mucin domain-3 (TIM3), promoting proliferation and

activation of DCs, and mediating Th1 and Th17 inflammatory responses.

AIM: To investigate the role of DCs in the development of IBS in a rat model and

to understand the regulation of DCs after C. butyricum intervention.

METHODS: An IBS animal model was established using C57BL/6 mice, and C.

butyricum was continuously administered via the intragastric route to simulate

different intestinal immune states. Intestinal visceral hypersensitivity and

histopathology were assessed using the abdominal withdrawal reflex (AWR) test

and hematoxylin & eosin (H&E) staining, respectively. The expression of

proinflammatory cytokines (IL-1尾 and IL-6) and TIM3 was analyzed by Western blot

analysis and real-time PCR. Flow cytometry was applied to analyze the quantity,

function, and membrane molecule TIM3 of the lamina propria dendritic cells

(LPDCs). The regulatory effect of C. butyricum was verified in bone

marrow-derived dendritic cells by in vitro experiments.

RESULTS: The secretion of proinflammatory cytokines (IL-1尾 and IL-6) in mice

with IBS was significantly increased compared with that of the control group,

which suggested that the intestinal mucosa in mice with IBS was in a low-grade

inflammatory state. The expression of CD11C+CD80+ and CD11c+TIM3+ in intestinal

LPDCs in mice with IBS increased significantly. Meanwhile, the cytokines (IL-1尾

and IL-6) were significantly reduced after the intervention with probiotic C.

butyricum. The amount and function of LPDCs and the TIM3 on the surface of the

LPDCs were decreased with the alleviation of the intestinal inflammatory

response.

CONCLUSION: The results suggest that C. butyricum regulates the amount and

functional status of LPDCs in the intestinal mucosa of mice with IBS, and

therefore modulates the local immune response in the intestine.

漏The Author(s) 2019. Published by Baishideng Publishing Group Inc. All rights

reserved.

DOI: 10.3748/wjg.v25.i36.5469

PMCID: PMC6767978

PMID: 31576093 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: The authors

declare no conflicts of interest related to this manuscript or its publication.

16. World J Gastroenterol. 2016 Jan 28;22(4):1331-4. doi: 10.3748/wjg.v22.i4.1331.

Is irritable bowel syndrome an infectious disease?

Thompson JR(1).

Author information:

(1)John Richard Thompson, Department of Pharmacy Practice, Lipscomb University

College of Pharmacy, One University Park Drive, Nashville, TN 37204, United

States.

Irritable bowel syndrome (IBS) is the most common of all gastroenterological

diseases. While many mechanisms have been postulated to explain its etiology, no

single mechanism entirely explains the heterogeneity of symptoms seen with the

various phenotypes of the disease. Recent data from both basic and clinical

sciences suggest that underlying infectious disease may provide a unifying

hypothesis that better explains the overall symptomatology. The presence of

small intestinal bowel overgrowth (SIBO) has been documented in patients with

IBS and reductions in SIBO as determined by breath testing correlate with IBS

symptom improvement in clinical trials. The incidence of new onset IBS symptoms

following acute infectious gastroenteritis also suggests an infectious cause.

Alterations in microbiota-host interactions may compromise epithelial barrier

integrity, immune function, and the development and function of both central and

enteric nervous systems explaining alterations in the brain-gut axis. Clinical

evidence from treatment trials with both probiotics and antibiotics also support

this etiology. Probiotics appear to restore the imbalance in the microflora and

improve IBS-specific quality of life. Antibiotic trials with both neomycin and

rifaximin show improvement in global IBS symptoms that correlates with breath

test normalization in diarrhea-predominant patients. The treatment response to

two weeks of rifaximin is sustained for up to ten weeks and comparable results

are seen in symptom reduction with retreatment in patients who develop recurrent

symptoms.

DOI: 10.3748/wjg.v22.i4.1331

PMCID: PMC4721968

PMID: 26819502 [Indexed for MEDLINE]

17. Cells. 2021 Jun 10;10(6):1459. doi: 10.3390/cells10061459.

A Distinct Faecal Microbiota and Metabolite Profile Linked to Bowel Habits in

Patients with Irritable Bowel Syndrome.

Ahluwalia B(1)(2), Iribarren C(1)(3), Magnusson MK(1), Sundin J(1), Clevers

E(3)(4), Savolainen O(5), Ross AB(5)(6), T枚rnblom H(3), Simr茅n M(3)(7), 脰hman

L(1).

Author information:

(1)Department of Microbiology and Immunology, Institute of Biomedicine,

University of Gothenburg, 405 30 Gothenburg, Sweden.

(2)Calmino Group AB, Research and Development, 413 46 Gothenburg, Sweden.

(3)Department of Molecular and Clinical Medicine, Institute of Medicine,

University of Gothenburg, 413 45 Gothenburg, Sweden.

(4)GI Motility and Sensitivity Research Group, Translational Research Centre for

Gastrointestinal Disorders (TARGID), KU Leuven, 3000 Leuven, Belgium.

(5)Chalmers Mass Spectrometry Infrastructure, Department of Biology and

Biological Engineering, Chalmers University of Technology, 412 96 Gothenburg,

Sweden.

(6)Proteins and Metabolites Team, AgResearch, Lincoln 7674, New Zealand.

(7)Center for Functional Gastrointestinal and Motility Disorders, Division of

Gastroenterology & Hepatology, School of Medicine, University of North Carolina

at Chapel Hill, Chapel Hill, NC 27599, USA.

Patients with irritable bowel syndrome (IBS) are suggested to have an altered

intestinal microenvironment. We therefore aimed to determine the intestinal

microenvironment profile, based on faecal microbiota and metabolites, and the

potential link to symptoms in IBS patients. The faecal microbiota was evaluated

by the GA-mapTM dysbiosis test, and tandem mass spectrometry (GC-MS/MS) was used

for faecal metabolomic profiling in patients with IBS and healthy subjects.

Symptom severity was assessed using the IBS Severity Scoring System and anxiety

and depression were assessed using the Hospital Anxiety and Depression Scale. A

principal component analysis based on faecal microbiota (n = 54) and metabolites

(n = 155) showed a clear separation between IBS patients (n = 40) and healthy

subjects (n = 18). Metabolites were the main driver of this separation.

Additionally, the intestinal microenvironment profile differed between IBS

patients with constipation (n = 15) and diarrhoea (n = 11), while no clustering

was detected in subgroups of patients according to symptom severity or anxiety.

Furthermore, ingenuity pathway analysis predicted amino acid metabolism and

several cellular and molecular functions to be altered in IBS patients. Patients

with IBS have a distinct faecal microbiota and metabolite profile linked to

bowel habits. Intestinal microenvironment profiling, based on faecal microbiota

and metabolites, may be considered as a future non-invasive diagnostic tool,

alongside providing valuable insights into the pathophysiology of IBS.

DOI: 10.3390/cells10061459

PMCID: PMC8230381

PMID: 34200772 [Indexed for MEDLINE]

Conflict of interest statement: B.A., C.I., M.K.M., J.S., E.C., O.S., A.B.R. and

H.T. declare no conflict of interest. L.脰. has received a financial support for

research by Danone Research and AstraZeneca and has served as

Consultant/Advisory Board member for Genetic Analysis AS, and as a speaker for

Ferring Pharmaceuticals, Takeda, AbbVie, and Meda. M.S. has received

unrestricted research grants from Danone Nutricia Research and Glycom A/S (now

DSM), and served as a Consultant/Advisory Board member for Danone Nutricia

Research, Ironwood, Menarini, Biocodex, Genetic Analysis AS, Glycom A/S (now

DSM), Tillotts, Arena, and Adnovate, and as in the speakers鈥? bureau for

Tillotts, Menarini, Kyowa Kirin, Takeda, Shire, Biocodex, Alimentary Health,

AlfaSigma, and Falk Foundation.

18. Dig Dis Sci. 2023 Nov;68(11):4166-4174. doi: 10.1007/s10620-023-08117-7. Epub

2023 Sep 26.

Intestinal Barrier and Gut Microbiota in Patients with Overlapping Irritable

Bowel Syndrome and Functional Dyspepsia.

Kovaleva A(1), Poluektova E(1), Maslennikov R(2), Karchevskaya A(1), Shifrin

O(1), Kiryukhin A(1), Tertychnyy A(1), Kovalev L(3), Kovaleva M(3), Lobanova

O(1), Kudryavtseva A(4), Krasnov G(4), Ivashkin V(1).

Author information:

(1)Sechenov University, Moscow, Russia, 119435.

(2)Sechenov University, Moscow, Russia, 119435.

maslennikov\_r\_v@staff.sechenov.ru.

(3)A.N. Bach Institute of Biochemistry, Leninsky Prospekt, 33, Bld. 2, Moscow,

Russia, 119071.

(4)Engelhardt Institute of Molecular Biology, Vavilova St., 32, Bld. 1, Moscow,

Russia, 119991.

BACKGROUND: Disturbances in the intestinal barrier and gut dysbiosis have been

observed in patients with functional bowel diseases.

AIMS: To investigate the correlation between biomarkers of intestinal barrier

disorders at different layers and the severity of symptoms in patients with

overlapping diarrhea-predominant irritable bowel syndrome and functional

dyspepsia (IDFO), as well as with gut microbiota taxa.

METHODS: This study included 45 patients with IDFO and 16 healthy controls.

Endoscopy with biopsy of the duodenum and sigmoid colon (SC) was performed to

count intraepithelial lymphocytes (IELs) and mucosal eosinophils (subepithelial

layer), assess fatty acid binding protein (FABP; epithelial layer) level, and

stain for mucin-2 (MUC-2; pre-epithelial layer). Composition of the gut

microbiota was evaluated using 16S rRNA gene sequencing.

RESULTS: Patients with IDFO exhibited an increase in biomarkers of intestinal

barrier disorders at all layers studied. IEL count in the duodenum was

correlated with the severity of bloating (r鈥?=鈥?0.336; p鈥?=鈥?0.024) and, in the SC,

was correlated with tenesmus severity (r鈥?=鈥?0.303; p鈥?=鈥?0.042). FABP-1 level in

the SC was correlated with the severity of diarrhea (r鈥?=鈥?0.577; p鈥?=鈥?0.001), and

FABP-5 concentration in the SC was correlated with abdominal distension

(r鈥?=鈥?0.477; p鈥?=鈥?0.010). MUC-2 concentration in the duodenum was correlated with

the severity of heartburn (r鈥?=鈥?0.572; p鈥?=鈥?0.025) and burning sensation in the

epigastrium (r鈥?=鈥?0.518; p鈥?=鈥?0.048). All biomarkers of intestinal barrier

permeability were correlated with the abundance of some gut microbiota taxa.

CONCLUSION: Patients with IDFO exhibited disrupted intestinal barrier function

in all layers, which was associated with clinical symptom severity and changes

in the gut microbiota.

漏 2023. The Author(s), under exclusive licence to Springer Science+Business

Media, LLC, part of Springer Nature.

DOI: 10.1007/s10620-023-08117-7

PMID: 37752368 [Indexed for MEDLINE]

19. Acta Gastroenterol Belg. 2016 Mar;79(1):29-38.

Irritable bowel syndrome and visceral hypersensitivity鈥?: risk factors and

pathophysiological mechanisms.

Deiteren A, de Wit A, van der Linden L, De Man JG, Pelckmans PA, De Winter BY.

Irritable bowel syndrome (IBS) is a common functional gastro-intestinal

disorder, characterized by abdominal pain and altered intestinal motility.

Visceral hypersensitivity is an important hallmark feature of IBS and is

believed to underlie abdominal pain in patients with IBS. The two main risk

factors associated with the development of IBS are gastrointestinal inflammation

and psychological distress. On a peripheral level, visceral sensitivity seems to

be modulated by several mechanisms. Immune cells in the mucosal wall, such as

mast cells, and enterochromaffin cells may sensitize afferent nerves by release

of their mediators. Furthermore, increased mucosal permeability, altered

intestinal microflora and dietary habits may contribute to this feature. On a

central level, an increased prevalence of psychiatric comorbidities is

demonstrated in IBS patients, alongside alterations in the hormonal brain-gut

axis, increased vigilance towards intestinal stimuli and functional and

structural changes in the brain. The pathogenesis of IBS is complicated and

multifactorial and the treatment remains clinically challenging. Dietary

measures and symptomatic control are the cornerstones for IBS treatment and may

be sufficient for patients experiencing mild symptoms, alongside education,

reassurance and an effective therapeutic physician-patient relationship. New

pharmacological therapies are aimed at interfering with mediator release and/or

blockade of the relevant receptors within the gut wall, while modulation of the

intestinal flora and diet may also be of therapeutic benefit. Tricyclic

anti-depressants and serotonin reuptake inhibitors act both on a central and

peripheral level by modulating pain signalling pathways.

漏 Acta Gastro-Enterologica Belgica.

PMID: 26852761 [Indexed for MEDLINE]

20. Lancet. 2020 Nov 21;396(10263):1675-1688. doi: 10.1016/S0140-6736(20)31548-8.

Epub 2020 Oct 10.

Irritable bowel syndrome.

Ford AC(1), Sperber AD(2), Corsetti M(3), Camilleri M(4).

Author information:

(1)Leeds Institute of Medical Research at St James's, University of Leeds,

Leeds, UK; Leeds Gastroenterology Institute, St James's University Hospital,

Leeds, UK. Electronic address: alexf12399@yahoo.com.

(2)Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva,

Israel.

(3)National Institute for Health Research, Nottingham Biomedical Research

Centre, Nottingham University Hospitals NHS Trust, Nottingham, UK; Nottingham

Digestive Diseases Centre, School of Medicine, University of Nottingham,

Nottingham, UK.

(4)Clinical Enteric Neuroscience Translational and Epidemiological Research,

Mayo Clinic, Rochester, MN, USA.

Irritable bowel syndrome is a functional gastrointestinal disorder with symptoms

including abdominal pain associated with a change in stool form or frequency.

The condition affects between 5% and 10% of otherwise healthy individuals at any

one point in time and, in most people, runs a relapsing and remitting course.

The best described risk factor is acute enteric infection, but irritable bowel

syndrome is also more common in people with psychological comorbidity and in

young adult women than in the rest of the general population. The

pathophysiology of irritable bowel syndrome is incompletely understood, but it

is well established that there is disordered communication between the gut and

the brain, leading to motility disturbances, visceral hypersensitivity, and

altered CNS processing. Other less reproducible mechanisms might include genetic

associations, alterations in gastrointestinal microbiota, and disturbances in

mucosal and immune function. In most people, diagnosis can be made on the basis

of clinical history with limited and judicious use of investigations, unless

alarm symptoms such as weight loss or rectal bleeding are present, or there is a

family history of inflammatory bowel disease or coeliac disease. Once the

diagnosis is made, an empathetic approach is key and can improve quality of life

and symptoms, and reduce health-care expenditure. The mainstays of treatment

include patient education about the condition, dietary changes, soluble fibre,

and antispasmodic drugs. Other treatments tend to be reserved for people with

severe symptoms and include central neuromodulators, intestinal secretagogues,

drugs acting on opioid or 5-HT receptors, or minimally absorbed antibiotics (all

of which are selected according to predominant bowel habit), as well as

psychological therapies. Increased understanding of the pathophysiology of

irritable bowel syndrome in the past 10 years has led to a healthy pipeline of

novel drugs in development.

Copyright 漏 2020 Elsevier Ltd. All rights reserved.

DOI: 10.1016/S0140-6736(20)31548-8

PMID: 33049223 [Indexed for MEDLINE]

21. Gastroenterology. 2017 Jan;152(1):111-123.e8. doi: 10.1053/j.gastro.2016.09.049.

Epub 2016 Oct 7.

Identification of an Intestinal Microbiota Signature Associated With Severity of

Irritable Bowel Syndrome.

Tap J(1), Derrien M(2), T枚rnblom H(3), Brazeilles R(4), Cools-Portier S(4), Dor茅

J(5), St枚rsrud S(6), Le Nev茅 B(4), 脰hman L(7), Simr茅n M(8).

Author information:

(1)Danone Nutricia Research, Palaiseau, France; French National Institute for

Agricultural Research (INRA) MetaGenoPolis, Jouy en Josas, France.

(2)Danone Nutricia Research, Palaiseau, France. Electronic address:

muriel.derrien@danone.com.

(3)Department of Internal Medicine and Clinical Nutrition, Institute of

Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden;

Centre for Person-Centered Care, Sahlgrenska Academy, University of Gothenburg,

Gothenburg, Sweden.

(4)Danone Nutricia Research, Palaiseau, France.

(5)French National Institute for Agricultural Research (INRA) MetaGenoPolis,

Jouy en Josas, France.

(6)Department of Internal Medicine and Clinical Nutrition, Institute of

Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

(7)Department of Internal Medicine and Clinical Nutrition, Institute of

Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden;

Department of Microbiology and Immunology, Sahlgrenska Academy, University of

Gothenburg, Gothenburg, Sweden; School of Health and Education, University of

Sk枚vde, Sk枚vde, Sweden.

(8)Department of Internal Medicine and Clinical Nutrition, Institute of

Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden;

Centre for Person-Centered Care, Sahlgrenska Academy, University of Gothenburg,

Gothenburg, Sweden; Center for Functional GI and Motility Disorders, University

of North Carolina, Chapel Hill, North Carolina. Electronic address:

magnus.simren@medicine.gu.se.

BACKGROUND & AIMS: We have limited knowledge about the association between the

composition of the intestinal microbiota and clinical features of irritable

bowel syndrome (IBS). We collected information on the fecal and

mucosa-associated microbiota of patients with IBS and evaluated whether these

were associated with symptoms.

METHODS: We collected fecal and mucosal samples from adult patients who met the

Rome III criteria for IBS at a secondary/tertiary care outpatient clinics in

Sweden, as well as from healthy subjects. The exploratory set comprised 149

subjects (110 with IBS and 39 healthy subjects); 232 fecal samples and 59

mucosal biopsy samples were collected and analyzed by 16S ribosomal RNA targeted

pyrosequencing. The validation set comprised 46 subjects (29 with IBS and 17

healthy subjects); 46 fecal samples, but no mucosal samples, were collected and

analyzed. For each subject, we measured exhaled H2 and CH4, oro-anal transit

time, and the severity of psychological and gastrointestinal symptoms. Fecal

methanogens were measured by quantitative polymerase chain reaction. Numerical

ecology analyses and a machine learning procedure were used to analyze the data.

RESULTS: Fecal microbiota showed covariation with mucosal adherent microbiota.

By using classic approaches, we found no differences in fecal microbiota

abundance or composition between patients with IBS vs healthy patients. A

machine learning procedure, a computational statistical technique, allowed us to

reduce the 16S ribosomal RNA data complexity into a microbial signature for

severe IBS, consisting of 90 bacterial operational taxonomic units. We confirmed

the robustness of the intestinal microbial signature for severe IBS in the

validation set. The signature was able to discriminate between patients with

severe symptoms, patients with mild/moderate symptoms, and healthy subjects. By

using this intestinal microbiota signature, we found IBS symptom severity to be

associated negatively with microbial richness, exhaled CH4, presence of

methanogens, and enterotypes enriched with Clostridiales or Prevotella species.

This microbiota signature could not be explained by differences in diet or use

of medications.

CONCLUSIONS: In analyzing fecal and mucosal microbiota from patients with IBS

and healthy individuals, we identified an intestinal microbiota profile that is

associated with the severity of IBS symptoms.

TRIAL REGISTRATION NUMBER: NCT01252550.

Copyright 漏 2017 AGA Institute. Published by Elsevier Inc. All rights reserved.

DOI: 10.1053/j.gastro.2016.09.049

PMID: 27725146 [Indexed for MEDLINE]

22. Neurogastroenterol Motil. 2020 Nov;32(11):e13891. doi: 10.1111/nmo.13891. Epub

2020 May 25.

Gut fungal dysbiosis and altered bacterial-fungal interaction in patients with

diarrhea-predominant irritable bowel syndrome: An explorative study.

Hong G(1), Li Y(1), Yang M(1), Li G(1), Qian W(1), Xiong H(1), Bai T(1), Song

J(1), Zhang L(1), Hou X(1).

Author information:

(1)Division of Gastroenterology, Union Hospital, Tongji Medical College,

Huazhong University of Science and Technology, Wuhan, China.

BACKGROUND: Little is known about intestinal fungi in IBS patients whose gut

bacteria have been investigated a lot. In order to explore causal relationship

between IBS and gut mycobiome, and use gut fungi to diagnose or even treat IBS,

further characterization of it in IBS is required.

METHODS: Fifty-five diarrhea-predominant IBS (D-IBS) patients fulfilling Rome

III criteria, and 16 healthy controls (HC) were recruited. Fresh fecal samples

were collected and used for 16s rRNA and ITS2 high-throughput sequencing.

Diversity and composition of gut bacteria and fungi, as well as bacterial-fungal

interactions in D-IBS patients, were characterized. Specific fungal taxa

differentiating D-IBS from HC were recognized by LEfSe and RandomForest methods,

and their association with clinical symptoms was assessed by Spearman's

correlation.

RESULTS: Diarrhea-predominant irritable bowel syndrome patients showed abnormal

(IBS-dysbiosis) or normal (HC-like IBS) fecal bacterial structure and diversity

compared with healthy controls. However, fecal fungal signatures differed

absolutely between D-IBS and HC, which indicated a more susceptible alteration

of gut fungi than bacteria in D-IBS. Fecal fungi showed significant correlations

with IBS symptoms, especially Mycosphaerella, Aspergillus, Sporidiobolus, and

Pandora which were identified to potentially differentiate D-IBS from HC.

Moreover, compared with HC there were markedly declined bacterial-fungal

interactions in D-IBS, in which Candida changed from negative to positive

correlations with bacteria, and Eurotium changed from positive correlations to

irrelevance, while Debaryomyces gained negative correlations with bacteria.

CONCLUSIONS: Gut fungal dysbiosis and altered bacterial-fungal interactions were

present in patients with D-IBS, and gut fungi could be used to diagnose D-IBS.

漏 2020 John Wiley & Sons Ltd.

DOI: 10.1111/nmo.13891

PMID: 32449259 [Indexed for MEDLINE]

23. Health Technol Assess. 2019 Apr;23(17):1-154. doi: 10.3310/hta23170.

Therapist telephone-delivered CBT and web-based CBT compared with treatment as

usual in refractory irritable bowel syndrome: the ACTIB three-arm RCT.

Everitt H(1), Landau S(2), Little P(1), Bishop FL(3), O'Reilly G(1), Sibelli

A(4), Holland R(2), Hughes S(1), Windgassen S(4), McCrone P(5), Goldsmith K(2),

Coleman N(6), Logan R(7), Chalder T(8), Moss-Morris R(4).

Author information:

(1)Primary Care and Population Sciences, University of Southampton, Southampton,

UK.

(2)Biostatistics, Institute of Psychiatry, Psychology & Neuroscience, King's

College London, London, UK.

(3)Centre for Applications of Health Psychology, University of Southampton,

Southampton, UK.

(4)Health Psychology Section, Institute of Psychiatry, Psychology &

Neuroscience, King's College London, London, UK.

(5)Institute of Psychiatry, Psychology & Neuroscience, King's College London,

London, UK.

(6)Department of Gastroenterology, Southampton University Hospital, Southampton,

UK.

(7)Department of Gastroenterology, King's College Hospital, London, UK.

(8)Academic Department of Psychological Medicine, King's College London, London,

UK.

Comment in

BMJ. 2019 Nov 4;367:l4962. doi: 10.1136/bmj.l4962.

BACKGROUND: Irritable bowel syndrome (IBS) affects 10-22% of people in the UK.

Abdominal pain, bloating and altered bowel habits affect quality of life and can

lead to time off work. Current treatment relies on a positive diagnosis,

reassurance, lifestyle advice and drug therapies, but many people suffer ongoing

symptoms. Cognitive-behavioural therapy (CBT) is recommended in guidelines for

patients with ongoing symptoms but its availability is limited.

OBJECTIVES: To determine the clinical effectiveness and cost-effectiveness of

therapist telephone-delivered CBT (TCBT) and web-based CBT (WCBT) with minimal

therapist support compared with treatment as usual (TAU) in refractory IBS.

DESIGN: This was a three-arm randomised controlled trial.

SETTING: This trial took place in UK primary and secondary care.

PARTICIPANTS: Adults with refractory IBS (clinically significant symptoms for 12

months despite first-line therapies) were recruited from 74 general practices

and three gastroenterology centres from May 2014 to March 2016.

INTERVENTIONS: TCBT - patient CBT self-management manual, six 60-minute

telephone sessions over 9 weeks and two 60-minute booster sessions at 4 and 8

months (8 hours' therapist time). WCBT - interactive, tailored web-based CBT,

three 30-minute telephone sessions over 9 weeks and two 30-minute boosters at 4

and 8 months (2.5 hours' therapist time).

MAIN OUTCOME MEASURES: Primary outcomes - IBS symptom severity score (IBS SSS)

and Work and Social Adjustment Scale (WSAS) at 12 months. Cost-effectiveness

[quality-adjusted life-years (QALYs) and health-care costs].

RESULTS: In total, 558 out of 1452 patients (38.4%) screened for eligibility

were recruited - 186 were randomised to TCBT, 185 were randomised to WCBT and

187 were randomised to TAU. The mean baseline Irritable Bowel Syndrome Symptom

Severity Score (IBS SSS) was 265.0. An intention-to-treat analysis with multiple

imputation was carried out at 12 months; IBS SSS were 61.6 points lower in the

TCBT arm [95% confidence interval (CI) 89.5 to 33.8; p鈥?<鈥?0.001] and 35.2 points

lower in the WCBT arm (95% CI 57.8 to 12.6; p鈥?=鈥?0.002) than in the TAU arm (IBS

SSS of 205.6). The mean WSAS score at 12 months was 10.8 in the TAU arm, 3.5

points lower in the TCBT arm (95% CI 5.1 to 1.9; p鈥?<鈥?0.001) and 3.0 points lower

in the WCBT arm (95% CI 4.6 to 1.3; p鈥?=鈥?0.001). For the secondary outcomes, the

Subject's Global Assessment showed an improvement in symptoms at 12 months

(responders) in 84.8% of the TCBT arm compared with 41.7% of the TAU arm [odds

ratio (OR) 6.1, 95% CI 2.5 to 15.0; p鈥?<鈥?0.001] and 75.0% of the WCBT arm (OR

3.6, 95% CI 2.0 to 6.3; p鈥?<鈥?0.001). Patient enablement was 78.3% (responders)

for TCBT, 23.5% for TAU (OR 9.3, 95% CI 4.5 to 19.3; p鈥?<鈥?0.001) and 54.8% for

WCBT (OR 3.5, 95% CI 2.0 to 5.9; p鈥?<鈥?0.001). Adverse events were similar between

the trial arms. The incremental cost-effectiveness ratio (ICER) (QALY) for TCBT

versus TAU was 拢22,284 and for WCBT versus TAU was 拢7724. Cost-effectiveness

reduced after imputation for missing values. Qualitative findings highlighted

that, in the CBT arms, there was increased capacity to cope with symptoms,

negative emotions and challenges of daily life. Therapist input was important in

supporting WCBT.

CONCLUSIONS: In this large, rigorously conducted RCT, both CBT arms showed

significant improvements in IBS outcomes compared with TAU. WCBT had lower costs

per QALY than TCBT. Sustained improvements in IBS symptoms are possible at an

acceptable cost. Suggested future research work is longer-term follow-up and

research to translate these findings into usual clinical practice.

FUTURE WORK: Longer-term follow-up and research to translate these findings into

usual clinical practice is needed.

TRIAL REGISTRATION: Current Controlled Trials ISRCTN44427879.

FUNDING: This project was funded by the National Institute for Health Research

(NIHR) Health Technology Assessment (HTA) programme and will be published in

full in Health Technology Assessment; Vol. 23, No. 17. See the NIHR Journals

Library website for further project information. The University of Southampton

sponsored this study. Funding was received from the NIHR HTA Board and the NIHR

Clinical Research Network and support was received from the NIHR Clinical

Research Network.

Plain Language Summary: Irritable bowel syndrome (IBS) is a common bowel

disorder causing pain, bloating and diarrhoea or constipation, which can affect

quality of life. Treatment relies on a positive diagnosis, reassurance,

lifestyle advice and drug therapies. However, many patients suffer ongoing

distressing symptoms. Guidelines recommend cognitive鈥揵ehavioural therapy (CBT)

for patients with ongoing IBS symptoms. However, access to therapy is limited

because of cost and therapist availability. We previously developed web-based

CBT (WCBT), which is more accessible, less expensive and requires less therapist

time than traditional therapist telephone-delivered CBT (TCBT). The aim of the

current trial was to assess the clinical effectiveness and cost-effectiveness of

these two approaches. Participants were randomly assigned to TCBT, WCBT or

treatment as usual (TAU). The TCBT group received a CBT manual and six 1-hour

telephone CBT sessions with trained therapists over 9 weeks and two booster

sessions at 4 and 8 months. The WCBT group received access to the interactive

CBT website with eight online sessions at home over 9 weeks, with similar

content to the therapist CBT, and received three 30-minute therapist

telephone-delivered CBT sessions and two boosters at 4 and 8 months. There were

558 adults with ongoing IBS symptoms who took part from 74 general practice

surgeries and three hospital clinics in London and the south of England. The

main study outcomes were the IBS Symptom Severity Score and the Work and Social

Adjustment Scale, which measures people鈥檚 ability to function and live their

lives. The results of these were collected at the start of the study and at 3, 6

and 12 months. Significant improvement in symptoms was found in the two therapy

groups compared with TAU at 3, 6 and 12 months. Cost-effectiveness and wider

benefits (e.g. ability to cope and mood) also showed positive results,

indicating that sustained improvements in IBS symptoms are possible at an

acceptable cost.

DOI: 10.3310/hta23170

PMCID: PMC6545494

PMID: 31042143 [Indexed for MEDLINE]

Conflict of interest statement: Paul Little was Programme Director of the

Programme Grants for Applied Research (PGfAR) programme, Editor-in-Chief for the

PGfAR journal and a member of the National Institute for Health Research (NIHR)

Journals Library Editorial Group and the NIHR PGfAR expressions of interest 鈥?

Health Technology Assessment Projects Remit Meeting. Trudie Chalder reports

grants from Guy鈥檚 and St Thomas鈥? Charity. She was a faculty member at the Third

International Conference on Functional (Psychogenic) Neurological Disorders,

September 2017, Edinburgh, UK; a member of the Improving Access to Psychological

Therapies (IAPT) Education and Training Evidence Review Group (2016); a member

of the IAPT Outcomes and Informatics Meeting (2016鈥損resent); and the president

of the British Association for Behavioural and Cognitive Psychotherapies

(2012鈥?15), for which she did not receive payment. She delivered workshops on

medically unexplained symptoms during the conduct of the study (money paid into

King鈥檚 College London for future research). Trudie Chalder has a patent for the

background intellectual property (IP) of the manuals that were developed prior

to the trial starting. The Trial Steering Committee Chairperson, Peter White,

was a colleague of Trudie Chalder in the past but he has recently retired. Rona

Moss-Morris reports personal fees from training in irritable bowel syndrome

interventions for Central and North West London NHS Foundation Trust and the

University of East Anglia outside the submitted work. The patient manual is

background IP developed by Rona Moss-Morris and Trudie Chalder in previous work.

The therapist manual was developed for the Assessing Cognitive鈥揵ehavioural

Therapy in Irritable Bowel (ACTIB) trial. These manuals were made available only

once the 12-month ACTIB follow-up was complete. Sabine Landau reports support

via the Biomedical Research Centre for Mental Health at South London and

Maudsley NHS Foundation Trust and King鈥檚 College London.

24. Physiol Int. 2019 Sep 1;106(3):225-235. doi: 10.1556/2060.106.2019.20. Epub 2019

Sep 27.

Ultrastructure of intestinal mucosa in diarrhea-predominant irritable bowel

syndrome.

Zhao DY(1), Qi QQ(2), Long X(2), Li X(2), Chen FX(2), Yu YB(2), Zuo XL(2).

Author information:

(1)Department of Gastroenterology, Puyang Oilfield General Hospital, Puyang, P.

R. China.

(2)Department of Gastroenterology, Qilu Hospital, Shandong University, Shandong

Province, P. R. China.

OBJECTIVES: Impaired intestinal barrier function has been demonstrated in the

pathophysiology of diarrhea-predominant irritable bowel syndrome (IBS-D). This

study aimed to describe the intestinal ultrastructural findings in the

intestinal mucosal layer of IBS-D patients.

METHODS: In total, 10 healthy controls and 10 IBS-D patients were analyzed in

this study. The mucosa of each patient's rectosigmoid colon was first assessed

by confocal laser endomicroscopy (CLE); next, biopsied specimens of these sites

were obtained. Intestinal tissues of IBS-D patients and healthy volunteers were

examined to observe cellular changes by transmission electron microscopy (TEM).

RESULTS: CLE showed no visible epithelial damage or inflammatory changes in the

colonic mucosa of IBS-D compared with healthy volunteers. On transmission

electron microscopic examination, patients with IBS-D displayed a larger apical

intercellular distance with a higher proportion of dilated (>20聽nm)

intercellular junctional complexes, which was indicative of impaired mucosal

integrity. In addition, microvillus exfoliation, extracellular vesicle as well

as increased presence of multivesicular bodies were visible in IBS-D patients.

Single epithelial cells appeared necrotic, as characterized by cytoplasmic

vacuolization, cytoplasmic swelling, and presence of autolysosome. A significant

association between bowel habit, frequency of abdominal pain, and enlarged

intercellular distance was found.

CONCLUSION: This study showed ultrastructural alterations in the architecture of

intestinal epithelial cells and intercellular junctional complexes in IBS-D

patients, potentially representing a pathophysiological mechanism in IBS-D.

DOI: 10.1556/2060.106.2019.20

PMID: 31560236 [Indexed for MEDLINE]

25. Ter Arkh. 2016;88(8):40-45. doi: 10.17116/terarkh201688840-45.

[Efficacy of Kolofort for the treatment of patients with irritable bowel

syndrome].

[Article in Russian; Abstract available in Russian from the publisher]

Tsukanov VV(1), Rzhavicheva OS(2), Vasjutin AV(1), Dunaevskaja OV(3), Tonkih

JL(1), Bronnikova EP(1).

Author information:

(1)Research Institute of Medical Problems of the North, Krasnoyarsk, Russia.

(2)Railway Clinical Hospital, Krasnoyarsk, Russia.

(3)Polyclinic, OAO "Krastvetmet", Krasnoyarsk, Russia.

AIM: to determine the efficacy and safety of Kolofort in the treatment of

patients with irritable bowel syndrome (IBS).

SUBJECTS AND METHODS: 52 patients (16 men and 36 women) aged 26 to 59 years were

examined over 4 months to rule out organic disease. The diagnosis of IBS was

established on the basis of the Rome III diagnostic criteria (2006). Seven

patients were diagnosed as having IBS with a preponderance of constipation; 3

had IBS with a preponderance of diarrhea, and 42 had mixed IBS. Thereafter they

were given Kolofort, a combination release-active antibody drug having

anxiolytic, anti-inflammatory, and spasmolytic effects. Kolofort affects the

ligand-receptor interactions of the brain-specific protein S-100 with serotonin

receptors and 蟽1-receptors in the central nervous system and that of histamine

with histamine H4 receptors in the gastrointestinal tract and modifies

(regulates) the functional activity of tumor necrosis factor-伪 (TNF-伪). The

regulatory action of the drug at the level of the central and autonomic nervous

system and the immune system manifests itself as spasmolytic, anti-inflammatory,

and sedative effects, which as a whole effectively normalizes gastrointestinal

motility. For 3 months, the patients took sublingual Kolofort in a dose of 2

tablets thrice daily for 2 weeks, then 2 tablets twice daily for 2.5 months.

Control was made 2 weeks, 1, 2, and 3 months after treatment initiation. The

investigators assessed abdominal pain syndrome, defecation disorders, abdominal

distension, and flatulence by the visual analogue scale (VAS-IBS questionnaire),

visceral sensitivity index (VSI questionnaire), quality of life (QL) in patients

with IBS (IBS-QoL questionnaire), and stool form according to the Bristol Stool

Chart and measured the levels of TNF-伪 and interleukin (IL)-1尾 and IL-10 before

and after treatment.

RESULTS: The efficacy of Kolofort showed itself within 2 weeks of its

administration against all the study functional parameters (pain, defecation

disorder, and flatulence). After one month of therapy, the efficacy of Kolofort

achieved meaningful statistical significance against abdominal pain, complaints

of flatulence, visceral sensitivity index, and QL. The statistically significant

restoration of a stool form was achieved 2 months after treatment and 3-month

Kolofort treatment showed a clear-cut positive clinical effect that appeared as

reductions in pain syndrome (214卤0.22; 褉 < 0.001) and visceral hypersensitivity

symptoms (from 30.33卤2.9 to 67.76卤6.5; 褉 < 0.001), improvements in subjective

sensations associated with defecation disorders (from 6.95卤0.71 to 2.74卤0.28; 褉

< 0.001), stool form, and QL indicators (from 103.48卤9.06 to 44.95卤5.4; 褉 <

0.001), and a decrease in blood TNF-伪 levels after treatment termination (from

9.16 to 7.02 pg/ml; 褉 < 0.026). A Kolofort treatment cycle for IBS produced no

clinically relevant side effects.

CONCLUSION: Kolofort was highly effective in relieving symptoms, in normalizing

the psychological status, and in lowering the levels of TNF-伪 in the treatment

of IBS. The efficacy of the drug was achieved because of its combined effect on

the main components of the pathogenesis of IBS.

Publisher: 笑械谢褜 懈褋褋谢械写芯胁邪薪懈褟. 袨锌褉械写械谢懈褌褜 褝褎褎械泻褌懈胁薪芯褋褌褜 懈 斜械蟹芯锌邪褋薪芯褋褌褜 锌褉械锌邪褉邪褌邪

袣芯谢芯褎芯褉褌 胁 谢械褔械薪懈懈 斜芯谢褜薪褘褏 褋 褋懈薪写褉芯屑芯屑 褉邪蟹写褉邪卸械薪薪芯谐芯 泻懈褕械褔薪懈泻邪 (小袪袣). 袦邪褌械褉懈邪谢褘

懈 屑械褌芯写褘. 袙 褌械褔械薪懈械 4 屑械褋 芯斜褋谢械写芯胁邪谢懈 52 锌邪褑懈械薪褌芯胁 (16 屑褍卸褔懈薪 懈 36 卸械薪褖懈薪) 胁

胁芯蟹褉邪褋褌械 芯褌 26 写芯 59 谢械褌 写谢褟 懈褋泻谢褞褔械薪懈褟 芯褉谐邪薪懈褔械褋泻芯泄 锌邪褌芯谢芯谐懈懈. 袛懈邪谐薪芯蟹 小袪袣

褍褋褌邪薪邪胁谢懈胁邪谢懈 薪邪 芯褋薪芯胁邪薪懈懈 袪懈屑褋泻懈褏 泻褉懈褌械褉懈械胁 III (2006). 校 7 锌邪褑懈械薪褌芯胁

写懈邪谐薪芯褋褌懈褉芯胁邪薪 小袪袣 褋 锌褉械芯斜谢邪写邪薪懈械屑 蟹邪锌芯褉邪, 褍 3 鈥? 小袪袣 褋 锌褉械芯斜谢邪写邪薪懈械屑 写懈邪褉械懈, 褍

42 鈥? 小袪袣 褋屑械褕邪薪薪芯谐芯 褌懈锌邪. 袩芯褋谢械 褝褌芯谐芯 薪邪蟹薪邪褔邪谢懈 袣芯谢芯褎芯褉褌 - 泻芯屑锌谢械泻褋薪褘泄 锌褉械锌邪褉邪褌

薪邪 芯褋薪芯胁械 褉械谢懈蟹-邪泻褌懈胁薪褘褏 邪薪褌懈褌械谢 邪薪泻褋懈芯谢懈褌懈褔械褋泻芯谐芯, 锌褉芯褌懈胁芯胁芯褋锌邪谢懈褌械谢褜薪芯谐芯 懈

褋锌邪蟹屑芯谢懈褌懈褔械褋泻芯谐芯 写械泄褋褌胁懈褟. 袣芯谢芯褎芯褉褌 胁谢懈褟械褌 薪邪 谢懈谐邪薪写-褉械褑械锌褌芯褉薪褘械 胁蟹邪懈屑芯写械泄褋褌胁懈褟

屑芯蟹谐芯褋锌械褑懈褎懈褔械褋泻芯谐芯 斜械谢泻邪 S-100 褋 褋械褉芯褌芯薪懈薪芯胁褘屑懈 懈 蟽1-褉械褑械锌褌芯褉邪屑懈 胁 褑械薪褌褉邪谢褜薪芯泄

薪械褉胁薪芯泄 褋懈褋褌械屑械, 谐懈褋褌邪屑懈薪邪 褋 谢芯泻邪谢懈蟹芯胁邪薪薪褘屑懈 胁 卸械谢褍写芯褔薪芯-泻懈褕械褔薪芯屑 褌褉邪泻褌械

谐懈褋褌邪屑懈薪芯胁褘屑懈 褉械褑械锌褌芯褉邪屑懈 袧4 懈 屑芯写懈褎懈褑懈褉褍械褌 (褉械谐褍谢懈褉褍械褌) 褎褍薪泻褑懈芯薪邪谢褜薪褍褞

邪泻褌懈胁薪芯褋褌褜 褎邪泻褌芯褉邪 薪械泻褉芯蟹邪 芯锌褍褏芯谢懈 - 伪 (肖袧袨-伪). 袪械谐褍谢懈褉褍褞褖械械 胁谢懈褟薪懈械 锌褉械锌邪褉邪褌邪

薪邪 褍褉芯胁薪械 褑械薪褌褉邪谢褜薪芯泄, 胁械谐械褌邪褌懈胁薪芯泄 薪械褉胁薪芯泄 懈 懈屑屑褍薪薪芯泄 褋懈褋褌械屑 锌褉芯褟胁谢褟械褌褋褟

褋锌邪蟹屑芯谢懈褌懈褔械褋泻懈屑, 锌褉芯褌懈胁芯胁芯褋锌邪谢懈褌械谢褜薪褘屑, 褍褋锌芯泻邪懈胁邪褞褖懈屑 写械泄褋褌胁懈械屑, 褔褌芯 胁

泻芯屑锌谢械泻褋械 褝褎褎械泻褌懈胁薪芯 薪芯褉屑邪谢懈蟹褍械褌 屑芯褌芯褉懈泻褍 卸械谢褍写芯褔薪芯-泻懈褕械褔薪芯谐芯 褌褉邪泻褌邪. 袘芯谢褜薪褘械

锌褉懈薪懈屑邪谢懈 袣芯谢芯褎芯褉褌 胁 褌械褔械薪懈械 3 屑械褋 锌芯写 褟蟹褘泻 锌芯 2 褌邪斜谢械褌泻懈 3 褉邪蟹邪 胁 写械薪褜 胁

褌械褔械薪懈械 2 薪械写, 蟹邪褌械屑 锌芯 2 褌邪斜谢械褌泻懈 2 褉邪蟹邪 胁 写械薪褜 2,5 屑械褋. 袣芯薪褌褉芯谢褜 锌褉芯胁芯写懈谢懈

褔械褉械蟹 2 薪械写, 1, 2 懈 3 屑械褋 芯褌 薪邪褔邪谢邪 谢械褔械薪懈褟. 袨褑械薪懈胁邪谢懈 邪斜写芯屑懈薪邪谢褜薪褘泄 斜芯谢械胁芯泄

褋懈薪写褉芯屑, 薪邪褉褍褕械薪懈械 褋褌褍谢邪, 胁蟹写褍褌懈械 卸懈胁芯褌邪 懈 屑械褌械芯褉懈蟹屑 锌芯 胁懈蟹褍邪谢褜薪芯泄 邪薪邪谢芯谐芯胁芯泄

褕泻邪谢械 (芯锌褉芯褋薪懈泻 VAS-IBS), 懈薪写械泻褋 胁懈褋褑械褉邪谢褜薪芯泄 褔褍胁褋褌胁懈褌械谢褜薪芯褋褌懈 (芯锌褉芯褋薪懈泻 VSI),

泻邪褔械褋褌胁芯 卸懈蟹薪懈 (袣袞) 锌邪褑懈械薪褌芯胁 褋 小袪袣 (芯锌褉芯褋薪懈泻 IBS-QoL) 懈 褎芯褉屑褍 褋褌褍谢邪 锌芯

袘褉懈褋褌芯谢褜褋泻芯泄 褕泻邪谢械, 邪 褌邪泻卸械 褋芯写械褉卸邪薪懈械 肖袧袨-伪 懈 懈薪褌械褉谢械泄泻懈薪邪-1尾 懈 -10 写芯 懈 锌芯褋谢械

谢械褔械薪懈褟. 袪械蟹褍谢褜褌邪褌褘. 协褎褎械泻褌懈胁薪芯褋褌褜 袣芯谢芯褎芯褉褌邪 锌褉芯褟胁懈谢邪褋褜 胁 褌械褔械薪懈械 2 薪械写 锌褉懈械屑邪 胁

芯褌薪芯褕械薪懈懈 胁褋械褏 懈褋褋谢械写褍械屑褘褏 褎褍薪泻褑懈芯薪邪谢褜薪褘褏 锌邪褉邪屑械褌褉芯胁 (斜芯谢褜, 薪邪褉褍褕械薪懈械 褋褌褍谢邪,

屑械褌械芯褉懈蟹屑). 效械褉械蟹 1 屑械褋 褌械褉邪锌懈懈 褝褎褎械泻褌懈胁薪芯褋褌褜 袣芯谢芯褎芯褉褌邪 写芯褋褌懈谐谢邪 胁褘褉邪卸械薪薪芯泄

褋褌邪褌懈褋褌懈褔械褋泻懈 蟹薪邪褔懈屑芯泄 褋褌械锌械薪懈 胁 芯褌薪芯褕械薪懈懈 邪斜写芯屑懈薪邪谢褜薪芯泄 斜芯谢懈, 卸邪谢芯斜 薪邪

屑械褌械芯褉懈蟹屑, 懈薪写械泻褋邪 胁懈褋褑械褉邪谢褜薪芯泄 褔褍胁褋褌胁懈褌械谢褜薪芯褋褌懈 懈 袣袞. 小褌邪褌懈褋褌懈褔械褋泻懈 蟹薪邪褔懈屑芯械

胁芯褋褋褌邪薪芯胁谢械薪懈械 褎芯褉屑褘 褋褌褍谢邪 写芯褋褌懈谐薪褍褌芯 褔械褉械蟹 2 屑械褋 谢械褔械薪懈褟, 邪 泻 3 屑械褋 谢械褔械薪懈褟

袣芯谢芯褎芯褉褌芯屑 胁褘褟胁谢械薪 芯褌褔械褌谢懈胁褘泄 锌芯谢芯卸懈褌械谢褜薪褘泄 泻谢懈薪懈褔械褋泻懈泄 褝褎褎械泻褌, 泻芯褌芯褉褘泄

锌褉芯褟胁谢褟谢褋褟 胁 褍屑械薪褜褕械薪懈懈 斜芯谢械胁芯谐芯 褋懈薪写褉芯屑邪 (2,14卤0,22; 褉<0,001), 褋薪懈卸械薪懈懈

锌褉芯褟胁谢械薪懈泄 胁懈褋褑械褉邪谢褜薪芯泄 谐懈锌械褉褔褍胁褋褌胁懈褌械谢褜薪芯褋褌懈 (芯褌 30,33卤2,9 写芯 67,76卤6,5;

褉<0,001), 褍谢褍褔褕械薪懈懈 褋褍斜褗械泻褌懈胁薪褘褏 芯褖褍褖械薪懈泄, 褋胁褟蟹邪薪薪褘褏 褋 薪邪褉褍褕械薪懈褟屑懈 褋褌褍谢邪 (芯褌

6,95卤0,71 写芯 2,74卤0,28; 褉<0,001), 褎芯褉屑褘 褋褌褍谢邪, 褍谢褍褔褕械薪懈懈 锌芯泻邪蟹邪褌械谢械泄 袣袞 (芯褌

103,48卤9,06 写芯 44,95卤5,4; 褉<0,001) 懈 褋薪懈卸械薪懈懈 褋芯写械褉卸邪薪懈褟 肖袧袨-伪 胁 泻褉芯胁懈 锌芯褋谢械

芯泻芯薪褔邪薪懈褟 谢械褔械薪懈褟 (芯褌 9,16 写芯 7,02 锌谐/屑谢; 褉<0,026). 袣谢懈薪懈褔械褋泻懈 蟹薪邪褔懈屑褘褏 锌芯斜芯褔薪褘褏

褝褎褎械泻褌芯胁 锌褉懈 泻褍褉褋芯胁芯屑 谢械褔械薪懈懈 小袪袣 锌褉械锌邪褉邪褌芯屑 袣芯谢芯褎芯褉褌 薪械 芯斜薪邪褉褍卸械薪芯. 袟邪泻谢褞褔械薪懈械.

袣芯谢芯褎芯褉褌 芯泻邪蟹邪谢 胁褘褋芯泻芯褝褎褎械泻褌懈胁薪芯械 写械泄褋褌胁懈械 胁 泻褍锌懈褉芯胁邪薪懈懈 褋懈屑锌褌芯屑芯胁, 薪芯褉屑邪谢懈蟹邪褑懈懈

锌褋懈褏芯谢芯谐懈褔械褋泻芯谐芯 褋褌邪褌褍褋邪 懈 褋薪懈卸械薪懈懈 褍褉芯胁薪褟 肖袧袨-伪 锌褉懈 谢械褔械薪懈懈 小袪袣. 协褎褎械泻褌懈胁薪芯褋褌褜

袣芯谢芯褎芯褉褌邪 写芯褋褌懈谐邪械褌褋褟 斜谢邪谐芯写邪褉褟 褋芯褔械褌邪薪薪芯屑褍 泻芯屑锌谢械泻褋薪芯屑褍 胁芯蟹写械泄褋褌胁懈褞 薪邪 芯褋薪芯胁薪褘械

蟹胁械薪褜褟 锌邪褌芯谐械薪械蟹邪 小袪袣.

DOI: 10.17116/terarkh201688840-45

PMID: 27636926 [Indexed for MEDLINE]

26. Best Pract Res Clin Gastroenterol. 2019 Jun-Aug;40-41:101620. doi:

10.1016/j.bpg.2019.05.007. Epub 2019 May 24.

Pathophysiology of the irritable bowel syndrome - Reflections of today.

Hellstr枚m PM(1).

Author information:

(1)Department of Medical Sciences, Gastroenterology Unit, Uppsala University,

Bldg 40, 5th Floor, SE-75185, Uppsala, Sweden. Electronic address:

Per.Hellstrom@medsci.uu.se.

Irritable bowel syndrome (IBS) is a chronic gastrointestinal symptom complex

defined by abdominal pain and disturbed bowel habits over 3 months within a

period of 6 months, in absence of any identifiable organic pathology. Over the

years, speculations of the pathophysiology of IBS has moved from elusive central

nervous symptoms impinging on psychosomatic disease, to objective signs of

intestinal fermentation with abdominal bloating and intestinal dysmotility. The

specific subgroup of post-infectious IBS is of special interest since it opens

the possibility of dysbiosis as the pivotal point for development of IBS in

association with traveler's diarrhea or antibiotic treatment with ensuing

dysbiosis and abdominal symptoms that may resolve over decades. The undefined

disease mechanisms that take place within the gut seem responsible for the

gut-brain signaling leading to activation of brain centers that drive the

clinical picture of IBS, further modulated by the patient's social background

and previous lifetime events.

Copyright 漏 2019. Published by Elsevier Ltd.

DOI: 10.1016/j.bpg.2019.05.007

PMID: 31594651 [Indexed for MEDLINE]

27. Neurogastroenterol Motil. 2019 Mar;31(3):e13531. doi: 10.1111/nmo.13531. Epub

2019 Jan 10.

Anhedonia in irritable bowel syndrome and in inflammatory bowel diseases and its

relationship with abdominal pain.

Carpinelli L(1), Bucci C(1), Santonicola A(1), Zingone F(1), Ciacci C(1), Iovino

P(1).

Author information:

(1)Gastroenterology Unit, Department of Medicine, Surgery and Dentistry "Scuola

Medica Salernitana", University of Salerno, Salerno, Italy.

BACKGROUND: Anhedonia is the lowered ability to experience pleasure from

rewarding or enjoyable activities and is considered a symptom of depression.

Inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) are

frequently accompanied by psychiatric disorders such as depression. However, to

our knowledge, studies have yet to investigate the anhedonia in these patients.

Our aim was to study the level of anhedonia in patients with IBD and IBS in

comparison with healthy controls (HC), and to relate anhedonia levels with the

severity of abdominal pain.

METHODS: We consecutively recruited IBD and IBS patients. All patients fulfilled

the Snaith-Hamilton Pleasure Scale (SHAPS), a self-rating scale consisting of 14

items that cover the domains of social interaction, food, and drink, sensory

experiences, achievement and pastimes, and the Beck Depression Inventory-II

(BDI-II) to screen for depression. Moreover, we calculated abdominal pain on a

(0-100) Visual Analog Scale (VAS) in all patients.

KEY RESULTS: We enrolled 120 patients (64 IBD and 56 IBS) and 81 HC. Among IBD

patients, 34 had Crohn's disease and 30 ulcerative colitis. All patients as a

whole had significantly higher SHAPS and BDI-II scores than HC (1.3聽卤聽1.5 vs

0.8聽卤聽0.1; P聽=聽0.01 and 10.4聽卤聽7.5 vs 5.9聽卤聽4.9; P聽<聽0.001, respectively), while

no significant differences were found among groups. SHAPS score showed a

significant correlation in only a few statements of BDI-II. In our cohort, a

multivariate regression analysis showed that SHAPS score was significantly

related to current abdominal pain (0-100 VAS) (P聽=聽0.03) independent of gender

and age.

CONCLUSIONS AND INFERENCES: The level of anhedonia was higher in all patients

compared to healthy controls. The more the subject is anhedonic, the higher the

VAS scale for abdominal pain. This study suggests that anhedonia would need to

be very carefully weighed in IBD and IBS patients.

漏 2018 John Wiley & Sons Ltd.

DOI: 10.1111/nmo.13531

PMID: 30628137 [Indexed for MEDLINE]

28. Digestion. 2017;96(1):29-38. doi: 10.1159/000471919. Epub 2017 Jun 21.

Bifidobacterium-Rich Fecal Donor May Be a Positive Predictor for Successful

Fecal Microbiota Transplantation in Patients with Irritable Bowel Syndrome.

Mizuno S(1), Masaoka T, Naganuma M, Kishimoto T, Kitazawa M, Kurokawa S,

Nakashima M, Takeshita K, Suda W, Mimura M, Hattori M, Kanai T.

Author information:

(1)Division of Gastroenterology and Hepatology, Department of Internal Medicine,

Keio University School of Medicine, Tokyo, Japan.

BACKGROUND/AIMS: Dysbiosis is associated with various systemic disorders

including irritable bowel syndrome (IBS). Fecal microbiota transplantation (FMT)

might restore intestinal microbial balance. The study aimed to determine the

safety and efficacy of FMT in IBS patients, as well as also positive predictors

for FMT.

METHODS: This was a single-arm, open-label study. Eligible patients were

diagnosed based on Rome III Diagnostic Criteria. Fecal materials were

administered to the patient via colonoscopy. The primary end point was a change

in the Bristol stool form scale at 4 weeks after FMT. Recovery to types 3-4 was

considered a clinical response. The secondary end point was a change in

intestinal microbiota and psychological status using the Hamilton Rating Scale.

RESULTS: Ten patients were enrolled. Six patients achieved a clinical response.

The diversity of patients 4 weeks after FMT increased significantly compared

with patients before FMT, and that of responding patients was significantly

higher than non-responder patients. The abundance of Bifidobacterium in

effective donors was significantly higher than in ineffective donors and

patients. Psychological status of all patients was significantly improved after

FMT.

CONCLUSIONS: FMT for patients with IBS is safe, and relatively effective.

Bifidobacterium-rich fecal donor may be a positive predictor for successful FMT.

Key Summary: (1) Dysbiosis is associated with various gastrointestinal disorders

including IBS. (2) FMT has potential to restore intestinal microbial balance.

(3) We showed that FMT improved stool form and psychological status of IBS

patients. (4) Bifidobacterium-rich donor efficiently induced symbiosis in IBS

patients.

漏 2017 The Author(s) Published by S. Karger AG, Basel.

DOI: 10.1159/000471919

PMCID: PMC5637308

PMID: 28628918 [Indexed for MEDLINE]

29. Am J Gastroenterol. 2021 Apr;116(4):769-779. doi: 10.14309/ajg.0000000000001038.

Cumulative Effect of Psychological Alterations on Gastrointestinal Symptom

Severity in Irritable Bowel Syndrome.

Midenfjord I(1), Borg A, T枚rnblom H, Simr茅n M.

Author information:

(1)1Department of Internal Medicine and Clinical Nutrition, Institute of

Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden;

2Centre for Functional GI and Motility Disorders, University of North Carolina,

Chapel Hill, North Carolina, USA.

INTRODUCTION: Psychological alterations are common and considered important for

symptom generation in irritable bowel syndrome (IBS). However, the possible

cumulative effect of having multiple psychological alterations on

gastrointestinal (GI) symptom severity in IBS is largely unknown.

METHODS: Patients with IBS (Rome IV) completed validated questionnaires

assessing GI symptoms (Gastrointestinal Symptom Rating Scale, IBS version and

IBS Severity Scoring System), personality traits (Big Five), posttraumatic

stress and psychological alterations, anxiety (Generalized Anxiety Disorder

7-item scale and State-Trait Anxiety Inventory), depression (Patient Health

Questionnaire, 9-item version), fatigue (Multidimensional Fatigue Inventory),

pain catastrophizing, somatization (Patient Health Questionnaire, 12-item

version), stress (Perceived Stress Scale), and GI-specific anxiety (Visceral

Sensitivity Index). Of the 18 possible psychological factors, those with

significant associations with GI symptom severity, corrected for multiple

comparisons, were identified. The associations between increasing number of

psychological alterations (validated cutoff values or uppermost tertile) and the

severity of GI symptoms were analyzed with linear trend analyses.

RESULTS: In total, 106 patients with IBS (Rome IV criteria) were included (72

[68%] women, median age of 35 [interquartile range: 26-45] years). Psychological

alterations were common and overlap among these factors were frequently seen.

Five psychological factors (physical fatigue, GI-specific anxiety, perceived

stress, pain catastrophizing, and trait anxiety) demonstrated significant,

noncollinear associations with GI symptom severity. With increasing number of

these psychological alterations, a gradual increase was seen in the overall

severity of GI symptoms (Gastrointestinal Symptom Rating Scale, IBS version:

partial 畏 = 0.268, P < 0.001; IBS Severity Scoring System: partial 畏 = 0.219, P

< 0.001, both large effect sizes).

DISCUSSION: Distinct associations were seen between the severity of GI symptoms

and individual, as well as an increasing number of psychological alterations.

This highlights the importance of understanding different psychological

alterations for the disease burden in IBS (visual abstract, Supplementary

Digital Content 1, http://links.lww.com/AJG/B756).

DOI: 10.14309/ajg.0000000000001038

PMID: 33982947 [Indexed for MEDLINE]

30. Scand J Pain. 2018 Jan 26;18(1):81-91. doi: 10.1515/sjpain-2017-0153.

Cognitive behavioral therapy for irritable bowel syndrome: the effects on state

and trait anxiety and the autonomic nervous system during induced rectal

distensions - An uncontrolled trial.

Edebol-Carlman H(1), Schrooten M(2), Lj贸tsson B(3), Boersma K(2), Linton S(2),

Brummer RJ(4).

Author information:

(1)Nutrition-Gut-Brain Interactions Research Centre, 脰rebro University, 脰rebro

701 82, Sweden, Phone: +46 (0) 19 30 33 22, Mobile: +46 (0) 732 707 624.

(2)Center for Health and Medical Psychology (CHAMP), School of Law, Psychology

and Social Work, 脰rebro University, 脰rebro, Sweden.

(3)Department of Clinical Neuroscience, Division of Psychology and Division of

Psychiatry, Karolinska Institutet, Stockholm, Sweden.

(4)Nutrition-Gut-Brain Interactions Research Centre, 脰rebro University, 脰rebro,

Sweden.

BACKGROUND AND AIMS: Irritable bowel syndrome (IBS), is a common multifactorial

gastrointestinal disorder linked to disturbances in the microbe gut-brain axis.

Cognitive behavioral therapy (CBT), in face-to-face format has showed promising

results on IBS and its associated psychological symptoms. The present study

explored for the first time if CBT for IBS affects the autonomic nervous system

(ANS) during experimentally induced visceral pain and cognitive stress,

respectively. The levels of state and trait anxiety, current and perceived

stress were also evaluated.

METHODS: In this uncontrolled trial, individual CBT was performed in

face-to-face format for 12 weeks in 18 subjects with IBS. Heart rate variability

and skin conductance were measured during experimentally induced visceral pain

and during a cognitive task (Stroop color-word test), before and after

intervention. The levels of state and trait anxiety as well as self-rated

current and perceived stress were also measured before and after the

intervention.

RESULTS: CBT did not affect ANS activity during experimentally induced visceral

pain and cognitive stress. The sympathetic activity was high, typical for IBS

and triggered during both visceral pain and cognitive stress. The levels of

state and trait anxiety significantly decreased after the intervention. No

significant changes in self-rated current or perceived stress were found.

CONCLUSIONS: Results suggest that face-to-face CBT for IBS improved anxiety- a

key psychological mechanism for the IBS pathophysiology, rather than the

autonomic stress response to experimentally induced visceral pain and cognitive

stress, respectively.

IMPLICATIONS: This study indicates that IBS patients present high levels of

stress and difficulties coping with anxiety and ANS activity during visceral

pain and a cognitive stress test, respectively. These manifestations of IBS are

however not targeted by CBT, and do not seem to be central for the study

participants IBS symptoms according to the current and our previous study.

Face-to-face CBT for IBS, it does not seem to affect modulation of ANS activity

in response to induced visceral pain or cognitive stress. Instead, face-to-face

CBT decreased levels of state and trait anxiety. Implications for further

studies include that anxiety seems to be important in the IBS pathophysiology,

and needs further scientific attention. This is in line with the fear-avoidance

model which suggests that anxious responses to pain and discomfort drive

hypervigilance to, and (behavioral) avoidance of, symptom provoking stimuli and

vice versa. Catastrophic cognitions, hypervigilance and avoidant behavioral

responses are proposed to produce vicious circles that withhold and exacerbate

pain-related symptoms and disability, and lead to lower quality of life. Larger

scale studies of potential autonomic changes are needed in order to elucidate

which mechanisms elicit its effects in face-to-face CBT for IBS, and provide new

avenues in understanding the pathophysiology of IBS.

DOI: 10.1515/sjpain-2017-0153

PMID: 29794287 [Indexed for MEDLINE]

31. World J Gastroenterol. 2019 Nov 21;25(43):6416-6429. doi:

10.3748/wjg.v25.i43.6416.

Altered profiles of fecal metabolites correlate with visceral hypersensitivity

and may contribute to symptom severity of diarrhea-predominant irritable bowel

syndrome.

Zhang WX(1), Zhang Y(1), Qin G(1), Li KM(2), Wei W(1), Li SY(3), Yao SK(4).

Author information:

(1)Graduate School, Peking Union Medical College and Chinese Academy of Medical

Sciences, Beijing 100730, China.

(2)School of Biological Science and Medical Engineering, Beihang University,

Beijing 100191, China.

(3)Department of Epidemiology and Health Statistics, School of Public Health,

Qingdao University, Qingdao 266071, Shandong Province, China.

(4)Department of Gastroenterology, China-Japan Friendship Hospital, Beijing

100029, China. shukunyao@126.com.

BACKGROUND: Fecal metabolites are associated with gut visceral sensitivity,

mucosal immune function and intestinal barrier function, all of which have

critical roles in the pathogenesis of irritable bowel syndrome (IBS). However,

the metabolic profile and pathophysiology of IBS are still unclear. We

hypothesized that altered profiles of fecal metabolites might be involved in the

pathogenesis of IBS with predominant diarrhea (IBS-D).

AIM: To investigate the fecal metabolite composition and the role of metabolites

in IBS-D pathophysiology.

METHODS: Thirty IBS-D patients and 15 age- and sex-matched healthy controls

(HCs) underwent clinical and psychological assessments, including the IBS

Symptom Severity System (IBS-SSS), an Italian modified version of the Bowel

Disease Questionnaire, the Bristol Stool Form Scale (BSFS), the Hospital Anxiety

and Depression Scale, and the Visceral Sensitivity Index. Visceral sensitivity

to rectal distension was tested using high-resolution manometry system by the

same investigator. Fecal metabolites, including amino acids and organic acids,

were measured by targeted metabolomics approaches. Correlation analyses between

these parameters were performed.

RESULTS: The patients presented with increased stool water content, more

psychological symptoms and increased visceral hypersensitivity compared with the

controls. In fecal metabolites, His [IBS-D: 0.0642 (0.0388, 0.1484), HC: 0.2636

(0.0780, 0.3966), P = 0.012], Ala [IBS-D: 0.5095 (0.2826, 0.9183), HC: 1.0118

(0.6135, 1.4335), P = 0.041], Tyr [IBS-D: 0.1024 (0.0173, 0.4527), HC: 0.5665

(0.2436, 1.3447), P = 0.018], Phe [IBS-D: 0.1511 (0.0775, 0.3248), HC: 0.3967

(0.1388, 0.7550), P = 0.028], and Trp [IBS-D: 0.0323 (0.0001, 0.0826), HC:

0.0834 (0.0170, 0.1759), P = 0.046] were decreased in IBS-D patients, but

isohexanoate [IBS-D: 0.0127 (0.0060, 0.0246), HC: 0.0070 (0.0023, 0.0106), P =

0.028] was significantly increased. Only Tyr was mildly correlated with BSFS

scores in all subjects (r = -0.347, P = 0.019). A possible potential biomarker

panel was identified to correlate with IBS-SSS score (R 2 Adjusted = 0.693, P <

0.001). In this regression model, the levels of Tyr, Val, hexanoate, fumarate,

and pyruvate were significantly associated with the symptom severity of IBS-D.

Furthermore, visceral sensation, including abdominal pain and visceral

hypersensitivity, was correlated with isovalerate, valerate and isohexanoate.

CONCLUSION: Altered profiles of fecal metabolites may be one of the origins or

exacerbating factors of symptoms in IBS-D via increasing visceral sensitivity.

漏The Author(s) 2019. Published by Baishideng Publishing Group Inc. All rights

reserved.

DOI: 10.3748/wjg.v25.i43.6416

PMCID: PMC6881512

PMID: 31798278 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: All authors

report no conflicts of interest.

32. Aliment Pharmacol Ther. 2016 Aug;44(3):246-58. doi: 10.1111/apt.13677. Epub 2016

May 30.

Effects of disturbed sleep on gastrointestinal and somatic pain symptoms in

irritable bowel syndrome.

Patel A(1), Hasak S(1), Cassell B(1), Ciorba MA(1), Vivio EE(1), Kumar M(1),

Gyawali CP(1), Sayuk GS(1)(2)(3).

Author information:

(1)Division of Gastroenterology, Washington University School of Medicine, St.

Louis, MO, USA.

(2)Department of Psychiatry, Washington University School of Medicine, St.

Louis, MO, USA.

(3)Gastroenterology Section, John Cochran Veterans Affairs Medical Center, St.

Louis, MO, USA.

BACKGROUND: Sleep disturbances are common, and perhaps are even more prevalent

in irritable bowel syndrome (IBS).

AIMS: To determine the effect of measured sleep on IBS symptoms the following

day, IBS-specific quality of life (IBS-QOL) and non-GI pain symptoms.

METHODS: IBS patients' sleep patterns were compared to healthy individuals via

wrist-mounted actigraphy over 7 days. Daily bowel pain logs (severity, distress;

10-point Likert) stool pattern (Bristol scale) and supporting symptoms (e.g.

bloating, urgency; 5-point Likert) were kept. Validated measures, including the

GI Symptom Rating Scale-IBS, Visceral Sensitivity Index, Pittsburgh Sleep

Quality Index and the IBS-Quality of Life were collected. Mediation analysis

explored the relationship between sleep, mood and bowel symptoms.

RESULTS: Fifty subjects (38.6 卤 1.0 years old, 44 female; 24 IBS and 26 healthy

controls) completed sleep monitoring. IBS patients slept more hours per day (7.7

卤 0.2 vs. 7.1 卤 0.1, P = 0.008), but felt less well-rested. IBS patients

demonstrated more waking episodes during sleep (waking episodes; 12.1 vs. 9.3, P

< 0.001). Waking episodes predicted worse abdominal pain (P 鈮? 0.01) and GI

distress (P < 0.001), but not bowel pattern or accessory IBS symptoms (P > 0.3

for each). Waking episodes negatively correlated with general- and IBS-specific

QOL in IBS (r = -0.58 and -0.52, P < 0.001 for each). Disturbed sleep effects on

abdominal pain were partially explained by mood as an intermediate.

CONCLUSIONS: Sleep disturbances are more common in irritable bowel syndrome, and

correlate with IBS-related pain, distress and poorer irritable bowel

syndrome-related quality of life. Disturbed sleep effects extend beyond the

bowel, leading to worse mood and greater somatic pain in patients with the

irritable bowel syndrome.

漏 2016 John Wiley & Sons Ltd.

DOI: 10.1111/apt.13677

PMCID: PMC5020700

PMID: 27240555 [Indexed for MEDLINE]

Conflict of interest statement: None of the authors have any conflicts of

interest to report. No writing assistance was obtained.

33. World J Gastroenterol. 2015 Jun 28;21(24):7362-6. doi: 10.3748/wjg.v21.i24.7362.

Immunomodulation of enteric neural function in irritable bowel syndrome.

O'Malley D(1).

Author information:

(1)Dervla O'Malley, Department of Physiology and Alimentary Pharmabiotic Centre,

University College Cork, Cork, Ireland.

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder

which is characterised by symptoms such as bloating, altered bowel habit and

visceral pain. It's generally accepted that miscommunication between the brain

and gut underlies the changes in motility, absorpto-secretory function and pain

sensitivity associated with IBS. However, partly due to the lack of

disease-defining biomarkers, understanding the aetiology of this complex and

multifactorial disease remains elusive. Anecdotally, IBS patients have noted

that periods of stress can result in symptom flares and many patients exhibit

co-morbid stress-related mood disorders such as anxiety and depression. However,

in addition to psychosocial stressors, infection-related stress has also been

linked with the initiation, persistence and severity of symptom flares. Indeed,

prior gastrointestinal infection is one of the strongest predictors of

developing IBS. Despite a lack of overt morphological inflammation, the

importance of immune factors in the pathophysiology of IBS is gaining

acceptance. Subtle changes in the numbers of mucosal immune cell infiltrates and

elevated levels of circulating pro-inflammatory cytokines have been reproducibly

demonstrated in IBS populations. Moreover, these immune mediators directly

affect neural signalling. An exciting new area of research is the role of

luminal microbiota in the modulation of neuro-immune signalling, resulting in

local changes in gastrointestinal function and alterations in central neural

functioning. Progress in this area has begun to unravel some of the complexities

of neuroimmune and neuroendocrine interactions and how these molecular exchanges

contribute to GI dysfunction.

DOI: 10.3748/wjg.v21.i24.7362

PMCID: PMC4481432

PMID: 26139983 [Indexed for MEDLINE]

34. World J Gastroenterol. 2021 Nov 21;27(43):7433-7445. doi:

10.3748/wjg.v27.i43.7433.

COVID-19 as a trigger of irritable bowel syndrome: A review of potential

mechanisms.

Settanni CR(1), Ianiro G(1), Ponziani FR(1), Bibb貌 S(1), Segal JP(2), Cammarota

G(1), Gasbarrini A(1).

Author information:

(1)Unit脿 Operativa Complessa Medicina Interna e Gastroenterologia, Dipartimento

di Scienze Mediche e Chirurgiche, Fondazione Policlinico Universitario "A.

Gemelli" IRCCS, Rome 00168, Italy.

(2)Department of Gastroenterology and Hepatology, Hillingdon Hospital, Uxbridge

HA1 3UJ, United Kingdom.

In December 2019 a novel coronavirus disease 2019 (COVID-19), caused by the

severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), started spreading

from Wuhan city of Chinese Hubei province and rapidly became a global pandemic.

Clinical symptoms of the disease range from paucisymptomatic disease to a much

more severe disease. Typical symptoms of the initial phase include fever and

cough, with possible progression to acute respiratory distress syndrome.

Gastrointestinal manifestations such as diarrhoea, vomiting and abdominal pain

are reported in a considerable number of affected individuals and may be due to

the SARS-CoV-2 tropism for the peptidase angiotensin receptor 2. The intestinal

homeostasis and microenvironment appear to play a major role in the pathogenesis

of COVID-19 and in the enhancement of the systemic inflammatory responses.

Long-term consequences of COVID-19 include respiratory disturbances and other

disabling manifestations, such as fatigue and psychological impairment. To date,

there is a paucity of data on the gastrointestinal sequelae of SARS-CoV-2

infection. Since COVID-19 can directly or indirectly affect the gut physiology

in different ways, it is plausible that functional bowel diseases may occur

after the recovery because of potential pathophysiological alterations

(dysbiosis, disruption of the intestinal barrier, mucosal microinflammation,

post-infectious states, immune dysregulation and psychological stress). In this

review we speculate that COVID-19 can trigger irritable bowel syndrome and we

discuss the potential mechanisms.

漏The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights

reserved.

DOI: 10.3748/wjg.v27.i43.7433

PMCID: PMC8613742

PMID: 34887641 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: The authors

declare no conflict of interests.

35. World J Gastroenterol. 2019 Aug 28;25(32):4696-4714. doi:

10.3748/wjg.v25.i32.4696.

Effect of mild moxibustion on intestinal microbiota and NLRP6 inflammasome

signaling in rats with post-inflammatory irritable bowel syndrome.

Bao CH(1), Wang CY(1), Li GN(1), Yan YL(1), Wang D(1), Jin XM(2), Wu LY(1), Liu

HR(1), Wang XM(1), Shi Z(1), Wu HG(3).

Author information:

(1)Key Laboratory of Acupuncture and Immunological Effects, Shanghai University

of Traditional Chinese Medicine, Shanghai 200030, China.

(2)Stark Neurosciences Research Institute, Indiana University School of

Medicine, Indianapolis, IN 46202, United States.

(3)Key Laboratory of Acupuncture and Immunological Effects, Shanghai University

of Traditional Chinese Medicine, Shanghai 200030, China. wuhuangan@126.com.

BACKGROUND: About one-third of refractory irritable bowel syndrome (IBS) cases

are caused by gastrointestinal (GI) infection/inflammation, known as

post-infectious/post-inflammatory IBS (PI-IBS). Although it is known that

intestinal microbiota and host NOD-like receptor family pyrin domain containing

6 (NLRP6) inflammsome signaling are closely related to PI-IBS and moxibustion

has a therapeutic effect on PI-IBS, whether moxibustion regulates the intestinal

flora and host NLRP6 events in PI-IBS remains unclear.

AIM: To examine the regulatory effect of moxibustion on intestinal microbiota

and host NLRP6 inflammatory signaling in PI-IBS.

METHODS: Sprague-Dawley rats were divided into a normal control group, a model

control group, a mild moxibustion group, and a sham mild moxibustion group.

PI-IBS rats in the mild moxibustion group were treated with moxibusiton at

bilateral Tianshu (ST 25) and Zusanli (ST36) for 7 consecutive days for 10 min

each time. The sham group rats were given the same treatment as the mild

moxibustion group except the moxa stick was not ignited. Abdominal withdrawal

reflex (AWR) score was measured to assess the visceral sensitivity, and colon

histopathology and ultrastructure, colonic myeloperoxidase (MPO) activity, and

serum C-reactive protein (CRP) level were measured to evaluate low-grade colonic

inflammation in rats. The relative abundance of selected intestinal bacteria in

rat feces was detected by 16S rDNA PCR and the NLRP6 inflammsome signaling in

the colon was detected by immunofluorescence, qRT-PCR, and Western blot.

RESULTS: The AWR score was significantly decreased and the low-grade intestinal

inflammation reflected by serum CRP and colonic MPO levels was inhibited in the

mild moxibustion group compared with the sham group. Mild moxibustion remarkably

increased the relative DNA abundances of Lactobacillus, Bifidobacterium, and

Faecalibacterium prausnitzii but decreased that of Escherichia coli in the gut

of PI-IBS rats. Additionally, mild moxibustion induced mRNA and protein

expression of intestine lectin 1 but inhibited the expression of IL-1尾, IL-18,

and resistance-like molecule 尾 by promoting the NLRP6 and reducing the mRNA and

protein expression of apoptosis-associated speck-like protein containing CARD

(ASC) and cysteinyl-aspartate-specific proteinase 1 (Caspase-1). The relative

DNA abundances of Lactobacillus, Bifidobacteria, Faecalibacterium prausnitzii,

and Escherichia coli in each group were correlated with the mRNA and protein

expression of NLRP6, ASC, and Caspase-1 in the colon.

CONCLUSION: These findings indicated that mild moxibustion can relieve low-grade

GI inflammation and alleviate visceral hypersensitivity in PI-IBS by regulating

intestinal microbes and controlling NLRP6 inflammasome signaling.

DOI: 10.3748/wjg.v25.i32.4696

PMCID: PMC6718040

PMID: 31528095 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: The authors

declare no conflict of interest related to this study.

36. Brain Behav Immun. 2018 Oct;73:403-415. doi: 10.1016/j.bbi.2018.05.024. Epub

2018 May 31.

Early life stress in mice is a suitable model for Irritable Bowel Syndrome but

does not predispose to colitis nor increase susceptibility to enteric

infections.

Riba A(1), Olier M(1), Lacroix-Lamand茅 S(2), Lencina C(1), Bacqui茅 V(1), Harkat

C(1), Van Langendonck N(3), Gillet M(1), Cartier C(1), Baron M(1), Sommer C(1),

Mallet V(1), Zill M(4), Robert H(5), Laurent F(2), Ellero-Simatos S(6),

Th茅odorou V(1), M茅nard S(7).

Author information:

(1)INRA, ToxAlim (Research Centre in Food Toxicology), Team

Neuro-Gastroenterology and Nutrition, Toulouse, France.

(2)Equipe Apicomplexes et Immunit茅 Mucosale (AIM), UMR 1282

INRA/Universit茅-Infectiologie et Sant茅 Publique (ISP), Centre INRA Val de Loire,

Nouzilly, France.

(3)Service de Parasitologie-Mycologie-M茅decine Tropicale, CHRU, Tours, France.

(4)Institut Universitaire de Technologie, Universit茅 Paul Sabatier, Auch,

France.

(5)INRA, ToxAlim (Research Centre in Food Toxicology), Team

Neuro-Gastroenterology and Nutrition, Toulouse, France; Institut Universitaire

de Technologie, Universit茅 Paul Sabatier, Auch, France.

(6)INRA, ToxAlim (Research Centre in Food Toxicology), Team Integrative

Toxicology and Metabolism, Toulouse, France.

(7)INRA, ToxAlim (Research Centre in Food Toxicology), Team

Neuro-Gastroenterology and Nutrition, Toulouse, France. Electronic address:

sandrine.menard@inra.fr.

Neonatal period is characterized by an immature intestinal barrier. Scattered

evidence suggests that early life stressful events induce long lasting

alterations of intestinal homeostasis mimicking Irritable Bowel Syndrome (IBS).

Those observations highlighting defect of intestinal barrier by early life

stress questioned its potential role as a risk factor for gastrointestinal

disorders such as colitis and infections. In this study, we aimed to analyze if

maternal separation (MS) in mice mimicks IBS main features. We next addressed

whether MS could trigger or exacerbate colitis in genetically predisposed mice

and/or enhance susceptibility to gastrointestinal infections in wild type mice.

MS induced main features of IBS in adult wild type male mice i.e. intestinal

hyperpermeability, visceral hypersensitivity, microbiota dysbiosis, bile acid

malabsorption and low grade inflammation in intestine associated with a defect

of Paneth cells and the ILC3 population. This breach in mucosal barrier

functions in adults was associated with a systemic IgG response against

commensal E. coli and increased IFN纬 secretion by splenocytes. However, in

IL10-/- mice, MS did not trigger nor worsen colitis. Furthermore, wild type mice

submitted to MS did not show increase susceptibility to gastrointestinal

infections (S. Typhimurium, L. monocytogenes or T. gondii) compared to controls.

Altogether, our results identify MS in mice as a good experimental model for IBS

mimicking all the main features. In addition, early life stress, even though it

has long lasting consequences on intestinal homeostasis, does not constitute a

facilitating factor to colitis in predisposed individuals nor to

gastrointestinal infections in wild type mice.

Copyright 漏 2018 Elsevier Inc. All rights reserved.

DOI: 10.1016/j.bbi.2018.05.024

PMID: 29860025 [Indexed for MEDLINE]

37. Gastroenterology. 2017 Oct;153(4):948-960.e3. doi: 10.1053/j.gastro.2017.06.051.

Epub 2017 Jul 13.

Vasoactive Intestinal Polypeptide and Mast Cells Regulate Increased Passage of

Colonic Bacteria in Patients With Irritable Bowel Syndrome.

Bednarska O(1), Walter SA(1), Casado-Bedmar M(2), Str枚m M(1), Salvo-Romero E(3),

Vicario M(3), Mayer EA(4), Keita 脜V(5).

Author information:

(1)Department of Clinical and Experimental Medicine, Link枚ping University,

Link枚ping, Sweden; Department of Gastroenterology, Link枚ping University,

Link枚ping, Sweden.

(2)Department of Clinical and Experimental Medicine, Link枚ping University,

Link枚ping, Sweden.

(3)Laboratory of Translational Mucosal Immunology, Digestive Diseases Research

Unit, Vall d'Hebron Institut de Recerca, Hospital Universitari Vall d'Hebron,

Universitat Aut貌noma de Barcelona, Spain.

(4)G Oppenheimer Center for Neurobiology of Stress & Resilience, Division of

Digestive Diseases, David Geffen School of Medicine at UCLA, Los Angeles,

California.

(5)Department of Clinical and Experimental Medicine, Link枚ping University,

Link枚ping, Sweden. Electronic address: asa.keita@liu.se.

BACKGROUND & AIMS: Irritable bowel syndrome (IBS) is associated with intestinal

dysbiosis and symptoms of IBS develop following gastroenteritis. We aimed to

study the passage of live bacteria through the colonic epithelium, and determine

the role of mast cells (MCs) and vasoactive intestinal polypeptide (VIP) in

barrier regulation in IBS and healthy individuals.

METHODS: Colon biopsies from 32 women with IBS and 15 age-matched healthy women

(controls) were mounted in Ussing chambers; we measured numbers of fluorescently

labeled Escherichia coli HS and Salmonella typhimurium that passed through from

the mucosal side to the serosal side of the tissue. Some biopsies were exposed

to agents that block the VIP receptors (VPAC1 and VPAC2) or MCs. Levels of VIP

and tryptase were measured in plasma and biopsy lysates. Number of MCs and MCs

that express VIP or VIP receptors were quantified by immunofluorescence.

Biopsies from an additional 5 patients with IBS and 4 controls were mounted in

chambers and Salmonella were added; we studied passage routes through the

epithelium by transmission electron microscopy and expression of tight junctions

by confocal microscopy.

RESULTS: In colon biopsies from patients with IBS, larger numbers of E coli HS

and S聽typhimurium passed through the epithelium than in biopsies from controls

(P < .0005). In transmission electron microscopy analyses, bacteria were found

to cross the epithelium via only the transcellular route. Bacterial passage was

reduced in biopsies from patients with IBS and controls after addition of

antibodies against VPACs or ketotifen, which inhibits MCs. Plasma samples from

patients with IBS had higher levels of VIP than plasma samples from controls.

Biopsies from patients with IBS had higher levels of tryptase, larger numbers of

MCs, and a higher percentage of MCs that express VPAC1 than biopsies from

controls. In biopsies from patients with IBS, addition of Salmonella

significantly reduced levels of occludin; subsequent addition of ketotifen

significantly reversed this effect.

CONCLUSIONS: We found that colonic epithelium tissues from patients with IBS

have increased translocation of commensal and pathogenic live bacteria compared

with controls. The mechanisms of increased translocation include MCs and VIP.

Copyright 漏 2017 AGA Institute. Published by Elsevier Inc. All rights reserved.

DOI: 10.1053/j.gastro.2017.06.051

PMCID: PMC5623149

PMID: 28711627 [Indexed for MEDLINE]

38. BMC Complement Altern Med. 2019 Nov 27;19(1):337. doi:

10.1186/s12906-019-2749-4.

Tong-Xie-Yao-Fang improves intestinal permeability in diarrhoea-predominant

irritable bowel syndrome rats by inhibiting the NF-魏B and notch signalling

pathways.

Hou Q(1)(2), Huang Y(3), Zhu Z(1), Liao L(1), Chen X(4), Han Q(5), Liu F(6).

Author information:

(1)Department of Gastroenterology, The First Affiliated Hospital of Guangzhou

University of Chinese Medicine, Guangzhou, 510405, Guangdong, China.

(2)School of Chinese Medicine, Hong Kong Baptist University, Hong Kong, China.

(3)Department of Orthopaedics, The Second Affiliated Hospital of Guangzhou

University of Chinese Medicine, Guangzhou, China.

(4)Department of Preventive Medicine and Health Statistics, Guangzhou University

of Chinese Medicine, Guangzhou, Guangdong, China.

(5)School of Chinese Medicine, Hong Kong Baptist University, Hong Kong, China.

simonhan74@126.com.

(6)Department of Gastroenterology, The First Affiliated Hospital of Guangzhou

University of Chinese Medicine, Guangzhou, 510405, Guangdong, China.

liufb163@126.com.

BACKGROUND: Tong-Xie-Yao-Fang (TXYF) has been shown to be effective in

diarrhoea-predominant irritable bowel syndrome (IBS-D) patients. However, the

underlying mechanism remains to be clarified. The aim of this study was to

investigate the efficacy and related mechanisms of TXYF in an IBS-D rat model.

METHODS: The IBS-D rat model was established with 4% acetic acid and evaluated

by haematoxylin-eosin (HE) staining. Then, IBS-D rats were divided into control,

TXYF and rifaximin groups and treated intragastrically with normal saline, TXYF

and rifaximin, respectively, for 14鈥塪ays. The following indicators were measured

before and after treatment: defecation frequency, faecal water content (FWC) and

colorectal distension (CRD). Histopathological changes in the distal colon were

observed after treatment. The expression of OCLN and ZO1 in the distal colon of

IBS-D rats reflected the intestinal mucosal permeability, as measured by

qRT-PCR, western blot, and enzyme-linked immunosorbent assays (ELISAs). The

NF-魏B and Notch signalling pathways and inflammation-related factors were

investigated.

RESULTS: After treatment with TXYF, the defecation frequency, FWC and CRD were

significantly lower than those in the model group (P鈥?<鈥?0.05). HE staining showed

that colonic epithelial cells (CECs) in the IBS-D rats displayed significant

oedema, impaired intestinal mucosal integrity and an increased influx of

inflammatory cells. A significant reduction in granulocyte and CEC oedema was

observed after the administration of TXYF and rifaximin compared to that of the

model group and blank group (P鈥?<鈥?0.05). TXYF significantly upregulated the

expression of OCLN and ZO-1 and downregulated inflammation-related factors

(IL-6, IL-1尾, and TNF-伪 and the chemokine KC) in IBS-D rats compared to those in

the model group rats (P鈥?<鈥?0.05). In terms of the NF-魏B and Notch signalling

pathways, the expression of NICD, p-ERK, Hes-1 and p-P65 decreased significantly

in the TXYF and rifaximin groups, while the expression of ATOH1 increased

significantly compared to that in the model group (P鈥?<鈥?0.05).

CONCLUSION: TXYF can effectively improve intestinal permeability and enhance

intestinal mucosal barrier function, which may be related to inhibition of the

inflammatory cascade and the NF-魏B and Notch signalling pathways.

DOI: 10.1186/s12906-019-2749-4

PMCID: PMC6882330

PMID: 31775739 [Indexed for MEDLINE]

Conflict of interest statement: The authors declare that they have no competing

interests.

39. Mol Med. 2023 Jan 12;29(1):5. doi: 10.1186/s10020-022-00599-x.

Evaluation of two laboratory model methods for diarrheal irritable bowel

syndrome.

Chen Q(1), Zhang H(2), Sun CY(1), He QY(3), Zhang RR(2), Luo BF(1), Zhou ZH(1),

Chen XF(#)(4).

Author information:

(1)Evidence-Based Medicine Research Centre, Jiangxi University of Chinese

Medicine, Nanchang, 330004, Jiangxi, China.

(2)Department of Food Nutrition and Safety, College of Pharmacy, Jiangxi

University of Chinese Medicine, Nanchang, 330004, Jiangxi, China.

(3)Chengdu University of Traditional Chinese Medicine, Chengdu, 611137, China.

(4)Evidence-Based Medicine Research Centre, Jiangxi University of Chinese

Medicine, Nanchang, 330004, Jiangxi, China. xiaofanci122306@163.com.

(#)Contributed equally

BACKGROUND: Diarrheal irritable bowel syndrome (IBS-D) is a common chronic

functional gastrointestinal disorder, and the underlying pathogenic mechanism is

still unclear. Animal models that mimic the pathological state of IBS-D patients

were constructed to provide a reference for later drug research and model

development.

METHODS: The IBS-D model was induced using restraint stress and chemical

stimulation (rhubarb), and rats were divided into normal control group (NC),

chemically stimulated group (CS), and restraint stress group (RS). Visceral

motility responses to Colorectal Balloon Dilation (CRD) were measured by

Abdominal Withdrawal Reflex (AWR); evaluation of faecal properties and water

content; determination of colonic tissue tight junction (TJ) mRNA expression by

RT-PCR; measurement of inflammatory cytokines by ELISA; and intestinal flora and

short chain fatty acids.

RESULTS: Compared to NC group, CS and RS group rats showed increased intestinal

sensitivity and Bristol stool score, significant diarrheal symptoms and weight

loss. Mucin 2, ZO-1, OCLN, CLDN4 mRNA expression was reduced and the intestinal

mucosal barrier function was diminished. In addition, the levels of inflammatory

factors IL-1尾, IL-6, IL-8, IL-10 and TNF-伪 increased, the abundance and

diversity of intestinal flora decreased, the content of beneficial bacteria such

as Bifidobacteria decreased, and SCFAs such as acetic acid, propionic acid and

butyric acid decreased to different degrees. Although, no significant difference

was observed for any molecular and inflammatory marker, but compared to CS

group, RS group had less water in the stool, higher visceral sensitivity, and

higher relative abundance of beneficial intestinal bacteria such as

Actinobacteria.

CONCLUSION: In conclusion, restraint stress combined with chemical stimulation

can mimic the pathological state of diarrhoea symptoms, visceral

hypersensitivity, reduced intestinal mucosal barrier permeability, immune

regulatory dysfunction and dysbiosis in IBS-D patients. However, herbs with

antibacterial effects such as rhubarb and senna, for example, are not suitable

as the first choice for chemical stimulation, as they may lead to a decrease in

harmful bacteria and an increase in beneficial bacteria in the intestinal

fraction and do not perfectly mimic the imbalanced state of intestinal flora in

IBS-D patients, while restraint stress may be a key factor in modelling.

漏 2023. The Author(s).

DOI: 10.1186/s10020-022-00599-x

PMCID: PMC9837933

PMID: 36635623 [Indexed for MEDLINE]

Conflict of interest statement: The authors declare that they have no competing

interests.

40. Am J Chin Med. 2020;48(1):77-90. doi: 10.1142/S0192415X20500044. Epub 2020 Jan

10.

Electroacupuncture Relieves Irritable Bowel Syndrome by Regulating IL-18 and Gut

Microbial Dysbiosis in a Trinitrobenzene Sulfonic Acid-Induced Post-Inflammatory

Animal Model.

Song YF(1), Pei LX(1), Chen L(1), Geng H(1), Yuan MQ(1), Xu WL(2), Wu J(3), Zhou

JY(3), Sun JH(1).

Author information:

(1)Department of Acupuncture, Jiangsu Province Hospital of Chinese Medicine,

Nanjing, Jiangsu 210029, P. R. China.

(2)Department of the First Clinical Medical College, Nanjing University of

Chinese Medicine, Nanjing, Jiangsu 210023, P. R. China.

(3)Department of Central Laboratory, Jiangsu Province Hospital of Chinese

Medicine, Nanjing, Jiangsu 210029, P. R. China.

Post inflammatory irritable bowel syndrome (PI-IBS), a subset of IBS, is

characterized by symptoms of visceral pain, bloating, and changed bowel habits

that occur post initial episode of intestinal infection. Gut microbial dysbiosis

or inflammation plays a key role in the pathogenesis of abdominal

hypersensitivity of PI-IBS. Electroacupuncture (EA) stimulation results in an

alleviated PI-IBS-associated symptom. This study investigated the effect of EA

on IL-18 and gut microbial dysbiosis in one visceral hypersensitive rat models

with PI-IBS. A trinitrobenzene sulfonic acid (TNBS)-induced visceral

hypersensitivity rat model was developed. EA stimulation was applied to the ST25

and ST36 acupoints. Animals were assessed using abdominal withdrawal reflex

(AWR) scores to determine the development of colonic visceral hypersensitivity.

The 16S rRNA was used to correlate microbial diversity. IL-18 expression in

colon was quantified by quantitative real-time PCR and western blotting. We

identified that model rats had an increased visceral hypersensitivity to

colorectal distention at different distention pressures compared with the normal

group. Sensitivity to colorectal distention decreased after EA stimulation. The

composition of the fecal microbiota was different between groups. Specifically,

in the model group Empedobacter, Psychrobacter, Enterococcus, Butyricimonas,

Vampirovibrio, Kurthia, Intestinimonas, Neisseria, Falsiporphyromonas,

Bilophila, Fusobacterium, Alistipes, Veillonella, Flavonifractor, Clostridium

XlVa were聽more abundant聽affected genera, whereas Lactobacillus was enriched in

normal rats. EA stimulation was correlated with significant decrease in the

phyla of Fusobacteria. The mRNA and protein levels of IL-18 were higher in the

model group. Meanwhile, EA stimulation attenuated this response. In a word, our

findings suggest that PI-IBS is associated with significant increase in IL-18

levels as well as an alteration in microbiome diversity. These changes can be

reversed with EA treatment. EA stimulation has a positive effect in alleviating

symptoms of visceral hypersensitivity and protecting the gastrointestinal tract.

DOI: 10.1142/S0192415X20500044

PMID: 31918565 [Indexed for MEDLINE]

41. World J Gastroenterol. 2023 Mar 7;29(9):1475-1491. doi: 10.3748/wjg.v29.i9.1475.

Adenosine 2A receptor contributes to the facilitation of post-infectious

irritable bowel syndrome by 纬未 T cells via the PKA/CREB/NF-魏B signaling pathway.

Dong LW(1), Chen YY(1), Chen CC(1), Ma ZC(1), Fu J(1), Huang BL(1), Liu FJ(1),

Liang DC(2), Sun DM(2), Lan C(3).

Author information:

(1)Department of Gastroenterology, Hainan General Hospital, Affiliated Hainan

Hospital, Hainan Medical University, Haikou 570311, Hainan Province, China.

(2)Doheny Eye Institute, Department of Ophthalmology, David Geffen School of

Medicine, University of California Los Angeles, Los Angeles, CA 90033, United

States.

(3)Department of Gastroenterology, Hainan General Hospital, Affiliated Hainan

Hospital, Hainan Medical University, Haikou 570311, Hainan Province, China.

lancheng71@163.com.

BACKGROUND: Immunological dysfunction-induced low-grade inflammation is regarded

as one of the predominant pathogenetic mechanisms in post-infectious irritable

bowel syndrome (PI-IBS). 纬未 T cells play a crucial role in innate and adaptive

immunity. Adenosine receptors expressed on the surface of 纬未 T cells participate

in intestinal inflammation and immunity regulation.

AIM: To investigate the role of 纬未 T cell regulated by adenosine 2A receptor

(A2AR) in PI-IBS.

METHODS: The PI-IBS mouse model has been established with Trichinella spiralis

(T. spiralis) infection. The intestinal A2AR and A2AR in 纬未 T cells were

detected by immunohistochemistry, and the inflammatory cytokines were measured

by western blot. The role of A2AR on the isolated 纬未 T cells, including

proliferation, apoptosis, and cytokine production, were evaluated in vitro.

Their A2AR expression was measured by western blot and reverse transcription

polymerase chain reaction (RT-PCR). The animals were administered with A2AR

agonist, or A2AR antagonist. Besides, 纬未 T cells were also injected back into

the animals, and the parameters described above were examined, as well as the

clinical features. Furthermore, the A2AR-associated signaling pathway molecules

were assessed by western blot and RT-PCR.

RESULTS: PI-IBS mice exhibited elevated ATP content and A2AR expression (P <

0.05), and suppression of A2AR enhanced PI-IBS clinical characteristics,

indicated by the abdominal withdrawal reflex and colon transportation test.

PI-IBS was associated with an increase in intestinal T cells, and cytokine

levels of interleukin-1 (IL-1), IL-6, IL-17A, and interferon-伪 (IFN-伪). Also, 纬未

T cells expressed A2AR in vitro and generated IL-1, IL-6, IL-17A, and IFN-伪,

which can be controlled by A2AR agonist and antagonist. Mechanistic studies

demonstrated that the A2AR antagonist improved the function of 纬未 T cells

through the PKA/CREB/NF-魏B signaling pathway.

CONCLUSION: Our results revealed that A2AR contributes to the facilitation of

PI-IBS by regulating the function of 纬未 T cells via the PKA/CREB/NF-魏B signaling

pathway.

漏The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights

reserved.

DOI: 10.3748/wjg.v29.i9.1475

PMCID: PMC10044852

PMID: 36998428 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: All the authors

report no relevant conflicts of interest for this article.

42. Turk J Gastroenterol. 2022 Dec;33(12):1033-1042. doi: 10.5152/tjg.2022.21651.

The Incidence of Post-infectious Irritable Bowel Syndrome, Anxiety, and

Depression in Iranian Patients with Coronavirus Disease 2019 Pandemic: A

Cross-Sectional Study.

Farsi F(1), Zonooz SR(2), Ebrahimi Z(2), Jebraili H(3), Morvaridi M(2), Azimi

T(3), Sikaroudi MK(4), Heshmati J(5), Khorrami S(6), Mokhtare M(7), Faghihi

A(7), Masoodi M(7).

Author information:

(1)Minimally Invasive Surgery Research Center, Iran University of Medical

Sciences, Tehran, Iran.

(2)Department of Nutrition, School of Public Health, Iran University of Medical

Sciences, Tehran, Iran.

(3)Department of Nutrition, Science and Research Branch, Islamic Azad

University, Tehran, Iran.

(4)Department of Health Sciences and Nutrition, Tehran University of Medical

Sciences, Tehran, Iran.

(5)Department of Nutritional Science, School of Nutritional Science and Food

Technology, Kermanshah University of Medical Sciences, Kermanshah, Iran.

(6)Colorectal Research Center, School of Medicine, Iran University of Medical

Sciences, Tehran, Iran.

(7)Colorectal Research Center, Iran University of Medical Sciences, Tehran,

Iran.

BACKGROUND: Irritable bowel syndrome refers to a subgroup of disorders of

gut-brain interaction associated with stress-related symptoms, but

gastrointestinal infection can also be considered the leading risk factor. It is

well reported that coronavirus disease 2019 can also result in gastroenteritis.

Therefore, this study aimed to evaluate the incidence of post-infectious

irritable bowel syndrome and stressful status among coronavirus disease 2019

patients.

METHODS: This cross-sectional study was conducted on adults with coronavirus

disease 2019 referred to the Infectious Disease Clinic in Iran from November

2020 to February 2021. Patients who met all eligibility criteria were included

in the study. The data were collected using a demographic questionnaire, Rome IV

criteria questionnaire, and Hospital Anxiety and Depression Scale.

RESULTS: Totally, the data obtained from 233 eligible patients (136 women, 97

men; mean age 38.41) 11.52 (years) were collected and analyzed, and 53.2% of the

cases had a moderate coronavirus disease 2019. The analysis showed that 27

(11.6%) patients suffered from irritable bowel syndrome symptoms based on Rome

IV criteria after the recovery from the infection. Also, Hospital Anxiety and

Depression Scale-based symptoms of depression and anxiety that occurred with

coronavirus disease 2019 were reported in 27.4% and 36.9%, respectively.

CONCLUSION: Our finding illustrated that irritable bowel syndrome symptoms based

on Rome IV could occur in post-infected coronavirus disease 2019 patients. Also,

Hospital Anxiety and Depression Scale-based symptoms of depression and anxiety

were more common in females and coronavirus disease 2019 infected patients with

clinical symptoms including cough, shortness of breath, and sore throat.

DOI: 10.5152/tjg.2022.21651

PMCID: PMC9797755

PMID: 36098366 [Indexed for MEDLINE]

43. Cells. 2022 Jun 28;11(13):2046. doi: 10.3390/cells11132046.

Mucosal Plasma Cell Activation and Proximity to Nerve Fibres Are Associated with

Glycocalyx Reduction in Diarrhoea-Predominant Irritable Bowel Syndrome: Jejunal

Barrier Alterations Underlying Clinical Manifestations.

Pardo-Camacho C(1)(2)(3), Ganda Mall JP(1)(4), Mart铆nez C(5), Pigrau M(2)(3),

Exp贸sito E(1)(2), Albert-Bayo M(1), Mel贸n-Ardanaz E(1), Nieto A(2)(6),

Rodi帽o-Janeiro B(2), Fortea M(1), Guagnozzi D(1)(2)(6), Rodriguez-Urrutia

A(3)(7)(8), Torres I(3)(9), Santos-Briones I(10), Azpiroz F(6)(11), Lobo

B(2)(3)(6), Alonso-Cotoner C(2)(3)(6)(11), Santos J(2)(3)(6)(11),

Gonz谩lez-Castro AM(1)(2), Vicario M(1)(12).

Author information:

(1)Laboratory of Translational Mucosal Immunology, Digestive System Research

Unit, Vall d'Hebron Institut de Recerca, Passeig Vall d'Hebron 119-129, 08035

Barcelona, Spain.

(2)Laboratory of Neuro-Immuno-Gastroenterology, Digestive System Research Unit,

Vall d'Hebron Institut de Recerca, Passeig Vall d'Hebron 119-129, 08035

Barcelona, Spain.

(3)Facultat de Medicina, Universitat Aut貌noma de Barcelona, 08193 Bellaterra,

Spain.

(4)Department of Biomedical and Clinical Sciences, Link枚ping University, 58185

Link枚ping, Sweden.

(5)Vascular and Renal Translational Research Group, Lleida Institute for

Biomedical Research Dr. Pifarr茅. Foundation (IRBLleida), Av. Alcalde Rovira

Roure 80, 25198 Lleida, Spain.

(6)Department of Gastroenterology, Vall d'Hebron Hospital Universitari, Passeig

Vall d'Hebron 119-129, 08035 Barcelona, Spain.

(7)Department of Mental Health, Vall d'Hebron Hospital Universitari, Passeig

Vall d'Hebron 119-129, 08035 Barcelona, Spain.

(8)Centro de Investigaci贸n Biom茅dica en Red de Salud Mental (CIBERSAM),

Instituto de Salud Carlos III, 28029 Madrid, Spain.

(9)Department of Pathology, Hospital Universitari Vall d'Hebr贸n, Passeig Vall

d'Hebron 119-129, 08035 Bar celona, Spain.

(10)Facultat Ci猫ncies de la Salut, Universitat Ramon LLull-Blanquerna, C/Padilla

326, 08025 Barcelona, Spain.

(11)Centro de Investigaci贸n Biom茅dica en Red de Enfermedades Hep谩ticas y

Digestivas (CIBEREHD), Instituto de Salud Carlos III, 28029 Madrid, Spain.

(12)Department of Gastrointestinal Health, Nestl茅 Institute of Health Sciences,

Soci茅t茅 des Produits Nestl茅 S.A., Nestl茅 Research, Vers-chez-les-Blanc, 1000

Lausanne, Switzerland.

Irritable bowel syndrome (IBS) is a disorder of brain-gut interaction

characterised by abdominal pain and changes in bowel habits. In the diarrhoea

subtype (IBS-D), altered epithelial barrier and mucosal immune activation are

associated with clinical manifestations. We aimed to further evaluate plasma

cells and epithelial integrity to gain understanding of IBS-D pathophysiology.

One mucosal jejunal biopsy and one stool sample were obtained from healthy

controls and IBS-D patients. Gastrointestinal symptoms, stress, and depression

scores were recorded. In the jejunal mucosa, RNAseq and gene set enrichment

analyses were performed. A morphometric analysis by electron microscopy

quantified plasma cell activation and proximity to enteric nerves and glycocalyx

thickness. Immunoglobulins concentration was assessed in the stool. IBS-D

patients showed differential expression of humoral pathways compared to

controls. Activation and proximity of plasma cells to nerves and IgG

concentration were also higher in IBS-D. Glycocalyx thickness was lower in IBS-D

compared to controls, and this reduction correlated with plasma cell activation,

proximity to nerves, and clinical symptoms. These results support humoral

activity and loss of epithelial integrity as important contributors to gut

dysfunction and clinical manifestations in IBS-D. Additional studies are needed

to identify the triggers of these alterations to better define IBS-D

pathophysiology.

DOI: 10.3390/cells11132046

PMCID: PMC9265332

PMID: 35805133 [Indexed for MEDLINE]

Conflict of interest statement: Fernando Azpiroz serves as a consultant or

advisory board member for Danone, Clasado, and Allergan; Javier Santos has

served as a consultant for Noventure SL, Devintecpharma, Reckitt, Ipsen Aboca &

Pileje and discloses present and past recent scientific collaborations with

Salvat, Norgine, Alfa-Sigma, Cosmo, Adare, Ordesa and Danone; Carmen Alonso

discloses past scientific collaboration with Noventure; Amanda Rodriguez-Urrutia

acted as a consultant for Janssen-Cilag and Organon in the last two years; Maria

Vicario is an employee of Soci茅t茅 des Produits Nestl茅 S.A., Switzerland. The

funders had no role in the design of the study; in the collection, analyses, and

interpretation of data; in the writing of the manuscript, and in the decision to

publish the results.

44. BMC Gastroenterol. 2021 May 22;21(1):235. doi: 10.1186/s12876-021-01820-7.

Somatization in patients with predominant diarrhoea irritable bowel syndrome:

the role of the intestinal barrier function and integrity.

Prospero L(#)(1), Riezzo G(#)(1), Linsalata M(1), Orlando A(1), D'Attoma B(1),

Di Masi M(2), Martulli M(1), Russo F(3).

Author information:

(1)Laboratory of Nutritional Pathophysiology, National Institute of

Gastroenterology "S. de Bellis" Research Hospital, Via Turi 27, 70013,

Castellana Grotte, BA, Italy.

(2)Scientific Direction, National Institute of Gastroenterology "S. de Bellis"

Research Hospital, 70013, Castellana Grotte, BA, Italy.

(3)Laboratory of Nutritional Pathophysiology, National Institute of

Gastroenterology "S. de Bellis" Research Hospital, Via Turi 27, 70013,

Castellana Grotte, BA, Italy. francesco.russo@irccsdebellis.it.

(#)Contributed equally

BACKGROUND: Irritable bowel syndrome (IBS) is characterised by gastrointestinal

(GI) and psychological symptoms (e.g., depression, anxiety, and somatization).

Depression and anxiety, but not somatization, have already been associated with

altered intestinal barrier function, increased LPS, and dysbiosis. The study

aimed to investigate the possible link between somatization and intestinal

barrier in IBS with diarrhoea (IBS-D) patients.

METHODS: Forty-seven IBS-D patients were classified as having low somatization

(LS鈥?=鈥?19) or high somatization (HS鈥?=鈥?28) according to the Symptom

Checklist-90-Revised (SCL-90-R), (cut-off score鈥?=鈥?63). The IBS Severity Scoring

System (IBS-SSS) and the Gastrointestinal Symptom Rating Scale (GSRS)

questionnaires were administered to evaluate GI symptoms. The intestinal barrier

function was studied by the lactulose/mannitol absorption test, faecal and serum

zonulin, serum intestinal聽fatty-acid binding protein, and diamine oxidase.

Inflammation was assessed by assaying serum Interleukins (IL-6, IL-8, IL-10),

and tumour necrosis factor-伪. Dysbiosis was assessed by the urinary

concentrations of indole and skatole and serum lipopolysaccharide (LPS). All

data were analysed using a non-parametric test.

RESULTS: The GI symptoms profiles were significantly more severe, both as a

single symptom and as clusters of IBS-SSS and GSRS, in HS than LS patients. This

finding was associated with impaired small intestinal permeability and increased

faecal zonulin levels. Besides, HS patients showed significantly higher IL-8 and

lowered IL-10 concentrations than LS patients. Lastly, circulating LPS levels

and the urinary concentrations of indole were higher in HS than LS ones,

suggesting a more pronounced imbalance of the small intestine in the former

patients.

CONCLUSIONS: IBS is a multifactorial disorder needing complete clinical,

psychological, and biochemical evaluations.

TRIAL REGISTRATION: https://clinicaltrials.gov/ct2/show/NCT03423069 .

DOI: 10.1186/s12876-021-01820-7

PMCID: PMC8141183

PMID: 34022802 [Indexed for MEDLINE]

Conflict of interest statement: The authors declare that they have no competing

interests.

45. Aliment Pharmacol Ther. 2017 Jan;45(1):100-114. doi: 10.1111/apt.13848. Epub

2016 Nov 9.

Increased expression of nerve growth factor correlates with visceral

hypersensitivity and impaired gut barrier function in diarrhoea-predominant

irritable bowel syndrome: a preliminary explorative study.

Xu XJ(1)(2), Zhang YL(2), Liu L(3), Pan L(4), Yao SK(1)(2).

Author information:

(1)Graduate School of Peking Union Medical College, Chinese Academy of Medical

Sciences, Beijing, China.

(2)Gastroenterology Department, China-Japan Friendship Hospital, Beijing, China.

(3)Jinan Central Hospital Affiliated to Shandong University, Jinan, China.

(4)Immunohistochemistry Laboratory of Clinical Medical Research Institute,

China-Japan Friendship Hospital, Beijing, China.

Comment in

Aliment Pharmacol Ther. 2017 Feb;45(4):567-568. doi: 10.1111/apt.13902.

Aliment Pharmacol Ther. 2017 Feb;45(4):568-569. doi: 10.1111/apt.13916.

BACKGROUND: Neural-immune-endocrine network mechanism has attracted increased

attention in diarrhoea-predominant irritable bowel syndrome (IBS-D).

Pre-clinical evidence indicates that nerve growth factor (NGF) mediates visceral

hypersensitivity and gut barrier dysfunction, via interactions with mast cells

and sensory nerve fibres.

AIM: To explore the role of nerve growth factor, as well as mast cell-nerve

growth factor-nerve interaction in IBS-D pathophysiology.

METHODS: In this cross-sectional study, IBS-D patients and healthy controls

first underwent clinical and psychological assessments. Visceral sensitivity to

rectal distension was tested. As gut barrier function markers, serum diamine

oxidase and d-lactate were detected. Rectosigmoid biopsies were taken for the

analyses of nerve growth factor expression, mast cell count and activation, and

sensory nerve fibres expressing transient receptor potential vanilloid 1 and

calcitonin gene-related peptide. Correlations between these parameters were

examined in patients.

RESULTS: Thirty-eight IBS-D patients (28 males, 10 females; average age 30.2

years) and 20 healthy controls (12 males, 8 females; average age 26.8 years)

participated in the study. The patients presented increased psychological

symptoms, visceral hypersensitivity and impaired gut barrier function. NGF gene

expression, mast cell count and sensory nerve fibres were significantly

increased in the patients (P < 0.05). In correlation analysis, NGF expression

was positively correlated with the disease severity, anxiety and serum diamine

oxidase; visceral sensitivity thresholds were negatively associated with NGF

expression (Bonferroni corrected P < 0.0029).

CONCLUSIONS: Elevated mucosal NGF may interact with mast cells and sensory nerve

fibres, contributing to visceral hypersensitivity and impaired gut barrier

function in IBS-D.

漏 2016 John Wiley & Sons Ltd.

DOI: 10.1111/apt.13848

PMID: 27862119 [Indexed for MEDLINE]

46. BMC Microbiol. 2021 Nov 13;21(1):316. doi: 10.1186/s12866-021-02380-2.

Involvement of mucosal flora and enterochromaffin cells of the caecum and

descending colon in diarrhoea-predominant irritable bowel syndrome.

Yang J(1)(2)(3), Wang P(1)(2)(3), Liu T(1)(2)(3), Lin L(1)(2)(3), Li L(1)(2)(3),

Kou G(1)(2)(3), Zhou R(1)(2)(3), Li P(1)(2)(3), Li Y(4)(5)(6).

Author information:

(1)Department of Gastroenterology, Qilu Hospital, Cheeloo College of Medicine,

Shandong University, No. 107, Wenhuaxi Road, Jinan, 250012, Shandong, China.

(2)Laboratory of Translational Gastroenterology, Qilu Hospital, Cheeloo College

of Medicine, Shandong University, No. 107, Wenhuaxi Road, Jinan, 250012,

Shandong, China.

(3)Robot Engineering Laboratory for Precise Diagnosis and Therapy of GI Tumor,

Qilu Hospital, Cheeloo College of Medicine, Shandong University, No. 107,

Wenhuaxi Road, Jinan, 250012, Shandong, China.

(4)Department of Gastroenterology, Qilu Hospital, Cheeloo College of Medicine,

Shandong University, No. 107, Wenhuaxi Road, Jinan, 250012, Shandong, China.

liyanqing@sdu.edu.cn.

(5)Laboratory of Translational Gastroenterology, Qilu Hospital, Cheeloo College

of Medicine, Shandong University, No. 107, Wenhuaxi Road, Jinan, 250012,

Shandong, China. liyanqing@sdu.edu.cn.

(6)Robot Engineering Laboratory for Precise Diagnosis and Therapy of GI Tumor,

Qilu Hospital, Cheeloo College of Medicine, Shandong University, No. 107,

Wenhuaxi Road, Jinan, 250012, Shandong, China. liyanqing@sdu.edu.cn.

BACKGROUND: Accumulating evidence supports the pivotal role of intestinal flora

in irritable bowel syndrome (IBS). Serotonin synthesis by enterochromaffin (EC)

cells is influenced by the gut microbiota and has been reported to have an

interaction with IBS. The comparison between the microbiota of the caecal and

colonic mucosa in IBS has rarely been studied. The aim of this study was to

investigate the relationship between the gut microbiota, EC cells in caecum and

descending colon, and diarrhoea-predominant IBS (IBS-D) symptoms.

RESULTS: A total of 22 IBS-D patients and 22 healthy controls (HCs) were

enrolled in our study. Hamilton anxiety (HAM-A) and Hamilton depression (HAM-D)

grades increased significantly in IBS-D patients. In addition, the frequency of

defecation in IBS-D patients was higher than that in HCs. Among the preponderant

bacterial genera, the relative abundance of the Ruminococcus\_torques\_ group

increased in IBS-D patients in caecum samples while Raoultella and Fusobacterium

were less abundant. In the descending colon, the abundance of the

Ruminococcus\_torques\_group and Dorea increased in IBS-D patients and

Fusobacterium decreased. No difference was observed between the descending colon

and caecum in regards to the mucosal-associated microbiota. The number of EC

cells in the caecum of IBS-D patients was higher than in HCs and the expression

of TPH1 was higher in IBS-D patients both in the caecum and in the descending

colon both at the mRNA and protein level. Correlation analysis showed that the

Ruminococcus\_torques\_group was positively associated with HAM-A, HAM-D, EC cell

number, IBS-SSS, degree of abdominal pain, frequency of abdominal pain and

frequency of defecation. The abundance of Dorea was positively associated with

EC cell number, IBS-SSS, HAM-A, HAM-D and frequency of abdominal pain.

CONCLUSIONS: EC cell numbers increased in IBS-D patients and the expression of

TPH1 was higher than in HCs. The Ruminococcus torques group and Dorea

furthermore seem like promising targets for future research into the treatment

of IBS-D patients.

漏 2021. The Author(s).

DOI: 10.1186/s12866-021-02380-2

PMCID: PMC8590216

PMID: 34773967 [Indexed for MEDLINE]

Conflict of interest statement: The authors declare that they have no competing

interests.

47. BMC Complement Med Ther. 2021 Jan 21;21(1):40. doi: 10.1186/s12906-021-03220-6.

Efficacy of a curcumin extract (Curcugen鈩?) on gastrointestinal symptoms and

intestinal microbiota in adults with self-reported digestive complaints: a

randomised, double-blind, placebo-controlled study.

Lopresti AL(1)(2), Smith SJ(3)(4), Rea A(4), Michel S(5).

Author information:

(1)Clinical Research Australia, Perth, Western Australia, 6023, Australia.

adrian@clinicalresearch.com.au.

(2)College of Science, Health, Engineering and Education, Murdoch University,

Perth, Western Australia, 6150, Australia. adrian@clinicalresearch.com.au.

(3)Clinical Research Australia, Perth, Western Australia, 6023, Australia.

(4)College of Science, Health, Engineering and Education, Murdoch University,

Perth, Western Australia, 6150, Australia.

(5)DolCas Biotech, LLC, Landing, NJ, 07850, USA.

BACKGROUND: There is preliminary evidence to suggest curcumin can alleviate

digestive symptoms in adults with self-reported digestive complaints and

irritable bowel syndrome. However, in all these trials, curcumin was used as a

component of a multi-herbal combination and there were consistent concerns

associated with risk of bias in most studies. The goal of this study was to

investigate the effects of a curcumin extract (Curcugen鈩?) on gastrointestinal

symptoms, mood, and overall quality of life in adults presenting with

self-reported digestive complaints. Moreover, to determine the potential

therapeutic mechanisms of action associated with curcumin, its effects on

intestinal microbiota and small intestinal bowel overgrowth (SIBO) were

examined.

METHODS: In this 8-week, parallel-group, double-blind, randomised controlled

trial, 79 adults with self-reported digestive complaints were recruited and

randomised to receive either a placebo or 500鈥塵g of the curcumin extract,

Curcugen鈩?. Outcome measures included the Gastrointestinal Symptom Rating Scale

(GSRS), intestinal microbial profile (16S rRNA), Depression, Anxiety, and Stress

Scale - 21 (DASS-21), Short Form-36 (SF-36), and SIBO breath test.

RESULTS: Based on self-report data collected from 77 participants, curcumin was

associated with a significantly greater reduction in the GSRS total score

compared to the placebo. There was also a greater reduction in the DASS-21

anxiety score. No other significant between-group changes in self-report data

were identified. An examination of changes in the intestinal microbial profile

and SIBO test revealed curcumin had no significant effect on these parameters.

Curcumin was well-tolerated with no significant adverse events.

CONCLUSIONS: The curcumin extract, Curcugen鈩?, administered for 8鈥墂eeks at a dose

of 500鈥塵g once daily was associated with greater improvements in digestive

complaints and anxiety levels in adults with self-reported digestive complaints.

Compared to the placebo, there were no significant changes in intestinal

microbiota or SIBO; however, further research using larger samples and testing

methods that allow more detailed microbial analyses will be important. An

investigation into other potential mechanisms associated with curcumin's

gastrointestinal-relieving effects will also be important such as examining its

influence on the intestinal barrier function, inflammation, neurotransmitter

activity, and visceral sensitivity.

TRIAL REGISTRATION: Australian New Zealand Clinical Trials Registry, Trial ID.

ACTRN12619001236189 . Registered 6 September 2019.

DOI: 10.1186/s12906-021-03220-6

PMCID: PMC7818735

PMID: 33478482 [Indexed for MEDLINE]

Conflict of interest statement: ALL has received either presentation honoraria

or clinical trial grants from nutraceutical companies to complete previous

clinical trials. SM is the director of medical & scientific affairs at

Dolcas-Biotech LLC. SJS and AR disclose no conflict of interest.

48. PLoS One. 2015 Sep 14;10(9):e0134836. doi: 10.1371/journal.pone.0134836.

eCollection 2015.

Cytokine Response after Stimulation with Key Commensal Bacteria Differ in

Post-Infectious Irritable Bowel Syndrome (PI-IBS) Patients Compared to Healthy

Controls.

Sundin J(1), Rangel I(1), Repsilber D(1), Brummer RJ(1).

Author information:

(1)School of Health and Medical Sciences, Faculty of Medicine and Health, 脰rebro

University, 脰rebro, Sweden.

BACKGROUND: Microbial dysbiosis and prolonged immune activation resulting in

low-grade inflammation and intestinal barrier dysfunction have been suggested to

be underlying causes of post-infectious irritable bowel syndrome (PI-IBS). The

aim of this study was to evaluate the difference in cytokine response between

mucosal specimens of PI-IBS patients and healthy controls (HC) after ex vivo

stimulation with key anaerobic bacteria.

METHODS: Colonic biopsies from 11 PI-IBS patients and 10 HC were stimulated ex

vivo with the commensal bacteria Bacteroides ovatus, Ruminococcus gnavus,

Akkermansia muciniphila, Subdoligranulum variabile and Eubacterium limosum,

respectively. The cytokine release (IL-1尾, IL-2, IL-8, IL-10, IL-13, IL-17,

TNF-伪 and IFN-纬) in stimulation supernatants was analyzed using the LUMINEX

assay. Comparison of cytokine release between PI-IBS patients and healthy

controls was performed taking both unstimulated and bacterially stimulated

mucosal specimens into account.

KEY RESULTS: IL-13 release from mucosal specimens without bacterial stimulation

was significantly lower in PI-IBS patients compared to HC (p < 0.05). After

stimulation with Subdoligranulum variabile, IL-1尾 release from PI-IBS patients

was significantly increased compared to HC (p < 0.05). Stimulation with

Eubacterium limosum resulted in a significantly decreased IL-10 release in HC

compared to PI-IBS patients (p < 0.05) and a tendency to decreased IL-13 release

in HC compared to PI-IBS patients (p = 0.07).

CONCLUSIONS & INFERENCES: PI-IBS patients differ from HC with regard to cytokine

release ex vivo after stimulation with selected commensal bacteria. Hence, our

results support that the pathogenesis of PI-IBS comprises an altered immune

response against commensal gut microbes.

DOI: 10.1371/journal.pone.0134836

PMCID: PMC4569289

PMID: 26366730 [Indexed for MEDLINE]

Conflict of interest statement: Competing Interests: The authors have declared

that no competing interests exist.

49. World J Gastroenterol. 2019 Jan 14;25(2):269-281. doi: 10.3748/wjg.v25.i2.269.

Increased expression of brain-derived neurotrophic factor is correlated with

visceral hypersensitivity in patients with diarrhea-predominant irritable bowel

syndrome.

Zhang Y(1), Qin G(1), Liu DR(1), Wang Y(1), Yao SK(1).

Author information:

(1)Graduate School, Peking Union Medical College and Chinese Academy of Medical

Sciences, Beijing 100730, China.

BACKGROUND: Visceral hypersensitivity is considered to play a vital role in the

pathogenesis of irritable bowel syndrome (IBS). Neurotrophins have drawn much

attention in IBS recently. Brain-derived neurotrophic factor (BDNF) was found to

mediate visceral hypersensitivity via facilitating sensory nerve growth in

pre-clinical studies. We hypothesized that BDNF might play a role in the

pathogenesis of diarrhea-predominant IBS (IBS-D).

AIM: To investigate BDNF levels in IBS-D patients and its role in IBS-D

pathophysiology.

METHODS: Thirty-one IBS-D patients meeting the Rome IV diagnostic criteria and

20 age- and sex-matched healthy controls were recruited. Clinical and

psychological assessments were first conducted using standardized

questionnaires. Visceral sensitivity to rectal distension was tested using a

high-resolution manometry system. Colonoscopic examination was performed and

four mucosal pinch biopsies were taken from the rectosigmoid junction. Mucosal

BDNF expression and nerve fiber density were analyzed using

immunohistochemistry. Mucosal BDNF mRNA levels were quantified by quantitative

real-time polymerase chain reaction. Correlations between these parameters were

examined.

RESULTS: The patients had a higher anxiety score [median (interquartile range),

6.0 (2.0-10.0) vs 3.0 (1.0-4.0), P = 0.003] and visceral sensitivity index score

[54.0 (44.0-61.0) vs 21.0 (17.3-30.0), P < 0.001] than controls. The defecating

sensation threshold [60.0 (44.0-80.0) vs 80.0 (61.0-100.0), P = 0.009], maximum

tolerable threshold [103.0 (90.0-128.0) vs 182.0 (142.5-209.3), P < 0.001] and

rectoanal inhibitory reflex threshold [30.0 (20.0-30.0) vs 30.0 (30.0-47.5), P =

0.032] were significantly lower in IBS-D patients. Intestinal mucosal BDNF

protein [3.46E-2 (3.06E-2-4.44E-2) vs 3.07E-2 (2.91E-2-3.48E-2), P = 0.031] and

mRNA [1.57 (1.31-2.61) vs 1.09 (0.74-1.42), P = 0.001] expression and nerve

fiber density [4.12E-2 (3.07E-2-7.46E-2) vs 1.98E-2 (1.21E-2-4.25E-2), P =

0.002] were significantly elevated in the patients. Increased BDNF expression

was positively correlated with abdominal pain and disease severity and

negatively correlated with visceral sensitivity parameters.

CONCLUSION: Elevated mucosal BDNF may participate in the pathogenesis of IBS-D

via facilitating mucosal nerve growth and increasing visceral sensitivity.

DOI: 10.3748/wjg.v25.i2.269

PMCID: PMC6337018

PMID: 30670915 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: The authors

declare no conflicts of interest.

50. Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2017 May 28;42(5):522-528. doi:

10.11817/j.issn.1672-7347.2017.05.007.

[Visceral sensitivity, gut barrier function and autonomic nerve function in

patients with diarrhea-predominant irritable bowel syndrome].

[Article in Chinese; Abstract available in Chinese from the publisher]

Xu X(1), Liu L(2), Yao S(1), Zhang Y(3).

Author information:

(1)Chinese Academy of Medical Sciences, Graduate School of Peking Union Medical

College, Beijing 100730; Department of Gastroenterology, China-Japan Friendship

Hospital, Beijing 100029, China.

(2)Department of Gastroenterology, Jinan Central Hospital Affiliated to Shandong

University, Jinan 250014, China.

(3)Department of Gastroenterology, China-Japan Friendship Hospital, Beijing

100029, China.

To evaluate visceral sensitivity, gut barrier function and autonomic nerve

function (ANF) in patients with diarrhea-predominant irritable bowel syndrome

(IBS-D), and to explore their roles in IBS-D pathophysiology.鈥? Methods: A total

of 46 IBS-D patients (IBS-D group) were selected from the Department of

Gastroenterology of China-Japan Friendship Hospital from October 2015 to March

2016, and 20 healthy volunteer were served as a control group (HC group).

Clinical and psychological symptoms were evaluated by questionnaire, and

visceral sensitivity to rectal balloon distention, gut barrier function and

autonomic nerve function (ANF) were examined. The difference in the

above-mentioned indexes were compared between the 2 groups, and the correlations

in the parameters were analyzed in the IBS-D group.鈥? Results: The scores of IBS

symptom severity scale (IBS-SSS), Hamilton anxiety scale (HAMA), Hamilton

depression scale (HAMD) and visceral sensitivity index (VSI) were significantly

higher in the IBS-D group than those in the HC group (P<0.01). In the visceral

sensitivity test, maximum tolerable threshold in the IBS-D group was

significantly decreased compared to that in the HC group (P<0.01); there was no

significant difference in first sensation threshold and defecating sensation

threshold between the two groups (P>0.05). As gut barrier function markers, the

serum diamine oxidase (DAO) and d-lactate were significantly increased in the

IBS-D group (P<0.05). In ANF test, the total score and parasympathetic score as

well as the proportion of abnormal scores in the IBS-D group were significantly

higher than those in the HC group (P<0.05). In IBS-D group, the HAMA, VSI and

serum DAO were positively correlated with IBS-SSS (r=0.528, 0.575, 0.507;

P<0.01), while the 3 visceral sensitivity thresholds were negatively correlated

with IBS-SSS (r=鈥?-0.636, -0.476, -0.697; P<0.01); in addition to the IBS-SSS,

the HAMA, HAMD, VSI and serum DAO were also significant negatively correlated

with the visceral sensitivity thresholds (all P<0.05); no significant

correlations were found between the ANF and the other parameters.鈥? Conclusion:

IBS-D patients show psychological symptoms, visceral hypersensitivity, impaired

gut barrier function and abnormal ANF characterized by parasympathetic

dysfunction; the former 3 factors are all associated with disease severity, and

thus may play vital roles in IBS-D pathophysiology.

Publisher: 鐩殑锛氳瘎浠疯吂娉诲瀷鑲犳槗婵€缁煎悎寰?(diarrhea-predominant irritable bowel

syndrome锛孖BS-D)鎮ｈ€呯殑鍐呰剰鏁忔劅鎬с€佽偁灞忛殰鍔熻兘鍜岃嚜涓荤缁忓姛鑳?(autonomic nerve

function锛孉NF)锛屾帰绱㈠畠浠湪IBS-D鐥呯悊鐢熺悊瀛︿腑鐨勪綔鐢ㄣ€傛柟娉曪細浠?2015骞?10鏈堣嚦2016骞?3鏈堝氨璇婁簬涓棩鍙嬪ソ鍖婚櫌娑堝寲鍐呯鐨?46渚婭BS-D鎮ｈ€?(IBS-D缁?)鍜?20渚嬪仴搴峰織鎰胯€?(瀵圭収缁?)涓虹爺绌跺璞★紝閲囩敤闂嵎璇勪及鍏朵复搴婂強绮剧蹇冪悊鐥囩姸锛屽苟妫€娴嬪唴鑴忔晱鎰熸€с€佽偁灞忛殰鍔熻兘鍙夾NF锛屾瘮杈冧袱缁勪笂杩板悇鎸囨爣鐨勫樊寮傦紝骞跺垎鏋怚BS-D缁勪腑鍚勬寚鏍囬棿鐨勭浉鍏虫€с€傜粨鏋滐細IBS-D缁勭殑鐥呮儏灏哄害璋冩煡琛?(IBS

symptom severity scale锛孖BS-SSS)銆佹眽瀵嗗皵椤跨劍铏戦噺琛?(Hamilton anxiety

scale锛孒AMA)銆佹眽瀵嗗皵椤挎姂閮侀噺琛?(Hamilton depression scale锛孒AMD)鍜屽唴鑴忔晱鎰熸寚鏁?(visceral sensitivity

index锛孷SI)璇勫垎鍧囨樉钁楅珮浜庡鐓х粍(P<0.01)銆傚唴鑴忔晱鎰熸€ф娴嬩腑锛孖BS-D缁勫鐩磋偁鎵╁紶鍒烘縺鐨勬渶澶ц€愬彈闃堝€兼樉钁椾綆浜庡鐓х粍(P<0.01)锛屽垵濮嬫劅瑙夐槇鍊煎拰鎸佺画鎺掍究闃堝€间袱缁勫樊寮傛棤缁熻瀛︽剰涔?(P>0.05)銆傝偁灞忛殰鍔熻兘琛€娓呮爣蹇楃墿浜岃兒姘у寲閰?(diamine

oxidase锛孌AO)鍜孌-涔抽吀鍦↖BS-D缁勪腑鍧囨樉钁楀崌楂?(鍧嘝<0.05)銆侷BS-D缁勭殑ANF鎬诲垎鍜屽壇浜ゆ劅璁″垎浠ュ強涓よ€呯殑寮傚父姣斾緥鍧囨樉钁楅珮浜庡鐓х粍(鍧嘝<0.05)銆傚湪IBS-D缁勫悇鎸囨爣鐩稿叧鎬у垎鏋愪腑锛孒AMA锛孷SI鍜岃娓匘AO涓嶪BS-SSS鍛堟樉钁楁鐩稿叧(鍒嗗埆r=0.528锛?0.575锛?0.507锛汸<0.01)锛?3涓唴鑴忔劅瑙夐槇鍊煎潎涓嶪BS-SSS鍛堟樉钁楄礋鐩稿叧(鍒嗗埆r=鈥?0.636锛屸€ㄢ€?0.476锛屸€?0.697锛孭<0.01)锛涗笌鍐呰剰鎰熻闃堝€煎憟鏄捐憲璐熺浉鍏崇殑鎸囨爣闄BS-SSS澶栵紝杩樻湁HAMA锛孒AMD锛孷SI鍜岃娓匘AO(鍧嘝<0.05)锛汚NF涓庡叾浠栨寚鏍囬棿鏈彂鐜板叧鑱斻€傜粨璁猴細IBS-D鎮ｈ€呭瓨鍦ㄧ簿绁炲績鐞嗗紓甯搞€佸唴鑴忛珮鏁忔劅銆佽偁灞忛殰鍙楁崯鍜屼互鍓氦鎰熺缁忓姛鑳藉紓甯镐负涓荤殑ANF澶辫皟锛屽墠涓夎€呭潎涓庣梾鎯呯▼搴︾浉鍏筹紝鍙兘鍦↖BS-D鐥呯悊鐢熺悊瀛︿腑鍙戞尌浜嗛噸瑕佷綔鐢ㄣ€?.

DOI: 10.11817/j.issn.1672-7347.2017.05.007

PMID: 28626097 [Indexed for MEDLINE]

51. Pak J Med Sci. 2016 Jan-Feb;32(1):116-9. doi: 10.12669/pjms.321.8628.

Post-infectious and non post-infectious irritable bowel syndrome: A comparative

study.

Wang J(1), Lu S(2), Zhao S(3).

Author information:

(1)Dr. Jianbo Wang, Department of Digestion Internal Medicine, The Affiliated

Hospital of Shandong University of, Traditional Chinese medicine, Jinan,

Shandong province, China.

(2)Dr. Shihua Lu, Department of Medical Affairs, The Affiliated Hospital of

Shandong University of, Traditional Chinese medicine, Jinan, Shandong province,

China.

(3)Dr. Shijie Zhao, Department of Digestion Internal Medicine, The Sixth

People's Hospital of Jinan, Jinan, Shandong province, China.

OBJECTIVE: To compare the post-infectious irritable bowel syndrome (PI-IBS) and

none post-infectious irritable bowel syndrome (NPI-IBS) clinically and

experimentally.

METHODS: From May 2013 to January 2015, eighty-nine patients with irritable

bowel syndrome (IBS)were recruited in the internal department of the affiliated

hospital of Shandong University of Traditional Chinese Medicine. The clinical

data were collected for all the patients, and a blood sample was collected to

detect the level of C-reactive protein (CRP) and intestinal fatty acid binding

protein (IFABP), an investigation questionnaire of gastrointestinal symptom

rating scale (GSRS) and self-rating anxiety scale (SAS) were carried out to

evaluate the gastrointestinal function and anxiety status.

RESULTS: In the study, forty-eight patients were included in PI-IBS group and 41

in Non-PI-IBS group. There was no significant difference in age, gender and GSRS

between the two groups (p>0.05). In PI-IBS group 70.8% patients presented with

the primary symptom of diarrhea and 60.4% presented with a SAS scores over 50,

but in Non-PI-IBS group, the values were only 19% (p<0.05) and 34.1% (p<0.05).

The level of IFABP and CRP were significantly higher in PI-IBS group than those

in Non-PI-IBS group (p<0.05).

CONCLUSION: The PI-IBS may be different from Non-PI-IBS in mechanism and should

be treated using different strategies.

DOI: 10.12669/pjms.321.8628

PMCID: PMC4795849

PMID: 27022357

52. Scand J Gastroenterol. 2020 May;55(5):537-542. doi:

10.1080/00365521.2020.1754455. Epub 2020 Apr 24.

Intestinal inflammatory profile shows increase in a diversity of biomarkers in

irritable bowel syndrome.

Berg LK(1)(2), Goll R(2), Fagerli E(1), Ludviksen JK(3)(4), Fure H(3)(4), Moen

OS(2), S酶rbye SW(5), Mollnes TE(3)(4)(6)(7)(8), Florholmen J(2).

Author information:

(1)Department of Medicine, Hospital of Helgeland, Mo i Rana, Norway.

(2)Research Group of Gastroenterology and Nutrition, Institute of Clinical

Medicine, Norwegian Arctic University, Troms酶, Norway.

(3)Research Laboratory, Nordland Hospital, Bod酶, Norway.

(4)K.G. Jebsen TREC, University of Troms酶, Troms酶, Norway.

(5)Clinical Pathology, University Hospital of North Norway, Troms酶, Norway.

(6)Department of Immunology, Oslo University Hospital, Oslo, Norway.

(7)K.G. Jebsen JIRC, University of Oslo, Oslo, Norway.

(8)Centre of Molecular Inflammation Research, Norwegian University of Science

and Technology, Trondheim, Norway.

Background: It has been proposed that irritable bowel syndrome (IBS) is a

low-grade mucosal inflammatory disease.Objective: To characterize the intestinal

inflammatory profile in IBS patients with or without fructose

intolerance.Design: Patients referred to colonoscopy with IBS complaints were

screened for participation. IBS patients diagnosed according to the Rome II

criteria and with no organic gastrointestinal disease were included in the

study. One subgroup was patients included in a fructose-reduced diet study for

2聽months with effects based on VAS symptom scores. Healthy controls were

subjects under investigation of colorectal cancer screening with no IBS or other

gastrointestinal diseases. All patients included had normal histology from

rectum. Mucosal cytokines, chemokines and growth factors were measured by

multiplex technology.Results: Of 27 inflammatory markers tested in the mucosal

tissue, 13 were significantly increased and none was significantly decreased in

IBS as compared to controls. Significantly increased were the proinflammatory

cytokines tumor necrosis factor, the typical TH1 markers IFN纬, IL-1尾, IL-2 and

RANTES, the typical TH2 markers IL-5 and IL-9, the TH17 marker IL-17, TNF, the

pleiotropic IL-15, and the growth factors bFGF and GM-CSF. In IBS patients with

fructose intolerance only IL-5 was significantly increased compared to patients

without fructose intolerance.Conclusions: A dysregulated mucosal inflammatory

profile with an increased level of TH1, TH2 and TH17 markers, and growth factors

were observed in bowel mucosa in of IBS patients when compared to healthy

controls.

DOI: 10.1080/00365521.2020.1754455

PMID: 32329383 [Indexed for MEDLINE]

53. World J Gastroenterol. 2022 Jul 7;28(25):2955-2967. doi:

10.3748/wjg.v28.i25.2955.

Upregulated adenosine 2A receptor accelerates post-infectious irritable bowel

syndrome by promoting CD4+ T cells' T helper 17 polarization.

Dong LW(1), Ma ZC(1), Fu J(1), Huang BL(1), Liu FJ(1), Sun D(2), Lan C(3).

Author information:

(1)Department of Gastroenterology, Hainan General Hospital, Affiliated Hainan

Hospital, Hainan Medical University, Haikou 570311, Hainan Province, China.

(2)Doheny Eye Institute, Department of Ophthalmology, David Geffen School of

Medicine, University of California Los Angeles, Los Angeles, CA 90033, United

States.

(3)Department of Gastroenterology, Hainan General Hospital, Affiliated Hainan

Hospital, Hainan Medical University, Haikou 570311, Hainan Province, China.

lancheng71@163.com.

BACKGROUND: Post-infectious irritable bowel syndrome (PI-IBS) is generally

regarded as a functional disease. Several recent studies have reported the

involvement of low-grade inflammation and immunological dysfunction in PI-IBS. T

helper 17 (Th17) polarization occurs in IBS. Adenosine and its receptors

participate in intestinal inflammation and immune regulation.

AIM: To investigate the role of Th17 polarization of CD4+ T cells regulated by

adenosine 2A receptor (A2AR) in PI-IBS.

METHODS: A PI-IBS model was established by infecting mice with Trichinella

spiralis. The intestinal A2AR and CD4+ T lymphocytes were detected by

immunohistochemistry, and the inflammatory cytokines were detected by

enzyme-linked immunoassay. CD4+ T lymphocytes present in the animal's spleen

were separated and cultured with or without A2AR agonist and antagonist. Western

blotting and real-time quantitative polymerase chain reaction were performed to

determine the effect of A2AR on the cells and intestinal tissue. Cytokine

production was determined. The protein and mRNA levels of A2AR associated

signaling pathway molecules were also evaluated. Furthermore, A2AR agonist and

antagonist were injected into the mouse model and the clinical features were

observed.

RESULTS: The PI-IBS mouse model showed increased expression of ATP and A2AR (P <

0.05), and inhibition of A2AR improved the clinical features in PI-IBS,

including the abdominal withdrawal reflex and colon transportation test (P <

0.05). The number of intestinal CD4+ T cells and interleukin-17 (IL-17) protein

levels increased during PI-IBS, which was reversed by administration of the A2AR

antagonist (P < 0.05). CD4+ T cells expressed A2AR and produced IL-17 in vitro,

which was regulated by the A2AR agonist and antagonist. The A2AR antagonist

increased the production of IL-17 by CD4+ T cells via the Janus kinase-signal

transducer and activator of transcription-receptor-related orphan receptor 纬

signaling pathway.

CONCLUSION: The results of the present study suggested that the upregulation of

A2AR increases PI-IBS by promoting the Th17 polarization of CD4+ T cells.

漏The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights

reserved.

DOI: 10.3748/wjg.v28.i25.2955

PMCID: PMC9280732

PMID: 35978875 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: All the authors

report no relevant conflicts of interest for this article.

54. Gut. 2015 Sep;64(9):1379-88. doi: 10.1136/gutjnl-2013-306236. Epub 2014 Sep 10.

Increased humoral immunity in the jejunum of diarrhoea-predominant irritable

bowel syndrome associated with clinical manifestations.

Vicario M(1), Gonz谩lez-Castro AM(2), Mart铆nez C(3), Lobo B(2), Pigrau M(2),

Guilarte M(4), de Torres I(5), Mosquera JL(6), Fortea M(2), Sevillano-Aguilera

C(2), Salvo-Romero E(2), Alonso C(1), Rodi帽o-Janeiro BK(2), S枚derholm JD(7),

Azpiroz F(1), Santos J(1).

Author information:

(1)Neuro-immuno-gastroenterology Laboratory, Digestive Diseases Research Unit,

Vall d'Hebron Institut de Recerca, Barcelona, Spain Department of

Gastroenterology, Hospital Universitari Vall d'Hebron & Facultat de Medicina,

Universitat Aut貌noma de Barcelona, Barcelona, Spain Centro de Investigaci贸n

Biom茅dica en Red de Enfermedades Hep谩ticas y Digestivas (CIBERehd).

(2)Neuro-immuno-gastroenterology Laboratory, Digestive Diseases Research Unit,

Vall d'Hebron Institut de Recerca, Barcelona, Spain Department of

Gastroenterology, Hospital Universitari Vall d'Hebron & Facultat de Medicina,

Universitat Aut貌noma de Barcelona, Barcelona, Spain.

(3)Department of Human Molecular Genetics, Institute of Human Genetics,

University of Heidelberg, Heidelberg, Germany.

(4)Department of Allergy, Hospital Universitari Vall d'Hebron & Facultat de

Medicina, Universitat Aut貌noma de Barcelona, Barcelona, Spain.

(5)Department of Pathology, Hospital Universitari Vall d'Hebron & Facultat de

Medicina, Universitat Aut貌noma de Barcelona, Barcelona, Spain.

(6)Department of Statistics, University of Barcelona, Barcelona, Spain.

(7)Department of Clinical and Experimental Medicine, Link枚ping University,

Link枚ping, Sweden.

Comment in

Nat Rev Gastroenterol Hepatol. 2014 Nov;11(11):643. doi:

10.1038/nrgastro.2014.169.

BACKGROUND AND AIMS: Altered intestinal barrier is associated with immune

activation and clinical symptoms in diarrhoea-predominant IBS (IBS-D). Increased

mucosal antigen load may induce specific responses; however, local antibody

production and its contribution to IBS aetiopathogenesis remain undefined. This

study evaluated the role of humoral activity in IBS-D.

METHODS: A single mucosal jejunal biopsy, luminal content and blood were

obtained from healthy volunteers (H; n=30) and IBS-D (n=49; Rome III criteria)

participants. Intraepithelial lymphocytes, mast cells, B lymphocytes and plasma

cells were studied by imaging techniques. Differential gene expression and

pathway analysis were assessed by microarray and PCR techniques. Blood and

luminal immunoglobulins (Igs) were quantified. Gastrointestinal symptoms,

respiratory atopy and stress and depression were also recorded.

RESULTS: Patients with IBS-D showed a higher number and activation of mucosal B

lymphocytes and plasma cells (p<0.05). Mast cell density was increased in

patients with IBS-D (non-atopic) and in close proximity to plasma cells

(p<0.05). Microarray profiling identified differential humoral activity in

IBS-D, involving proliferation and activation of B lymphocytes and Igs

production (p<0.001). Mucosal humoral activity was higher in IBS-D, with

upregulation of germline transcripts and Ig genes (1.3-fold-1.7-fold increase;

p<0.05), and increased IgG(+) cells and luminal IgG compared with H (p<0.05),

with no differences in blood. Biological markers of humoral activity correlated

positively with bowel movements, stool form and depression.

CONCLUSIONS: Enhanced small bowel humoral immunity is a distinctive feature of

IBS-D. Mucosal Ig production contributes to local inflammation and clinical

manifestations in IBS-D.

Published by the BMJ Publishing Group Limited. For permission to use (where not

already granted under a licence) please go to

http://group.bmj.com/group/rights-licensing/permissions.

DOI: 10.1136/gutjnl-2013-306236

PMID: 25209656 [Indexed for MEDLINE]

55. Am J Gastroenterol. 2016 Aug;111(8):1165-76. doi: 10.1038/ajg.2016.223. Epub

2016 Jun 7.

Global Cytokine Profiles and Association With Clinical Characteristics in

Patients With Irritable Bowel Syndrome.

Bennet SM(1)(2), Polster A(1), T枚rnblom H(1), Isaksson S(1)(2), Capronnier S(3),

Tessier A(3), Le Nev茅 B(3), Simr茅n M(1)(4), 脰hman L(1)(2)(5).

Author information:

(1)Department of Internal Medicine and Clinical Nutrition, Sahlgrenska Academy,

University of Gothenburg, Gothenburg, Sweden.

(2)Department of Microbiology and Immunology, Sahlgrenska Academy, University of

Gothenburg, Gothenburg, Sweden.

(3)Department of Life Science, Danone Nutricia Research, Palaiseau, France.

(4)Center for Functional GI and Motility Disorders, University of North

Carolina, Chapel Hill, North Carolina, USA.

(5)School of Health and Education, University of Sk枚vde, Sk枚vde, Sweden.

OBJECTIVES: Evidence suggests that patients with irritable bowel syndrome (IBS)

have an altered cytokine profile, although it is unclear whether cytokines are

linked with symptom severity. We aimed to determine whether global serum and

mucosal cytokine profiles differ between IBS patients and healthy subjects and

whether cytokines are associated with IBS symptoms.

METHODS: Serum from 144 IBS patients and 42 healthy subjects was analyzed for

cytokine levels of interleukin (IL)-5, IL-6, IL-8, IL-10, IL-12p70, IL-13,

IL-17A, interferon (IFN)-纬, and tumor necrosis factor (TNF) by MSD MULTI-ARRAY.

In total, 109 IBS and 36 healthy sigmoid colon biopsies were analyzed for mRNA

expression of IL-8, IL-10, TNF, and FOXP3 by quantitative reverse transcription

PCR. Multivariate discrimination analysis evaluated global cytokine profiles.

Rectal sensitivity, oroanal transit time, and psychological and gastrointestinal

symptom severity were also assessed.

RESULTS: Global cytokine profiles of IBS patients and healthy subjects

overlapped, but cytokine levels varied more in IBS patients. Serum levels of

IL-6 and IL-8 tended to be increased and levels of IFN-纬 tended to be decreased

in IBS patients. Mucosal mRNA expression of IL-10 and FOXP3 tended to be

decreased in IBS patients. Within both the full study cohort and IBS patients

alone, serum level of TNF was associated with looser stool pattern, while

subjects with more widespread somatic symptoms had increased serum levels of

IL-6. Although neither IBS bowel habit subgroups nor patients with possible

post-infectious IBS were associated with distinct cytokine profiles, a small

cluster of IBS patients with comparatively elevated immune markers was

identified.

CONCLUSIONS: Global cytokine profiles did not discriminate IBS patients from

healthy subjects, but cytokine profiles were more varied among IBS patients than

among healthy subjects, and a small subgroup of patients with enhanced immune

activity was identified. Also, association of inflammatory cytokines with some

clinical symptoms suggests that immune activation may be of importance in a

subset of IBS patients.

DOI: 10.1038/ajg.2016.223

PMID: 27272011 [Indexed for MEDLINE]

56. Eur J Intern Med. 2024 Jul;125:10-18. doi: 10.1016/j.ejim.2024.03.011. Epub 2024

Mar 11.

Gender-specific insights into the irritable bowel syndrome pathophysiology.

Focus on gut dysbiosis and permeability.

JohnBritto JS(1), Di Ciaula A(1), Noto A(1), Cassano V(2), Sciacqua A(2), Khalil

M(1), Portincasa P(3), Bonfrate L(1).

Author information:

(1)Clinica Medica "A. Murri", Department of Precision and Regenerative Medicine

and Jonian Area (DiMePre-J), University of Bari Aldo Moro, Bari, Italy.

(2)Department of Medical and Surgical Sciences, University "Magna Graecia" of

Catanzaro, 88100 Catanzaro, Italy.

(3)Clinica Medica "A. Murri", Department of Precision and Regenerative Medicine

and Jonian Area (DiMePre-J), University of Bari Aldo Moro, Bari, Italy.

Electronic address: piero.portincasa@uniba.it.

Irritable bowel syndrome (IBS) is the most common functional gastrointestinal

disorder involving the brain-gut interaction. IBS is characterized by persistent

abdominal pain and changes in bowel habits. IBS exerts significant impacts on

quality of life and imposes huge economic costs. Global epidemiological data

reveal variations in IBS prevalence, both globally and between genders,

necessitating comprehensive studies to uncover potential societal and cultural

influences. While the exact pathophysiology of IBS remains incompletely

understood, the mechanism involves a dysregulation of the brain-gut axis,

leading to disturbed intestinal motility, local inflammation, altered intestinal

permeability, visceral sensitivity, and gut microbiota composition. We reviewed

several gender-related pathophysiological aspects of IBS pathophysiology, by

focusing on gut dysbiosis and intestinal permeability. This perspective paves

the way to personalized and multidimensional clinical management of individuals

with IBS.

Copyright 漏 2024 European Federation of Internal Medicine. Published by Elsevier

B.V. All rights reserved.

DOI: 10.1016/j.ejim.2024.03.011

PMID: 38467533 [Indexed for MEDLINE]

Conflict of interest statement: Declaration of competing interest The authors

report no conflicts of interest. The authors alone are responsible for the

content and writing of the paper.

57. Gastroenterol Hepatol. 2022 Jan;45(1):66-76. doi:

10.1016/j.gastrohep.2021.02.022. Epub 2021 May 21.

Irritable bowel syndrome in inflammatory bowel disease. Synergy in alterations

of the gut-brain axis?

[Article in English, Spanish]

P茅rez de Arce E(1), Quera R(2), Beltr谩n CJ(3), Madrid AM(4), Nos P(5).

Author information:

(1)Departamento de Medicina Interna, Servicio de Gastroenterolog铆a, Hospital

Cl铆nico Universidad de Chile, Santiago, Chile. Electronic address:

eperezdearce@hcuch.cl.

(2)Programa Enfermedad Inflamatoria Intestinal, Departamento de

Gastroenterolog铆a, Cl铆nica Universidad de los Andes, Santiago, Chile.

(3)Laboratorio de Inmuno-gastroenterolog铆a, Servicio de Gastroenterolog铆a,

Hospital Cl铆nico Universidad de Chile, Santiago, Chile.

(4)Departamento de Medicina Interna, Servicio de Gastroenterolog铆a, Hospital

Cl铆nico Universidad de Chile, Santiago, Chile.

(5)Unidad de Enfermedad Inflamatoria Intestinal, Servicio de Medicina Digestiva,

Hospital Universitari i Polit猫cnic La Fe, Valencia, Espa帽a.

The presence of digestive symptoms associated with irritable bowel syndrome

(IBS) in patients with inflammatory bowel disease (IBD) in remission is a topic

of growing interest. Although there is heterogeneity in clinical studies

regarding the use of IBD remission criteria and the diagnosis of IBS, the

available data indicate that the IBD-IBS overlap would affect up to one third of

patients in remission, and they agree on the finding of a negative impact on the

mental health and quality of life of the individuals who suffer from it. The

pathophysiological bases that would explain this potential overlap are not

completely elucidated; however, an alteration in the gut-brain axis associated

with an increase in intestinal permeability, neuroimmune activation and

dysbiosis would be common to both conditions. The hypothesis of a new clinical

entity or syndrome of "Irritable Inflammatory Bowel Disease" or

"Post-inflammatory IBS" is the subject of intense investigation. The clinical

approach is based on certifying the remission of IBD activity and ruling out

other non-inflammatory causes of potentially treatable persistent functional

digestive symptoms. In the case of symptoms associated with IBS and in the

absence of sufficient evidence, comprehensive and personalized management of the

clinical picture (dietary, pharmacological and psychotherapeutic measures)

should be carried out, similar to a genuine IBS.

Copyright 漏 2021 Elsevier Espa帽a, S.L.U. All rights reserved.

DOI: 10.1016/j.gastrohep.2021.02.022

PMID: 34023477 [Indexed for MEDLINE]

58. Aliment Pharmacol Ther. 2017 Sep;46(5):529-539. doi: 10.1111/apt.14207. Epub

2017 Jul 3.

Mixture model analysis identifies irritable bowel syndrome subgroups

characterised by specific profiles of gastrointestinal, extraintestinal somatic

and psychological symptoms.

Polster A(1), Van Oudenhove L(2), Jones M(3), 脰hman L(4), T枚rnblom H(1), Simr茅n

M(1)(5).

Author information:

(1)Department of Internal Medicine and Clinical Nutrition, Institute of

Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

(2)Translational Research Center for Gastrointestinal Disorders (TARGID),

University of Leuven, Leuven, Belgium.

(3)Psychology Department, Faculty of Human Sciences, Macquarie University, North

Ryde, NSW, Australia.

(4)Department of Microbiology and Immunology, Sahlgrenska Academy, University of

Gothenburg, Gothenburg, Sweden.

(5)Center for Functional Gastrointestinal and Motility Disorders, University of

North Carolina at Chapel Hill, Chapel Hill, NC, USA.

Erratum in

Aliment Pharmacol Ther. 2018 Apr;47(7):1049. doi: 10.1111/apt.14556.

Comment in

Aliment Pharmacol Ther. 2017 Oct;46(7):698-699. doi: 10.1111/apt.14260.

Aliment Pharmacol Ther. 2017 Oct;46(7):697. doi: 10.1111/apt.14238.

BACKGROUND: Current subgrouping of Irritable Bowel Syndrome (IBS) is exclusively

based on stool consistency without considering other relevant gastrointestinal

(GI), extraintestinal somatic or psychological features.

AIM: To identify subgroups based on a comprehensive set of IBS-related

parameters.

METHODS: Mixture model analysis was used, with the following input variables: 13

single-item scores from the IBS-specific Gastrointestinal Symptom Rating Scale,

average stool consistency and frequency from a 7-day Bristol Stool Form diary,

12 single-item extraintestinal symptom scores from the Patient Health

Questionnaire-12, and anxiety and depression subscale scores from the Hospital

Anxiety and Depression scale. The resulting latent subgroups were compared

regarding symptom profiles using analysis of variance followed by pair-wise

comparisons.

RESULTS: One hundred and seventy-two IBS patients (Rome III; 69% female; mean

age 33.7 [range 18-60] years) were included. The optimal subgrouping showed six

latent groups, characterised by: (I) constipation with low comorbidities, (II)

constipation with high comorbidities, (III) diarrhoea with low comorbidities,

(IV) diarrhoea and pain with high comorbidities, (V) mixed GI symptoms with high

comorbidities, (VI) a mix of symptoms with overall mild severity. The subgroups

showed differences in the distribution of Rome III-subtypes, IBS severity,

presence of anxiety and depression, and gender, but not regarding age, IBS

duration or reported post-infectious onset of IBS.

CONCLUSIONS: This model-based subgrouping of IBS partly supports the distinction

of subgroups based on bowel habits, but additionally distinguishes subgroups

with or without co-morbid extraintestinal somatic and psychological symptoms.

The resulting groups show specific profiles of symptom combinations.

漏 2017 John Wiley & Sons Ltd.

DOI: 10.1111/apt.14207

PMID: 28671338 [Indexed for MEDLINE]

59. mSystems. 2024 Mar 19;9(3):e0129923. doi: 10.1128/msystems.01299-23. Epub 2024

Feb 8.

The function of the gut microbiota-bile acid-TGR5 axis in diarrhea-predominant

irritable bowel syndrome.

Zhan K(1), Wu H(2)(3)(4), Xu Y(5), Rao K(2), Zheng H(2)(3)(4), Qin S(2)(3)(4),

Yang Y(1), Jia R(2), Chen W(2), Huang S(2)(3)(4)(6).

Author information:

(1)Dongguan Hospital of Guangzhou University of Chinese Medicine, Dongguan,

China.

(2)The Second Clinical College of Guangzhou University of Chinese Medicine,

Guangzhou, China.

(3)State Key Laboratory of Dampness Syndrome of Chinese Medicine, The Second

Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou,

China.

(4)Collaborative Innovation Team of Traditional Chinese Medicine in Prevention

and Treatment of Functional Gastrointestinal Diseases, Guangzhou University of

Chinese Medicine, Guangzhou, China.

(5)Science and Technology Innovation Center, Guangzhou University of Chinese

Medicine, Guangzhou, China.

(6)The First School of Clinical Medicine, Guangzhou University of Chinese

Medicine, Guangzhou, China.

Imbalanced gut microbiota (GM) and abnormal fecal bile acid (BA) are thought to

be the key factors for diarrhea-predominant irritable bowel syndrome (IBS-D),

but the underlying mechanism remains unclear. Herein, we explore the influence

of the GM-BA-Takeda G-protein-coupled receptor 5 (TGR5) axis on IBS-D.

Twenty-five IBS-D patients and fifteen healthy controls were recruited to

perform BA-related metabolic and metagenomic analyses. Further, the

microbiota-humanized IBS-D rat model was established by fecal microbial

transplantation (FMT) to investigate the GM-BA-TGR5 axis effects on the colonic

barrier and visceral hypersensitivity (VH) in IBS-D. Finally, we used

chenodeoxycholic acid (CDCA), an important BA screened out by metabolome, to

evaluate whether it affected diarrhea and VH via the TGR5 pathway. Clinical

research showed that GM associated with bile salt hydrolase (BSH) activity such

as Bacteroides ovatus was markedly reduced in the GM of IBS-D, accompanied by

elevated total and primary BA levels. Moreover, we found that CDCA not only was

increased as the most important primary BA in IBS-D patients but also could

induce VH through upregulating TGR5 in the colon and ileum of normal rats. TGR5

inhibitor could reverse the phenotype, depression-like behaviors, pathological

change, and level of fecal BSH in a microbiota-humanized IBS-D rat model. Our

findings proved that human-associated FMT could successfully induce the IBS-D

rat model, and the imbalanced GM-BA-TGR5 axis may promote colonic mucosal

barrier dysfunction and enhance VH in IBS-D.

IMPORTANCE: Visceral hypersensitivity and intestinal mucosal barrier damage are

important factors that cause abnormal brain-gut interaction in

diarrhea-predominant irritable bowel syndrome (IBS-D). Recently, it was found

that the imbalance of the gut microbiota-bile acid axis is closely related to

them. Therefore, understanding the structure and function of the gut microbiota

and bile acids and the underlying mechanisms by which they shape visceral

hypersensitivity and mucosal barrier damage in IBS-D is critical. An examination

of intestinal feces from IBS-D patients revealed that alterations in gut

microbiota and bile acid metabolism underlie IBS-D and symptom onset. We also

expanded beyond existing knowledge of well-studied gut microbiota and bile acid

and found that Bacteroides ovatus and chenodeoxycholic acid may be potential

bacteria and bile acid involved in the pathogenesis of IBS-D. Moreover, our data

integration reveals the influence of the microbiota-bile acid-TGR5 axis on

barrier function and visceral hypersensitivity.

DOI: 10.1128/msystems.01299-23

PMCID: PMC10949424

PMID: 38329942 [Indexed for MEDLINE]

Conflict of interest statement: The authors declare no conflict of interest.

60. Gastroenterology. 2017 Oct;153(4):1026-1039. doi: 10.1053/j.gastro.2017.06.004.

Epub 2017 Jun 15.

Intestinal Fungal Dysbiosis Is Associated With Visceral Hypersensitivity in

Patients With Irritable Bowel Syndrome and Rats.

Botschuijver S(1), Roeselers G(2), Levin E(2), Jonkers DM(3), Welting O(1),

Heinsbroek SEM(1), de Weerd HH(2), Boekhout T(4), Fornai M(5), Masclee AA(3),

Schuren FHJ(2), de Jonge WJ(1), Seppen J(1), van den Wijngaard RM(6).

Author information:

(1)Tytgat Institute for Liver and Intestinal Research, Department of

Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The

Netherlands.

(2)Microbiology and Systems Biology, The Netherlands Organization for Applied

Scientific Research (TNO), Zeist, The Netherlands.

(3)Division Gastroenterology-Hepatology, Department of Internal Medicine, NUTRIM

School for Nutrition, and Translational Research in Metabolism, Maastricht

University Medical Center, Maastricht, The Netherlands.

(4)Westerdijk Fungal Biodiversity Institute, Utrecht, The Netherlands; Institute

for Biodiversity and Ecosystems Dynamics (IBED), University of Amsterdam,

Amsterdam, The Netherlands.

(5)Tytgat Institute for Liver and Intestinal Research, Department of

Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The

Netherlands; Division of Pharmacology, Department of Clinical & Experimental

Medicine, University of Pisa, Pisa, Italy.

(6)Tytgat Institute for Liver and Intestinal Research, Department of

Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The

Netherlands. Electronic address: R.vandenWijngaard@AMC.UVA.NL.

BACKGROUND & AIMS: Visceral hypersensitivity is one feature of irritable bowel

syndrome (IBS). Bacterial dysbiosis might be involved in the activation of

nociceptive sensory pathways, but there have been few studies of the role of the

mycobiome (the fungal microbiome) in the development of IBS. We analyzed

intestinal mycobiomes of patients with IBS and a rat model of visceral

hypersensitivity.

METHODS: We used internal transcribed spacer 1-based metabarcoding to compare

fecal mycobiomes of 18 healthy volunteers with those of 39 patients with IBS

(with visceral hypersensitivity or normal levels of sensitivity). We also

compared the mycobiomes of Long-Evans rats separated from their mothers

(hypersensitive) with non-handled (normally sensitive) rats. We investigated

whether fungi can cause visceral hypersensitivity using rats exposed to

fungicide (fluconazole and nystatin). The functional relevance of the gut

mycobiome was confirmed in fecal transplantation experiments: adult maternally

separated rats were subjected to water avoidance stress (to induce visceral

hypersensitivity), then given fungicide and donor cecum content via oral gavage.

Other rats subjected to water avoidance stress were given soluble 尾-glucans,

which antagonize C-type lectin domain family 7 member A (CLEC7A or DECTIN1)

signaling via spleen-associated tyrosine kinase (SYK), a SYK inhibitor to reduce

visceral hypersensitivity, or vehicle (control). The sensitivity of mast cells

to fungi was tested with mesenteric windows (ex聽vivo) and the human mast cell

line HMC-1.

RESULTS: 伪 diversity (Shannon index) and mycobiome signature (stability

selection) of both groups of IBS patients differed from healthy volunteers, and

the mycobiome signature of hypersensitive patients differed from that of

normally sensitive patients. We observed mycobiome dysbiosis in rats that had

been separated from their mothers compared with non-handled rats. Administration

of fungicide to hypersensitive rats reduced their visceral hypersensitivity to

normal levels of sensitivity. Administration of cecal mycobiomes from rats that

had been separated from their mothers (but not non-handled mycobiome) restored

hypersensitivity to distension. Administration of soluble 尾-glucans or a SYK

inhibitor reduced visceral hypersensitivity, compared with controls. Particulate

尾-glucan (a DECTIN-1 agonist) induced mast cell degranulation in mesenteric

windows and HMC-1 cells responded to fungal antigens by release of histamine.

CONCLUSIONS: In an analysis of patients with IBS and controls, we associated

fungal dysbiosis with IBS. In studies of rats, we found fungi to promote

visceral hypersensitivity, which could be reduced by administration of

fungicides, soluble 尾-glucans, or a SYK inhibitor. The intestinal fungi might

therefore be manipulated for treatment of IBS-related visceral hypersensitivity.

Copyright 漏 2017 AGA Institute. Published by Elsevier Inc. All rights reserved.

DOI: 10.1053/j.gastro.2017.06.004

PMID: 28624575 [Indexed for MEDLINE]

61. BMC Gastroenterol. 2017 Apr 14;17(1):53. doi: 10.1186/s12876-017-0605-x.

Lactobacillus casei DG and its postbiotic reduce the inflammatory mucosal

response: an ex-vivo organ culture model of post-infectious irritable bowel

syndrome.

Compare D(1), Rocco A(1), Coccoli P(1), Angrisani D(1), Sgamato C(1), Iovine

B(1), Salvatore U(1), Nardone G(2).

Author information:

(1)Department of Clinical Medicine and Surgery, Gastroenterology Unit,

University Federico II of Naples, Via S. Pansini 5, 80131, Naples, Italy.

(2)Department of Clinical Medicine and Surgery, Gastroenterology Unit,

University Federico II of Naples, Via S. Pansini 5, 80131, Naples, Italy.

nardone@unina.it.

BACKGROUND: The evidence on the role of gut microbiota in post-infectious

irritable bowel syndrome (PI-IBS) is convincing. Lactobacillus spp. positively

affect IBS symptoms, although the mechanisms through which probiotics exert

their beneficial effects are largely unknown. The aim of the study is to

evaluate the role of Lactobacillus casei DG (LC-DG) and its postbiotic (PB) in

modulating the inflammatory/immune-response in PI-IBS in an ex-vivo organ

culture model.

METHODS: Ex vivo cultures of ileal and colonic mucosa from 10 PI-IBS, diarrhea

predominant subtype (D) patients, and 10 healthy controls (HC) were treated with

LPS, LC-DG and PB. Interleukin (IL)-1伪, IL-6, IL-8 and IL-10 mRNA levels were

assessed by real-time PCR and Toll like receptor 4 (TLR-4) protein expression by

Western blotting.

RESULTS: At baseline, IL-1伪, IL-6 and IL-8 mRNA levels as well as TLR-4 protein

expression were significantly higher while IL-10 mRNA levels were lower in

PI-IBS D than in HC in both ileum and colon. LC-DG and PB significantly reduced

the mRNA levels of pro-inflammatory cytokines and TLR-4 while increased that of

IL-10 after LPS stimulation. The protective effect was more pronounced for PB

than LC-DG treatment.

CONCLUSION: LC-DG and its PB attenuate the inflammatory mucosal response in an

ex-vivo organ culture model of PI-IBS D.

DOI: 10.1186/s12876-017-0605-x

PMCID: PMC5391611

PMID: 28410580 [Indexed for MEDLINE]

62. World J Gastroenterol. 2024 Apr 28;30(16):2258-2271. doi:

10.3748/wjg.v30.i16.2258.

Chitin-glucan improves important pathophysiological features of irritable bowel

syndrome.

Valibouze C(1), Dubuquoy C(2), Chavatte P(3), Genin M(4), Maquet V(5), Modica

S(5), Desreumaux P(6), Rousseaux C(7).

Author information:

(1)Department of Digestive Surgery and Transplantation, Lille University, Lille

59037, France.

(2)Intestinal Biotech Development, Facult茅 de M茅dicine, Lille 59045, France.

(3)U1286-INFINITE-Institute for Translational Research in Inflammation,

Universit茅 de Lille, Lille 59000, France.

(4)ULR 2694-METRICS, 脡valuation des Technologies de sant茅 et des Pratiques

M茅dicales, University of Lille, Lille 59000, France.

(5)KitoZyme SA, Institution Soci茅t茅 Anonyme, Zone 2, Parc des Hauts Sarts, Rue

de Milmort, Herstal 4040, Belgium.

(6)Hepato-Gastroenterology Department, Lille University Hospital, Lille 59037,

France.

(7)Intestinal Biotech Development, Facult茅 de M茅dicine, Lille 59045, France.

crousseaux@ibd-biotech.com.

BACKGROUND: Irritable bowel syndrome (IBS) is one of the most frequent and

debilitating conditions leading to gastroenterological referrals. However,

recommended treatments remain limited, yielding only limited therapeutic gains.

Chitin-glucan (CG) is a novel dietary prebiotic classically used in humans at a

dosage of 1.5-3.0 g/d and is considered a safe food ingredient by the European

Food Safety Authority. To provide an alternative approach to managing patients

with IBS, we performed preclinical molecular, cellular, and animal studies to

evaluate the role of chitin-glucan in the main pathophysiological mechanisms

involved in IBS.

AIM: To evaluate the roles of CG in visceral analgesia, intestinal inflammation,

barrier function, and to develop computational molecular models.

METHODS: Visceral pain was recorded through colorectal distension (CRD) in a

model of long-lasting colon hypersensitivity induced by an intra-rectal

administration of TNBS [15 milligrams (mg)/kilogram (kg)] in 33 Sprague-Dawley

rats. Intracolonic pressure was regularly assessed during the 9 wk-experiment

(weeks 0, 3, 5, and 7) in animals receiving CG (n = 14) at a human equivalent

dose (HED) of 1.5 g/d or 3.0 g/d and compared to negative control (tap water, n

= 11) and positive control (phloroglucinol at 1.5 g/d HED, n = 8) groups. The

anti-inflammatory effect of CG was evaluated using clinical and histological

scores in 30 C57bl6 male mice with colitis induced by dextran sodium sulfate

(DSS) administered in their drinking water during 14 d. HT-29 cells under basal

conditions and after stimulation with lipopolysaccharide (LPS) were treated with

CG to evaluate changes in pathways related to analgesia (碌-opioid receptor

(MOR), cannabinoid receptor 2 (CB2), peroxisome proliferator-activated receptor

alpha, inflammation [interleukin (IL)-10, IL-1b, and IL-8] and barrier function

[mucin 2-5AC, claudin-2, zonula occludens (ZO)-1, ZO-2] using the real-time PCR

method. Molecular modelling of CG, LPS, lipoteichoic acid (LTA), and

phospholipomannan (PLM) was developed, and the ability of CG to chelate

microbial pathogenic lipids was evaluated by docking and molecular dynamics

simulations. Data were expressed as the mean 卤 SEM.

RESULTS: Daily CG orally-administered to rats or mice was well tolerated without

including diarrhea, visceral hypersensitivity, or inflammation, as evaluated at

histological and molecular levels. In a model of CRD, CG at a dosage of 3 g/d

HED significantly decreased visceral pain perception by 14% after 2 wk of

administration (P < 0.01) and reduced inflammation intensity by 50%, resulting

in complete regeneration of the colonic mucosa in mice with DSS-induced colitis.

To better reproduce the characteristics of visceral pain in patients with IBS,

we then measured the therapeutic impact of CG in rats with TNBS-induced

inflammation to long-lasting visceral hypersensitivity. CG at a dosage of 1.5

g/d HED decreased visceral pain perception by 20% five weeks after colitis

induction (P < 0.01). When the CG dosage was increased to 3.0 g/d HED, this

analgesic effect surpassed that of the spasmolytic agent phloroglucinol,

manifesting more rapidly within 3 wk and leading to a 50% inhibition of pain

perception (P < 0.0001). The underlying molecular mechanisms contributing to

these analgesic and anti-inflammatory effects of CG involved, at least in part,

a significant induction of MOR, CB2 receptor, and IL-10, as well as a

significant decrease in pro-inflammatory cytokines IL-1b and IL-8. CG also

significantly upregulated barrier-related genes including muc5AC, claudin-2, and

ZO-2. Molecular modelling of CG revealed a new property of the molecule as a

chelator of microbial pathogenic lipids, sequestering gram-negative LPS and

gram-positive LTA bacterial toxins, as well as PLM in fungi at the lowesr energy

conformations.

CONCLUSION: CG decreased visceral perception and intestinal inflammation through

master gene regulation and direct binding of microbial products, suggesting that

CG may constitute a new therapeutic strategy for patients with IBS or IBS-like

symptoms.

漏The Author(s) 2024. Published by Baishideng Publishing Group Inc. All rights

reserved.

DOI: 10.3748/wjg.v30.i16.2258

PMCID: PMC11056916

PMID: 38690023 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: Desreumaux

reports personal fees from Abbvie, personal fees from Abbott, personal fees from

Amgen, personal fees from Biocodex, personal fees from Biofortis, personal fees

from Biogen, personal fees from Biokuris, personal fees from Dr Falk, personal

fees from Ferring, personal fees from Galapagos, personal fees from Fresenius,

personal fees from Janssen, personal fees from Intestinal Biotech Development,

personal fees from Kitozyme, personal fees from Lesaffre, personal fees from

MSD, personal fees from Norgine, personal fees from Pfizer, personal fees from

Sandoz, personal fees from Shire, personal fees from Takeda, personal fees from

Tillotts, and personal fees from UCB outside the submitted work; Dr. Desreumaux

has issued a patent (WO2009103884) issued; Christel Rousseaux is Chief Executive

Officer at Intestinal Biotech Development; Veronique Maquet is a Product

Development Manager at Kitozyme; Salvatore Modica is Chief Operating Officer at

Biokuris, a spin-off company of Kitozyme; The other authors have nothing to

disclose.

63. United European Gastroenterol J. 2019 Jun;7(5):709-715. doi:

10.1177/2050640619826419. Epub 2019 Jan 19.

Serum zonulin is elevated in IBS and correlates with stool frequency in IBS-D.

Singh P(1), Silvester J(1)(2), Chen X(1), Xu H(1), Sawhney V(1), Rangan V(1),

Iturrino J(1), Nee J(1), Duerksen DR(3), Lembo A(1).

Author information:

(1)Division of Gastroenterology, Department of Medicine, Beth Israel Deaconess

Medical Center, Boston, United States of America.

(2)Division of Gastroenterology, Hepatology and Nutrition, Boston Children's

Hospital, Boston, United States of America.

(3)Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Canada.

BACKGROUND: Studies have shown increased intestinal permeability in irritable

bowel syndrome. Validating serum biomarkers for altered intestinal permeability

in irritable bowel syndrome will facilitate research and pathophysiology-based

therapy.

OBJECTIVE: To measure serum zonulin and intestinal fatty acid binding protein

levels in diarrhea-predominant irritable bowel syndrome and

constipation-predominant irritable bowel syndrome and compare with healthy

controls and celiac disease.

METHODS: Serum zonulin and intestinal fatty acid binding protein levels were

measured using enzyme-linked immunosorbent assays in constipation-predominant

irritable bowel syndrome (n鈥?=鈥?50), diarrhea-predominant irritable bowel syndrome

(n鈥?=鈥?50), celiac disease (n鈥?=鈥?53) and healthy controls (n鈥?=鈥?42). Irritable bowel

syndrome symptom severity was measured using the irritable bowel

syndrome-symptom severity scale.

RESULTS: Patients with constipation-predominant irritable bowel syndrome and

diarrhea-predominant irritable bowel syndrome had higher zonulin levels compared

with healthy controls (p鈥?=鈥?0.006 and 0.009 respectively), which was comparable

to those with active celiac disease. Although zonulin levels did not correlate

with the overall irritable bowel syndrome symptom severity scale, it positively

correlated with stool frequency per week (p鈥?=鈥?0.03) and dissatisfaction with

bowel habits (p鈥?=鈥?0.007) in diarrhea-predominant irritable bowel syndrome.

Patients with diarrhea-predominant irritable bowel syndrome and

constipation-predominant irritable bowel syndrome had lower intestinal fatty

acid binding protein levels compared with celiac patients (p鈥?=鈥?0.005 and

p鈥?=鈥?0.047 respectively).

CONCLUSION: Serum zonulin is upregulated in irritable bowel syndrome and the

levels are comparable to those in celiac disease. Zonulin levels correlated with

severity of bowel habits in diarrhea-predominant irritable bowel syndrome.

Intestinal fatty acid binding protein levels in irritable bowel syndrome

patients were not increased suggesting no significant increase in enterocyte

death.

DOI: 10.1177/2050640619826419

PMCID: PMC6545708

PMID: 31210949 [Indexed for MEDLINE]

64. Neurogastroenterol Motil. 2016 Apr;28(4):463-86. doi: 10.1111/nmo.12717. Epub

2015 Nov 11.

The joint power of sex and stress to modulate brain-gut-microbiota axis and

intestinal barrier homeostasis: implications for irritable bowel syndrome.

Pigrau M(1)(2), Rodi帽o-Janeiro BK(2), Casado-Bedmar M(2), Lobo B(2), Vicario

M(2)(3), Santos J(2)(3), Alonso-Cotoner C(2)(3).

Author information:

(1)Farncombe Family Digestive Health Research Institute, McMaster University,

Hamilton, ON, Canada.

(2)Laboratory of Neuro-immuno-gastroenterology, Digestive Diseases Research

Unit. Vall d'Hebron Institut de Recerca, Department of Gastroenterology,

Hospital Universitario Vall d'Hebron & Facultat de Medicina, Universitat

Aut貌noma de Barcelona, Barcelona, Spain.

(3)Centro de Investigaci贸n Biom茅dica en Red de Enfermedades Hep谩ticas y

Digestivas (CIBERehd), Madrid, Spain.

BACKGROUND: Intestinal homeostasis is a dynamic process that takes place at the

interface between the lumen and the mucosa of the gastrointestinal tract, where

a constant scrutiny for antigens and toxins derived from food and microorganisms

is carried out by the vast gut-associated immune system. Intestinal homeostasis

is preserved by the ability of the mucus layer and the mucosal barrier to keep

the passage of small-sized and antigenic molecules across the epithelium highly

selective. When combined and preserved, immune surveillance and barrier's

selective permeability, the host capacity of preventing the development of

intestinal inflammation is optimized, and viceversa. In addition, the

brain-gut-microbiome axis, a multidirectional communication system that

integrates distant and local regulatory networks through neural, immunological,

metabolic, and hormonal signaling pathways, also regulates intestinal function.

Dysfunction of the brain-gut-microbiome axis may induce the loss of gut mucosal

homeostasis, leading to uncontrolled permeation of toxins and immunogenic

particles, increasing the risk of appearance of intestinal inflammation, mucosal

damage, and gut disorders. Irritable bowel syndrome is prevalent

stress-sensitive gastrointestinal disorder that shows a female predominance.

Interestingly, the role of stress, sex and gonadal hormones in the regulation of

intestinal mucosal and the brain-gut-microbiome axis functioning is being

increasingly recognized.

PURPOSE: We aim to critically review the evidence linking sex, and stress to

intestinal barrier and brain-gut-microbiome axis dysfunction and the

implications for irritable bowel syndrome.

漏 2015 John Wiley & Sons Ltd.

DOI: 10.1111/nmo.12717

PMID: 26556786 [Indexed for MEDLINE]

65. J Gastroenterol Hepatol. 2018 Feb;33(2):443-452. doi: 10.1111/jgh.13841.

Beneficial effects of Rifaximin in post-infectious irritable bowel syndrome

mouse model beyond gut microbiota.

Jin Y(1), Ren X(2), Li G(1), Li Y(1), Zhang L(1), Wang H(1), Qian W(1), Hou

X(1).

Author information:

(1)Division of Gastroenterology, Union Hospital, Tongji Medical College,

Huazhong University of Science and Technology, Wuhan, China.

(2)The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China.

BACKGROUND AND AIMS: Rifaximin is a minimally absorbed antibiotic, which has

shown efficacy in irritable bowel syndrome (IBS) patients. However, the

mechanism on how it effects in IBS is still incompletely defined. In this study,

Trichinella spiralis-infected post-infectious (PI) IBS mouse model was used, to

assess the action of rifaximin on visceral hypersensitivity, barrier function,

gut inflammation, and microbiota.

METHODS: Post-infectious IBS model was established by T.聽spiralis infection in

mice. Rifaximin were administered to PI-IBS mice for seven consecutive days. The

abdominal withdrawal reflex and threshold of colorectal distention were employed

to evaluate visceral sensitivity. Smooth muscle contractile response was

recorded in the organ bath. Intestinal permeability was measured by Ussing

chamber. Expression of tight junction protein and cytokines were measured by

Western blotting. Ilumina miseq platform was used to analyze bacterial 16S

ribosomal RNA.

RESULTS: Post-infectious IBS mice treated with rifaximin exhibited decreased

abdominal withdrawal reflex score, increased threshold, reduced contractile

response, and intestinal permeability. Rifaximin also suppressed the expression

of interleukin-12 and interleukin-17 and promoted the expression of the major

tight junction protein occludin. Furthermore, rifaximin did not change the

composition and diversity, and the study reavealed that rifaximin had a tiny

effect on the relative abundance of Lactobacillus and Bifidobacterium in this

PI-IBS model.

CONCLUSIONS: Rifaximin alleviated visceral hypersensitivity, recovered

intestinal barrier function, and inhibited low-grade inflammation in colon and

ileum of PI-IBS mouse model. Moreover, rifaximin exerts anti-inflammatory

effects with only a minimal effect on the overall composition and diversity of

the gut microbiota in this model.

漏 2017 Journal of Gastroenterology and Hepatology Foundation and John Wiley &

Sons Australia, Ltd.

DOI: 10.1111/jgh.13841

PMID: 28573746 [Indexed for MEDLINE]

66. Int J Parasitol. 2017 May;47(6):311-326. doi: 10.1016/j.ijpara.2016.11.010. Epub

2017 Feb 22.

Giardia duodenalis induces pathogenic dysbiosis of human intestinal microbiota

biofilms.

Beatty JK(1), Akierman SV(1), Motta JP(2), Muise S(1), Workentine ML(1),

Harrison JJ(1), Bhargava A(1), Beck PL(3), Rioux KP(3), McKnight GW(4), Wallace

JL(5), Buret AG(6).

Author information:

(1)Department of Biological Sciences, University of Calgary, 2500 University

Drive NW, Calgary, Alberta T2N 4N1, Canada.

(2)Department of Biological Sciences, University of Calgary, 2500 University

Drive NW, Calgary, Alberta T2N 4N1, Canada; Department of Physiology &

Pharmacology, University of Calgary, 3330 Hospital Drive NW, Calgary, Alberta

T2N 4N1, Canada.

(3)Department of Medicine, Division of Gastroenterology, University of Calgary,

3330 Hospital Drive NW, Calgary, Alberta T2N 4N1, Canada.

(4)Department of Medicine, McMaster University, 1280 Main Street West, Hamilton,

Ontario L8S 4K1, Canada.

(5)Department of Physiology & Pharmacology, University of Calgary, 3330 Hospital

Drive NW, Calgary, Alberta T2N 4N1, Canada.

(6)Department of Biological Sciences, University of Calgary, 2500 University

Drive NW, Calgary, Alberta T2N 4N1, Canada; Department of Physiology &

Pharmacology, University of Calgary, 3330 Hospital Drive NW, Calgary, Alberta

T2N 4N1, Canada. Electronic address: aburet@ucalgary.ca.

Giardia duodenalis is a prevalent cause of acute diarrheal disease worldwide.

However, recent outbreaks in Italy and Norway have revealed a link between

giardiasis and the subsequent development of chronic post-infectious irritable

bowel syndrome. While the mechanisms underlying the causation of post-infectious

irritable bowel syndrome remain obscure, recent findings suggest that

alterations in gut microbiota communities are linked to the pathophysiology of

irritable bowel syndrome. In the present study, we use a laboratory biofilm

system to culture and enrich mucosal microbiota from human intestinal biopsies.

Subsequently, we show that co-culture with Giardia induces disturbances in

biofilm species composition and biofilm structure resulting in microbiota

communities that are intrinsically dysbiotic - even after the clearance of

Giardia. These microbiota abnormalities were mediated in part by

secretory-excretory Giardia cysteine proteases. Using in vitro cell culture and

germ-free murine infection models, we show that Giardia-induced disruptions of

microbiota promote bacterial invasion, resulting in epithelial apoptosis, tight

junctional disruption, and bacterial translocation across an intestinal

epithelial barrier. Additionally, these dysbiotic microbiota communities

resulted in increased activation of the Toll-like receptor 4 signalling pathway,

and overproduction of the pro-inflammatory cytokine IL-1beta in humanized

germ-free mice. Previous studies that have sought explanations and risk factors

for the development of post-infectious irritable bowel syndrome have focused on

features of enteropathogens and attributes of the infected host. We propose that

polymicrobial interactions involving Giardia and gut microbiota may cause

persistent dysbiosis, offering a new interpretation of the reasons why those

afflicted with giardiasis are predisposed to gastrointestinal disorders

post-infection.

Copyright 漏 2017 The Author(s). Published by Elsevier Ltd.. All rights reserved.

DOI: 10.1016/j.ijpara.2016.11.010

PMID: 28237889 [Indexed for MEDLINE]

67. Lancet Gastroenterol Hepatol. 2016 Oct;1(2):133-146. doi:

10.1016/S2468-1253(16)30023-1. Epub 2016 Sep 8.

Pathophysiology of irritable bowel syndrome.

Holtmann GJ(1), Ford AC(2), Talley NJ(3).

Author information:

(1)Department of Gastroenterology and Hepatology, Princess Alexandra Hospital

Brisbane, and Translational Research Institute, University of Queensland,

Brisbane, QLD, Australia.

(2)Leeds Gastroenterology Institute, St James's University Hospital, Leeds, UK;

Leeds Institute of Biomedical and Clinical Sciences, University of Leeds, Leeds,

UK.

(3)Faculty of Health and Medicine, University of Newcastle, NSW, Australia;

Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN, USA.

Electronic address: nicholas.talley@newcastle.edu.au.

Traditionally, irritable bowel syndrome has been considered to be a disorder

with no known underlying structural or biochemical explanation, but this concept

is likely to be outdated. In this Review we challenge the widely accepted view

that irritable bowel syndrome is an unexplained brain-gut disorder. There is

epidemiological evidence that, in a major subset of patients, gastrointestinal

symptoms arise first and only later do incident mood disorders occur.

Additionally, possible mechanisms for gut-brain dysfunction have been

identified, suggesting primary gut disturbances might be the underlying cause in

a subgroup. Underlying mechanisms that could lead to irritable bowel syndrome

include genetic factors (most notably an identified mutation of SCN5A);

post-infectious changes, chronic infections and disturbances in the intestinal

microbiota; low-grade mucosal inflammation, immune activation, and altered

intestinal permeability; disordered bile salt metabolism (in 10-20% of cases

with diarrhoea); abnormalities in serotonin metabolism; and alterations in brain

function, which could be primary or secondary factors. Identical irritable bowel

syndrome symptoms are probably due to different disease processes; grouping

patients with this disorder into either diarrhoea-predominant or

constipation-predominant subtypes promotes heterogeneity. An approach based on

the underlying pathophysiology could help to develop therapies that target

causes and ultimately provide a cure for patients with irritable bowel syndrome.

Copyright 漏 2016 Elsevier Ltd. All rights reserved.

DOI: 10.1016/S2468-1253(16)30023-1

PMID: 28404070 [Indexed for MEDLINE]

68. Chin J Integr Med. 2015 Nov;21(11):855-65. doi: 10.1007/s11655-015-2049-x. Epub

2015 Apr 6.

Comparison of electroacupuncture and moxibustion on brain-gut function in

patients with diarrhea-predominant irritable bowel syndrome: A randomized

controlled trial.

Zhao JM(1), Lu JH(2), Yin XJ(1), Chen XK(3), Chen YH(4), Tang WJ(5), Jin XM(6),

Wu LY(7), Bao CH(7), Wu HG(7), Shi Y(8).

Author information:

(1)Yueyang Clinical School of Medicine, Shanghai University of Traditional

Chinese Medicine, Shanghai, 201203, China.

(2)Medical Imaging Department, Jinhua Municipal Central Hospital, Jinhua,

Zhejiang Province, 321000, China.

(3)Department of Acupuncture and Moxibustion, Jinhua Municipal Central Hospital,

Jinhua, Zhejiang Province, 321000, China.

(4)Department of Digestive System, Jinhua Municipal Central Hospital, Jinhua,

Zhejiang Province, 321000, China.

(5)Radiology Department, Huashan Hospital, Fudan University, Shanghai, 200040,

China.

(6)Department of Anatomy and Cell Biology, Indiana University School of

Medicine, Indianapolis, 46202, USA.

(7)Shanghai Research Institute of Acupuncture and Meridian, Shanghai University

of Traditional Chinese Medicine, Shanghai, 200437, China.

(8)Shanghai Research Institute of Acupuncture and Meridian, Shanghai University

of Traditional Chinese Medicine, Shanghai, 200437, China. flysy0636@163.com.

OBJECTIVE: To compare the effects of electroacupuncture (EA) and moxibustion

therapies on patients with diarrhea-predominant irritable bowel syndrome

(D-IBS).

METHODS: A total of 60 D-IBS patients were randomly allocated to the EA group

(30 cases) and moxibustion group (30 cases). Before and after treatment, the

gastrointestinal symptoms and psychological symptoms were scored by Visual

Analogue Scale, Bristol Stool Form Scale, Hamilton Anxiety Rating Scale (HAMA),

and Hamilton Depression Rating Scale (HAMD); the expressions of

5-hydroxytryptamine (5-HT), 5-HT3 receptor (5-HT3R), and 5-HT4 receptor (5-HT4R)

in the sigmoid mucosal tissue were measured by immunohistochemical staining.

Additionally, the effects on the functional brain areas of the anterior

cingulate cortex (ACC), insular cortex (IC) and prefrontal cortex (PFC) were

observed by functional magnetic resonance imaging.

RESULTS: Compared with before treatment, both EA and moxibustion groups reported

significant improvements in abdominal pain and abdominal bloating after

treatment (P<0.01 or P<0.05). The moxibustion group reported greater

improvements in defecation emergency, defecation frequency, and stool feature

than the EA group (P<0.01). Both HAMA and HAMD scores were significantly

decreased in the moxibustion group than in the EA group (P<0.01). Both groups

demonstrated significantly reduced expressions of 5-HT, 5-HT3R and 5-HT4R in the

colonic mucosa after treatment (P<0.01), with a greater reduction of 5-HT in the

moxibustion group (P<0.05). Finally, decreased activated voxel values were

observed in the left IC, right IC and PFC brain regions of patients in the

moxibustion group under stimulation with 150 mL colorectal distension after

treatment (P<0.05 or P<0.01), while in the EA group only PFC area demonstrated a

reduction (P<0.05).

CONCLUSION: Moxibustion can significantly improve the symptoms of D-IBS,

suggesting that moxibustion may be a more effective therapy than EA for D-IBS

patients.

DOI: 10.1007/s11655-015-2049-x

PMID: 25847778 [Indexed for MEDLINE]

69. Nutrients. 2021 Jul 19;13(7):2469. doi: 10.3390/nu13072469.

Psychological and Gastrointestinal Symptoms of Patients with Irritable Bowel

Syndrome Undergoing a Low-FODMAP Diet: The Role of the Intestinal Barrier.

Prospero L(1), Riezzo G(1), Linsalata M(1), Orlando A(1), D'Attoma B(1), Russo

F(1).

Author information:

(1)Laboratory of Nutritional Pathophysiology, National Institute of

Gastroenterology "S. de Bellis" Research Hospital, Castellana Grotte, 70013

Bari, Italy.

A diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and

polyols (LFD) improves both gastrointestinal (GI) symptoms and the psychological

profile of patients with irritable bowel syndrome with diarrhea (IBS-D). The

effects of 12 weeks of LFD on GI symptom and psychological profiles in relation

to inflammation and the involvement of the intestinal barrier were studied in

twenty IBS-D patients. The IBS Severity Scoring System, the Symptom

Checklist-90-Revised, the Italian version of the 36-Item Short-Form Health

Survey, the IBS-Quality of Life (QoL) questionnaire, and the Psychophysiological

questionnaire were administered. The GI barrier function was assessed by sugar

absorption test, the serum and fecal zonulin levels, and the serum levels of

intestinal fatty-acid binding protein and diamine oxidase. Interleukins (ILs)

and lipopolysaccharide (LPS) serum levels were evaluated along with dysbiosis.

At the end of LFD, GI symptoms, psychological state (mainly anxiety,

somatization, psychoticism, and interpersonal sensitivity), and QoL

significantly improved in these patients. Simultaneously, an improvement in

small intestinal permeability and intestinal mucosal integrity occurred, while

IL-6, Il-10, LPS, and fermentative dysbiosis significantly decreased. The LFD

can modify the immune-inflammatory features and enhance intestinal permeability

and mucosal integrity, thus determining a concurrent improvement in the clinical

and psychological conditions.

DOI: 10.3390/nu13072469

PMCID: PMC8308851

PMID: 34371976 [Indexed for MEDLINE]

Conflict of interest statement: The authors declare no conflict of interest.

70. Gut Microbes. 2022 Jan-Dec;14(1):2022997. doi: 10.1080/19490976.2021.2022997.

AhR/IL-22 pathway as new target for the treatment of post-infectious irritable

bowel syndrome symptoms.

Meynier M(1)(2), Baudu E(1)(2), Rolhion N(3)(4), Defaye M(2)(5)(6), Straube

M(3), Daugey V(2), Modoux M(3), Wawrzyniak I(6), Delbac F(6), Vill茅ger R(1),

M茅leine M(2), Borras Nogues E(7), Godfraind C(1)(8), Barnich N(1), Ardid D(2),

Poirier P(1)(9), Sokol H(3)(4)(7), Chatel JM(7), Langella P(7), Livrelli

V(1)(9), Bonnet M(1), Carvalho FA(2).

Author information:

(1)M2iSH, UMR 1071 INSERM, University of Clermont Auvergne, INRAE USC 2018,

Clermont-Ferrand 63001, France.

(2)NeuroDol, UMR 1107 INSERM, University of Clermont Auvergne, Clermont-Ferrand

63001, France.

(3)Sorbonne University, INSERM, Centre de Recherche Saint-Antoine, CRSA, AP-HP,

Saint Antoine Hospital, Gastroenterology Department, F-75012 Paris, France.

(4)Paris Centre for Microbiome Medicine FHU, Paris, France.

(5)Department of Physiology and Pharmacology, Inflammation Research Network,

Snyder Institute for Chronic Diseases, Cumming School of Medicine, University of

Calgary, Calgary, AB, T2N 4N1, Canada.

(6)LMGE, CNRS 6023, University of Clermont Auvergne, Clermont-Ferrand 63001,

France.

(7)Universit茅 Paris-Saclay, Institut National de la Recherche Agronomique et

Environnementale (INRAE), AgroParisTech UMR 1319 MICALIS, Jouy-en-Josas, France.

(8)CHU Clermont-Ferrand, Neuropathology Unit, Clermont-Ferrand, France.

(9)CHU Clermont-Ferrand, Laboratoire de Parasitologie et de Mycologie,

Clermont-Ferrand, France.

Alterations in brain/gut/microbiota axis are linked to Irritable Bowel Syndrome

(IBS) physiopathology. Upon gastrointestinal infection, chronic abdominal pain

and anxio-depressive comorbidities may persist despite pathogen clearance

leading to Post-Infectious IBS (PI-IBS). This study assesses the influence of

tryptophan metabolism, and particularly the microbiota-induced AhR expression,

on intestinal homeostasis disturbance following gastroenteritis resolution, and

evaluates the efficacy of IL-22 cytokine vectorization on PI-IBS symptoms. The

Citrobacter rodentium infection model in C57BL6/J mice was used to mimic

Enterobacteria gastroenteritis. Intestinal homeostasis was evaluated as

low-grade inflammation, permeability, mucosa-associated microbiota composition,

and colonic sensitivity. Cognitive performances and emotional state of animals

were assessed using several tests. Tryptophan metabolism was analyzed by

targeted metabolomics. AhR activity was evaluated using a luciferase reporter

assay method. One Lactococcus lactis strain carrying an eukaryotic expression

plasmid for murine IL-22 (L. lactisIL-22) was used to induce IL-22 production in

mouse colonic mucosa. C. rodentium-infected mice exhibited persistent colonic

hypersensitivity and cognitive impairments and anxiety-like behaviors after

pathogen clearance. These post-infectious disorders were associated with

low-grade inflammation, increased intestinal permeability, decrease of

Lactobacillaceae abundance associated with the colonic layer, and increase of

short-chain fatty acids (SCFAs). During post-infection period, the indole

pathway and AhR activity were decreased due to a reduction of tryptophol

production. Treatment with L. lactisIL-22 restored gut permeability and

normalized colonic sensitivity, restored cognitive performances and decreased

anxiety-like behaviors. Data from the video-tracking system suggested an upgrade

of welfare for mice receiving the L.lactisIL-22 strain. Our findings revealed

that AhR/IL-22 signaling pathway is altered in a preclinical PI-IBS model. IL-22

delivering alleviate PI-IBS symptoms as colonic hypersensitivity, cognitive

impairments, and anxiety-like behaviors by acting on intestinal mucosa

integrity. Thus, therapeutic strategies targeting this pathway could be

developed to treat IBS patients suffering from chronic abdominal pain and

associated well-being disorders.

DOI: 10.1080/19490976.2021.2022997

PMCID: PMC8803069

PMID: 35090380 [Indexed for MEDLINE]

Conflict of interest statement: HS received consultancy, or lecture fees from

Carenity, Abbvie, Astellas, Danone, Ferring, Mayoly Spindler, MSD, Novartis,

Roche, Tillots, Enterome, Maat, BiomX, Biose, Novartis, and Takeda; and is a

co-founder of Exeliom Bioscience. PL has led research projects with several

agro-food (Danone, General Mills, Dupond and Lallemand), food supplements

(Pil猫je), biotech (Ysopia) and pharmaceutical (Biocodex and Merck) companies. PL

has received consultancy or lecture fees from Ipsen, Mayoly Spindler, Iprad,

Itak, BINC Geneva, Lesaffre, l鈥橭r茅al, Bonduelle and Second Genome and is a

co-founder of Exeliom Bioscience. The other authors declare n慰 competing

interests.

71. World J Gastroenterol. 2024 Sep 21;30(35):3985-3995. doi:

10.3748/wjg.v30.i35.3985.

Correlation between the neuroendocrine axis, microbial species, inflammatory

response, and gastrointestinal symptoms in irritable bowel syndrome.

Zhang X(1), Jin WW(2), Wang HG(3).

Author information:

(1)Department of Gastroenterology, Tongde Hospital of Zhejiang Province, Taizhou

524333, Zhejiang Province, China.

(2)Department of Nutrition, Tongde Hospital of Zhejiang Province, Taizhou

524333, Zhejiang Province, China.

(3)Department of Gastroenterology, Taizhou Municipal Hospital, Taizhou 524333,

Zhejiang Province, China. woxia09949287@163.com.

BACKGROUND: This study examines the complex relationships among the

neuroendocrine axis, gut microbiome, inflammatory responses, and

gastrointestinal symptoms in patients with irritable bowel syndrome (IBS). The

findings provide new insights into the pathophysiology of IBS and suggest

potential therapeutic targets for improving patient outcomes.

AIM: To investigate the interactions between the neuroendocrine axis, gut

microbiome, inflammation, and gastrointestinal symptoms in patients with IBS.

METHODS: Patients diagnosed with IBS between January 2022 and January 2023 were

selected for the study. Healthy individuals undergoing routine check-ups during

the same period served as the control group. Data were collected on

neuroendocrine hormone levels, gut microbiome profiles, inflammatory biomarkers,

and gastrointestinal symptomatology to analyze their interrelations and their

potential roles in IBS pathogenesis.

RESULTS: IBS patients exhibited significant dysregulation of the neuroendocrine

axis, with altered levels of cortisol, serotonin, and neuropeptides compared to

healthy controls. The gut microbiome of IBS patients showed reduced diversity

and specific alterations in bacterial genera, including Bifidobacterium,

Lactobacillus, and Faecalibacterium, which were associated with neuroendocrine

disturbances. Additionally, elevated levels of inflammatory markers, such as

C-reactive protein, interleukin-6, and tumor necrosis factor-伪, were observed

and correlated with the severity of gastrointestinal symptoms like abdominal

pain, bloating, and altered bowel habits.

CONCLUSION: The findings suggest that targeting the neuroendocrine axis, gut

microbiome, and inflammatory pathways may offer novel therapeutic strategies to

alleviate symptoms and improve the quality of life in IBS patients.

漏The Author(s) 2024. Published by Baishideng Publishing Group Inc. All rights

reserved.

DOI: 10.3748/wjg.v30.i35.3985

PMCID: PMC11438665

PMID: 39351052 [Indexed for MEDLINE]

Conflict of interest statement: Conflict-of-interest statement: The authors have

no conflicts of interest to declare.

72. Zhonghua Yi Xue Za Zhi. 2016 Aug 9;96(30):2398-403. doi:

10.3760/cma.j.issn.0376-2491.2016.30.007.

[Associations of sigmoid colon mucosal mast cells with bowel symptoms and

psychological status in patients with irritable bowel syndrome with diarrhea].

[Article in Chinese]

Xu D(1), Chen W, Zhou WX, Wang CD, Fei GJ, Zhu LM, Xin HW, Zhong DR, Sun G, Fang

XC.

Author information:

(1)Department of Gastroenterology, Peking Union Medical College Hospital,

Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing

100730, China.

OBJECTIVE: To investigate the bowel symptoms and psychological status of

patients with irritable bowel syndrome (IBS) with diarrhea (IBS-D), and to

verify whether sigmoid colon mucosal mast cells (MCs) and their activation have

effect on the symptoms and psychological status of IBS-D patients.

METHODS: Patients meeting Rome 鈪? diagnostic and subtyping criteria of IBS-D who

visited the outpatient clinic of gastroenterology of Peking Union Medical

College Hospital were consecutively enrolled between July 2009 and June 2012.

IBS symptoms questionnaire was completed using face-to-face interview, and

Hamilton Anxiety Scale (HAMA)/ Hamilton Depression Scale (HAMD) were

administrated to evaluate psychological status, both by well-trained

investigators. Mast cell tryptase monoclonal antibody was used for

immunohistochemical staining to detect MCs and degranulated MCs in mucosal

biopsy of sigmoid colon. MCs and degranulated MCs were blindly counted by a

senior pathologist, and presented as number of cells in high power field (HPF)

and percentage of activated MCs. Correlation analysis was performed using

Spearman rank correlation analysis.

RESULTS: Ninety-seven patients with IBS-D were enrolled in this study, with mean

age of (44卤11) years. 70.10%(68 cases) of the IBS-D patients had comorbid

anxiety and/or depression. The median total numbers of MCs, activated MCs, and

percentage of activated MCs in sigmoid mucosa were 11.60 (7.09)/HPF, 2.00 (1.40)

/HPF, and 17.50% (10.90%), respectively. Patients having abdominal

pain/discomfort before bowel movement "every day with intermediate to high

severity" had significantly larger numbers of total MCs in sigmoid colon

compared with those with pain or discomfort "not every day and mild"

[13.80(4.85)vs 7.60(5.90)/HPF, P=0.019]; the patient having "frequent" urge to

have a bowel movement and mushy stools showed significantly higher percentage of

activated MCs in sigmoid colon mucosa compared to those having the symptoms

"some of the time" [18.75%(9.12%) vs 14.50%(13.14%), P=0.031; 21.33%(7.43%)vs

11.51%(10.65%)vs 18.42%(8.61%), P=0.030]. There was a positive correlation

between the bowel movement during IBS-D onset and the percentage of activated

MCs (r=0.221, P=0.030). There were no statistically significant differences in

the total number of MCs and percentage of activated MCs between the patients

with anxiety/depression and those without anxiety/depression (P=0.255, P=0.315).

Scores of HAMA and HAMD were found not correlated with either total MCs number

or percentage of activated MCs in sigmoid colon mucosa(all P>0.05).

CONCLUSIONS: The majority of IBS-D patients had comorbid anxiety and/or

depression. The total number and activation status of MCs in sigmoid colon

mucosa might be related with some intestinal symptoms in IBS-D patients.

Psychological disorders might influence the pathogenesis and regression of IBS-D

through brain-gut axis other than MCs in sigmoid colon mucosa.

DOI: 10.3760/cma.j.issn.0376-2491.2016.30.007

PMID: 27545031 [Indexed for MEDLINE]