● G1148

TROPHIC ROLE OF CCK B-GASTRIN RECEPTORS IN INTACT AND ULCERATED OXYNTIC MUCOSA IN RATS. A. Schmassmann, P. Schuchert, B. Flogerzi, F. Halter. Gastrointestinal Unit, University Hospital, Bern, Switzerland.

Background: The trophic role of CCK B-gastrin receptors (GR) in the intact and ulcerated gastric oxyntic mucosa is not entirely clear. The proton pump inhibitor omeprazole (OME) causes acid inhibition and hypergastrinemia and causes growth promoting effects on the oxyntic mucosa (Schmassmann et al., Gastroenterology 1997; 133: No. 12). We speculated that the GR antagonist YF476 which also causes acid-inhibition and hyper-gastrinemia, would not have such effects due to YF476-induced inhibition of gastrin-GR interactions on stem cells.

Methods: We assessed the time-sequence of CCK B-gastrin receptors (mRNA and protein) after cryoinjury of the oxyntic rat mucosa. Furthermore, 96 rats were treated with placebo (PLA), OME (40 µmol/kg-day), YF476 (100 µmol/kg-day) and OME+YF476 for 3, 8 and 15 days. Epithelial cell proliferation was assessed in the intact and ulcerated oxyntic mucosa.

Results: Whereas GR mRNA and protein were down-regulated on day 3, GR protein was up-regulated on days 8 and 15. Compared with PLA, OME, YF476 and OME+YF476 caused a > four-fold increase of serum gastrin on days 3, 8 and 15 and a > two-fold decrease of ulcer size on day 15. OME increased ($P < 0.01$) epithelial cell proliferation in the ulcer margin on days 3, 8 and 15 by 23, 30 and 46%, respectively and in the intact mucosa (day 15) by 22%. In contrast, YF476 had no significant effect on epithelial cell proliferation in the intact or ulcerated mucosa. OME-induced effects on epithelial cell proliferation were partly reversed by co-therapy with YF476.

Conclusion: The proton pump inhibitor omeprazole but not the gastrin receptor antagonist YF476 have trophic effects on the intact and ulcerated oxyntic mucosa. Our data suggest a trophic role of CCK B-gastrin receptors both in the intact and ulcerated oxyntic mucosa.

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● G1149

HIGH GRADE DYSPLASIA STILL IS NOT AN INDICATION FOR SURGERY IN PATIENTS WITH BARRETT'S ESOPHAGUS: AN UPDATE. T. Schnell, S.J. Sontag, G. Chejfec, C. Kurucar, S. O'Connell, G. Levine, J. Karpf, K. Adelman, L. Brand, J. Seidel. Depts of Medicine and Pathology, VA Hospital, Hines, IL. and Loyola U. Stritch School of Medicine, Maywood, IL.

INTRODUCTION: Barrett's esophagus (BE) remains a premalignant metaplasia of the esophageal mucosa with a spectrum of cellular behavior ranging from **no dysplasia** to **low grade dysplasia** (LGD) to **high grade dysplasia** (HGD) to **cancer** (AdCa). The management of HGD (without AdCa) is still controversial, yet surgical esophageal resection is still being recommended based on the erroneous misconception that 40% of patients (pts) with HGD already have AdCa. Indeed, the factors that encourage or discourage HGD's leap to AdCa remain unidentified, and recent evidence suggests that HGD existing without AdCa may follow a relatively benign course. We now update the results of our ongoing 18 year screening and surveillance program for identification and detection of Barrett's AdCa. **METHODS: Definitions: (1) BE:** specialized columnar epithelium (SCE) from the tubular esophagus or SCE from the GE junction area IF the biopsy contained as one specimen the squamo-SCE junction. **(2)** Short segment (SS):≤ 1cm of BE, which often appeared as tiny tongues, spicules or irregularly shaped squamocolumnar junction (SCJ). **(3)** Long Segment (LS): > 1cm of BE. Endoscopies and biopsies were performed by one of two endoscopists using pre-defined criteria. Attempts were made to biopsy the SCJ regardless of its appearance. Location and detailed configuration of the BE were drawn and mapped by hand on to 1 of 22 different figures that adjusted for HH size and shape. Histological specimens were read in detail by one pathologist (GC). **RESULTS:** A total of 1175 pts with BE have been identified. 59 had HGD without cancer as their worst lesion. 29 had prevalent HGD and 30 had incident HGD. EGD and bx was repeated every 3 to 6 months until AdCa was discovered or until two consecutive EGDs showed only LGD (without HGD). Pts were grouped according to their worst lesion (e.g., HGD and AdCa occurring together were considered as AdCa). In the pts with incident HGD, the mean time to diagnose the HGD was 5.1 ± 3.8 years (range 1.2 - 17 years). AdCa has developed in 9 of the 59 HGD pts (15.3%): 4 of the Prevalent HGD pts developed AdCa at 1, 1, 3, and 9 years after diagnosis of HGD, and 5 of the incident HGD pts developed AdCa at 9 mos, 1 yr, 1 yr, 2.3 yrs and 3 yrs after diagnosis of HGD. **One** pt had no surgery and died 2 years later of an unrelated cause; **7** pts had surgical resection and are considered cured. One pt was lost to follow up after the diagnosis of HGD and returned 10 years later with an unresectable AdCa. AdCa has **not** developed in the remaining 50 HGD pts over a period of 223 pt years (mean 6.2 years; range 1 to 11.5 years). There have been 3 HGD patterns: 1)HGD lost and not found; 2) HGD lost and then found; 3) HGD lost, found, and then lost. **CONCLUSION:** HGD occurs without AdCa in 5.0% (59/1175) of pts with BE. A minority of pts with HGD progress to develop AdCa (9/59) and almost all of these are curable. Frequent EGD exams with bx - rather than immediate esophagectomy - remains with us the management of choice for most HGD pts without AdCa.

● *G1150*

CHANGES IN GENE EXPRESSION DURING GASTRIC ULCER HEALING IN RATS. P. Schuchert, A. Etter, B. Flogerzi, F. Halter, A. Schmassmann. University Hospital, Gastrointestinal Unit, Bern, Switzerland.

Background: It is unclear which genes are primarily responsible for mediating gastric ulcer healing. We used randomly amplified DNA (Differential Display PCR, ddPCR) to identify genes specifically upor down-regulated during gastric ulcer healing.

Method: Gastric ulcers were induced in Wistar rats by cryoprobe injury. Tissue samples were taken from the ulcerated region after 8 days and compared with intact oxyntic mucosa. Total RNA from both samples was isolated and reverse transcribed. These cDNA samples were then used for ddPCR (Delta RNA Fingerprinting Kit, Clontech, Palo Alto). About 40 different primer combinations were assayed.

Results: The majority of specific bands was detectd in RNA from intact oxyntic mucosa and only few bands were detected in RNA from the ulcerated region. DNA from 31 bands was cloned and sequenced and a selection of 12 clones are shown in table 1. Four bands from RNA from the ulcerated region could not be homologized to any known sequence. *In situ* hybridization and quantitative PCR was used to confirm the expression of some of our cloned gene fragments.

Conclusion: Differential display techniques allowed us to clone potentially new genes up-regulated during gastric ulcer healing. The significance of these genes in the repair process needs to be clarified.

Table 1: Results of sequencing clones derived from ddPCR

Mucosa specific bands	Ulcus specific or up-regulated
Pepsinogen precursor	SPARC (wound healing, angiogenesis)
H^+/K^+ ATPase (proton pump)	Collagen α-1
Mucin	Carboxypeptidase (intracellular digestion)
Phospholipase A2	Macroglobulin α-2 (inflammatory response)
Neurofibromin (RAS negative receptor)	Apolipoprotein E
Colipase	DRM protein (function in growth control and cell death)

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G1151

LONG-TERM FOLLOW-UP AFTER ITALIAN TRIPLE H.P.-ERADICATION UNDER PRIMARY CARE CONDITIONS. M. Schumacher, H. Wetzel, K. Fünfhausen, V. Huß, Study-Group Wolmirstedt, Germany

Purpose: Eradication of Helicobacter pylori is mainly a task of primary care medicine. After the so called Italian Triple therapy has proved high efficacy in clinical trials we prospectively investigated the long-term outcome of this regimen in a gastroenterological setting which is supported by the surrounding general practitioners.

Method: From January 1995 consecutive patients with acute duodenal ulcer were treated with 30 mg lansoprazole, 250 mg clarithromycin and 400 mg metronidazole all given bid for seven days orally, followed by another two weeks 30 mg lansoprazole oad. H. pylori infection was first diagnosed by rapid urease test and histology. Endoscopy was strived for after four weeks to confirm ulcer healing and after three months for histological controll of the H.p.-status. All patients who had refused to appear to the controll visits were invited to ^{13}urea breath (UBT) testing two years after treatment. Major symptoms were asked at entry and at the controll visits.

Results: 81 patients were included. 61 patients returned to endoscopy after 4 weeks and ulcer healing was confirmed in 98% (65/66). 37 patients returned for endoscopy after three months of whom 36 were H.p. negative by histology. In 25 of 44 invited patients UBT was performed. In 21 of these absence of H.p. infection was diagnosed. Summed up eradication rate was 92% (57/62).

All patients in whom eradication was successful felt benefit for their quality of life. Only minor side effects were reported during therapy.

Conclusion: Eradication of H. pylori with the Italian triple regimen is well suitable for primary care medicine on condition that there is a good cooperation of gastroenterological specialists and general practitioners.

G1152

RATIONAL PRESCRIBING OF PROPHYLAXIS IN PATIENTS TAKING NSAIDs. JM Seager, CJ Hawkey, Div Gastroenterology, University Hospital, Nottingham, UK.

INTRODUCTION: Since NSAID ulcers are often asymptomatic, decisions about the use of prophylactic co-therapy should be based on an assessment of the patient's risk of ulceration. We investigated the extent to which well-established risk factors were associated with the use, by British general practitioners, of effective prophylactic drugs (proton pump inhibitors [PPI's] or misoprostol [MISO]) and less effective treatment (H_2 receptor antagonists [H_2RA's]).