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·BASIC RESEARCH·

Effect of compound total extract ginseng and tall gastrodia tuber on content of monoamine transmitters in brain tissue of rats with vascular dementia**★

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Abstract

BACKGROUND: During vascular dementia, ischemia, hypoxia, energy expenditure, abnormal metabolism of neurons, decrease of generation of Adenosine Triphosphate and disorder of ionic environment in and out of cells are observed in brain tissue, which can cause abnormal release of monoamine transmitter.

OBJECTIVE: To probe into effect of *shenma yizhi* capsule on content of monoamine transmitter in brain tissue of rat models with vascular dementia induced by multiple cerebral infarction.

DESIGN: Randomized controlled study.

SETTING: Pathological and Physiological Department o Liaoning Basic Medical Institute.

MATERIALS: Totally 96 Wistar rats of either gender, aged 8-12 months, weighing 270-500 g, were selected.

METHODS: The experiment was completed in the Pathological and Physiological Department of Vocational-technical College, Liaoning College of Traditional Chinese Medicine from April to July 2001. All rats of either gender were divided into 6 groups with 16 in each group. Wistar rats in 5 groups were injected with cruor embolus in internal carotid artery to make animal model of vascular dementia induced by multiple cerebral infarction. After modeling, rats were randomly divided into 3.2 g/kg, 1.6 g/kg and 0.8 g/kg *shenma yizhi* capsule groups (*shenma yizhi* capsule was extracted from ginseng and tall gastrodia tuber with 2.7 g raw materials and provide by Xiyuan Hospital of Chinese Academy of Traditional Chinese Medicine), positive control group and dementia control group. Animals without modeling were regarded as normal control group. Rats in each dosage group were perfused with the corresponding dosage of *shenma yizhi* capsule; rats in positive control group were perfused with 1 mg/kg hydergine dihydroergotoxine; rats in dementia control group and normal control group were perfused with the same volume of saline solution. One week after modeling, rats were medicated once a day for 6 weeks. Content of monoamine transmitter was measured with high performance liquid chromatograpy.

MAIN OUTCOME MEASURES: Content of monoamine transmitter such as levarterenol, adnephrin, dopamine, indoleacetic acid, homovanillic acid and 5-serotonin.

RESULTS: Nine rats died because of self-body quality and environmental change, and totally 87 animals entered the final analysis. Content of levarterenol of rats in dementia control group was lower than that in normal control group [(0.40±0.23), (0.70±0.14) ng/g, t=2.712, P < 0.01]; content of levarterenol of rats of 3.2 and 1.6 g/kg dosage groups was higher than that of dementia control group [(0.57±0.09), (0.58±0.19), (0.40±0.23) ng/g, t=2.211, P < 0.05], but was lower than that of normal control group. Content of levarterenol of rats of 0.8 g/kg dosage group was lower than that of normal control group [(0.48±0.23) ng/g, t=2.213, P < 0.05], but was higher than that of dementia control group and positive control group [(0.41 ±0.19) ng/g]. Differences of other neurotransmitters were not significant.

CONCLUSION: Content of levarterenol in brain tissue of rats of dementia control group is decreased obviously, but *shenma yizhi* capsule can increase content of levarterenol in brain tissue of rats. The mechanism of *shenma yizhi* capsule on treating vascular dementia is possibly related with increasing content of levarterenol in brain tissue.

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INTRODUCTION

Vascular dementia is the only model for preventing and curing dementia. On the aspect of neuro-biochemistry, cholinergic system has been paid too much attention in the researches of vascular dementia, but relationship between monoamine system and vascular dementia is studied rarely. This study aims to observe the content of monoamine transmitters in brain tissue of rats with vascular dementia on the basis of intervention of *shenma yizhi* capsule on animal models with vascular dementia induced by multiple cerebral infarction.

MATERIALS AND METHODS

Materials

The experiment was completed in the Pathological and Physiological Department of Vocational-technical College, Liaoning College of Traditional Chinese Medicine from April to July 2001. Totally 96 Wistar rats, aged 8-12 months, weighing 270-500 g, of either gender, were provided by Animal Experimental Center of Shenyang University of Traditional Chinese Medicine (certification: 033). All rats of either gender were divided into 6 groups with 16 in each group. Rats in 5 groups were used to establish model of vascular dementia induced by multiple cerebral infarction. The 6 groups were regarded as follows: 3.2 g/kg, 1.6 g/kg and 0.8 g/kg *shenma yizhi* capsule groups, positive control group, dementia control group and normal control group. Rats ate and drank freely with 8 in each cage. The temperature was (22±2) ℃ and the humidity was (50±5)%.

Main reagent and equipment: Levarterenol, adnephrin, dopamine, indoleacetic acid, homovanillic acid and 5-serotonin of monoamine transmitter were provided by Sigma Company. *Shenma yizhi* capsule was extracted from ginseng and tall gastrodia tuber (per gram corresponding to 2.7 g raw materials) and provide by Xiyuan Hospital of Chinese Academy of Traditional Chinese Medicine. *Hydergine dihydroergotoxine* was provided by Shandeshi Pharmaceutical Factory of Switzerland and Tianjin Hualv Pharmaceutical Factory [certification: (91) wei yao zhun zi X-156, 1 mg/pill].

Methods

Establishment of animal models with multiple cerebral infarction: Blood clotting of isotype rats was dehydrated under sterile and natural condition and cribrated with 200 μm screen mes. 100 mL saline and 0.2 g blood clotting were mixed to make emboli

suspension, and the diameter of emboli was 40-200 μm under microscope. 100 g/L chloral hydrate was injected into rats according to 3.5 mg/kg body mass. Left common carotid artery was exposured and blocked with metal artery clamp to ligate left external carotid artery. 0.5 mL suspension of blood clotting was injected antidromicly near cardiac end of left external carotid artery which was ligated tightly. Meanwhile, artery clamp was opened up to let emboli go into anterior, middle artery and its branches of brain through internal artery to cause multiple cerebral infarction on the left side. Rats stayed at water maze after modeling, and if the tolerant time was longer than that of normal group, the modeling was successful. Rats in normal control group were treated with the same method except the injection of saline.

Intervention of *shenma yizhi* capsule on experimental animals: Rats of each dosage group were perfused with the corresponding dosage of *shenma yizhi* capsule; rats of positive control group were perfused with 1 mg/kg hydergine dihydroergotoxine; rats of dementia control group and normal control group were perfused with the same volume of saline. One week after operation, rats were medicated once a day for 6 weeks.

Contents of levarterenol, adnephrin, dopamine, indoleacetic acid, homovanillic acid and 5-serotonin were measured with high performance liquid chromatograpy [1]. Column of color pattern: Resolve C18, Waters Company; Streaming movement: 0.1 mmol/L sodium acetate-citromalic acid buffer (pH 3.5) containing 10 mL/L methyl alcohol, paired ion B8, 1.3 mmol/L Di(n-butyl) amine; flow rate: 0.8 mL/minute, running voltage: 0.7 V.

Contents of levarterenol, adnephrin, dopamine, indoleacetic acid, homovanillic acid and 5-serotonin were compared among groups. SPSS software was used by the first author. Data among groups were compared with ANOVA analysis and with *t*-test between groups. All data were expressed with Mean±SD.

RESULTS

Quantitative analysis of the experimental animals

Nine rats died because of self-body quality and environmental change, and totally 87 animals entered the final analysis.

Contents of monoamine neurotransmitter in brain tissue of rats in each group (Table 1)

Table 1 Contents of monoamine neurotransmitter in brain tissue of rats in each group (n=12, $\bar{x}\pm s$)

Group	Levarterenol (ng/g)	Adnephrin (Pg/g)	Dopamine (ng/g)
3.2 g/kg *shenma yizhi* capsule	0.57±0.09[a]	201±131	1.29±0.37
1.6 g/kg *shenma yizhi* capsule	0.58±0.19[a]	198±94	1.25±0.46
0.8 g/kg *shenma yizhi* capsule	0.48±0.23[c]	201±121	1.20±0.31
Positive control	0.41±0.19[b]	148±104	1.23±0.47
Dementia control	0.40±0.23[b]	133±109	1.25±0.54
Normal control	0.70±0.14	111±85	1.09±0.41

Group	Indoleacetic acid(ng/g)	Homovanillic acid(Pg/g)	5-serotonin (Pg/g)
3.2 g/kg *shenma yizhi* capsule	1.36±0.36	157±96	136±80
1.6 g/kg *shenma yizhi* capsule	1.48±0.57	165±101	148±78
0.8 g/kg *shenma yizhi* capsule	1.28±0.6 1	183±139	157±106
Positive control	1.45±0.50	190±119	157±92
Dementia control	1.39±0.47	195±132	159±86
Normal control	1.50±0.42	209±159	149±58

[a] t=2.211, P < 0.05, *vs* dementia group; [b] t=2.712, P < 0.01, [c] t=2.213, P < 0.05, *vs* normal control group

Content of levarterenol of rats of dementia control group was lower than that of normal control group; content of levarterenol of rats of 3.2 and 1.6 g/kg dosage groups was higher than that of dementia control group, but was lower than that of normal control group. Content of levarterenol of rats of 0.8 g/kg dosage group was lower than that of normal control group, but was higher than that of dementia control group and positive control group. Differences of other neurotransmitter were not significant.

DISCUSSION

Vascular dementia, *i.e.* multiple infarct dementia, is a common kind of dementia of aging people and has severe harm on physical and mental health of aging people. Whether monoamine neurotransmitter is related with the onset and development of vascular dementia or not is still not clear up to now. During vascular dementia, ischemia, hypoxia, energy expenditure, abnormal metabolism of neurons, decrease of generation of adenosine triphosphate and disorder of ionic environment in and out of cells are observed in brain tissue, which can cause abnormal release of monoamine transmitter. Some researches find that contents of monoamine transmitter including levarterenol, dopamine and 5-serotonin in brain tissue of rats were lower than those of rats in normal control group[1]. This study aims to prove the effect of *shenma yizhi* capsule on vascular dementia on the basis of measuring contents of monoamine neurotransmitter and its metabolite in brain tissue of model rats with vascular dementia. Results have been proved that content of levarterenol in brain tissue of rats in dementia control group is decreased obviously, but *shenma yizhi* capsule can increase content of levarterenol in brain tissue of rats. Differences of other neurotransmitters among groups were not significant. On other hand, results also show that the modeling of this study is successful[2], and the mechanism of *shenma yizhi* capsule on treating vascular dementia is possibly related with increasing content of levarterenol in brain tissue. Decrease of content of monoamine neurotransmitter in brain tissue is possibly related with cerebral ischemia and hypoxia induced by multiple cerebral infarction. Abnormal releasing of monoamine neurotransmitter not only affects postsynaptic neurons and causes neural dysfunction, but also induces cerebral vascular spasm, accelerates decrease of cerebral blood flow, aggravates ischemia and hypoxia of brain tissue, and accelerates onset and development of dementia[3].

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人参、天麻等复方总提取物对血管性痴呆大鼠脑组织单胺递质含量的影响 **

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车前子对抗高脂血症大鼠脂质过氧化作用*☆

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摘要

背景:近年研究发现,车前草种子外壳是很好的可溶性膳食纤维源,可用来添加到食品中,调整胆固醇含量。

目的:观察车前子对高脂血症大鼠血脂及其体内脂质过氧化作用的干预结果。

设计:完全随机分组设计,对照动物实验。

单位:河北省新药药理毒理实验室。

材料:①选用健康一级SD大鼠24只,鼠龄60~70 d,体质量(210±22) g,雌雄不拘。②基础饲料由河北省实验动物中心配制,各成分质量分数:面粉0.25,麸皮0.1,玉米面0.22,豆饼0.22,鱼粉0.08,骨粉0.02,草粉0.05,食盐0.01,酵母粉0.02,葵花子0.03。高脂饲料由河北省实验动物中心配制,各成分质量分数:基础饲料0.9,胆固醇0.015,猪油0.08,猪胆盐0.003。③测定血脂试剂盒由保定长城临床试剂公司出品;测超氧化物歧化酶、过氧化氢酶、谷胱甘肽过氧化物酶活力和丙二醛水平试剂盒由南京建成生物工程研究所提供。

方法:实验于2004-06/12在河北省新药药理毒理研究实验室完成。①随机将24只大鼠分为3组:正常对照组,模型组,车前子组,每组8只。正常对照组:进食基础饲料。模型组:进食高脂饲料。车前子组:进食高脂饲料+车前子15 g/kg,普通饮水。实验动物分笼饲养,每只摄食25 g/d,自由饮水,实验周期为12周。②实验结束时,麻醉大鼠,采用相应试剂盒测定血清三酰甘油、总胆固醇、高密度脂蛋白胆固醇水平;采用相应试剂盒测血清超氧化物歧化酶、过氧化氢酶活力和丙二醛水平,心肌组织超氧化物歧化酶活力及丙二醛含量,肝组织过氧化氢酶和谷胱甘肽过氧化物酶活力。③两组间计量资料差异比较采用t检验。

主要观察指标:造模12周后,各组大鼠血脂水平及机体抗氧化能力比较。

结果:大鼠24只均进入结果分析。①造模12周后,模型组大鼠血清和心肌组织超氧化物歧化酶活力明显低于正常对照组和车前子组($P < 0.05$),血清丙二醛水平和心肌丙二醛含量均明显高于正常对照组和车前子组($P < 0.05$)。②造模12周后,模型组大鼠血清和心肌组织过氧化氢酶和肝组织谷胱甘肽过氧化物酶活力均明显低于正常对照组和车前子组($P < 0.05$)。③造模12周后,模型组大鼠血清总胆固醇和三酰甘油水平明显高于正常对照组和车前子组($P < 0.05$),血清高密度脂蛋白胆固醇水平和高密度脂蛋白胆固醇/总胆固醇明显低于正常对照组和车前子组($P < 0.05$)。

结论:提示15 g/kg剂量车前子可明显降低高脂血症大鼠血脂,增加机体抗氧化能力。

主题词:车前子;高脂血症/中药疗法;脂质过氧化作用
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摘要

背景:在血管性痴呆时,脑组织缺血、缺氧,能量消耗,神经元代谢异常,三磷酸腺苷生成减少,细胞内外离子环境的紊乱等导致突触结构破坏,可能引起单胺神经递质的释放异常。

目的:观察参麻益智胶囊干预的多发性脑梗塞引起的血管性痴呆动物模型脑组织单胺递质含量的变化,分析其对血管性痴呆的影响。

设计:随机对照观察。

单位:辽宁省基础医学研究所病生研究室。

材料:Wistar种系大鼠96只,鼠龄为8~12个月,体质量为270~500 g,雄雌各半。

方法:实验于2001-04/07在辽宁中医学院职业技术学院病理生理研究室完成。将实验动物分为6组,每组大鼠16只,雄雌各半。其中5组采用Wistar大鼠颈内动脉注入凝血栓子的方法,制作出多发性脑梗塞引起的血管性痴呆动物模型,造模后随机分为参麻益智胶囊3.2 g/kg,1.6 g/kg,0.8 g/kg剂量组(参麻益智胶囊由人参、天麻等总提取物组成,每克药粉含生药2.7 g,由中国中医研究院西苑医院提供。),阳性药对照组,痴呆对照组;未造模动物为正常对照组。对参麻益智胶囊各剂量组分别施以相应剂量的参麻益智胶囊灌胃;阳性药对照组应用喜得镇甲磺酸双氢麦角毒碱片灌胃,剂量为1 mg/kg;痴呆对照组和正常对照组应用同等剂量的生理盐水灌胃。各组动物在造模后1周开始给药,1次/d,连续给药6周。应用高效液相色谱法测定单胺类神经递质含量。

主要观察指标:测定各组大鼠脑组织单胺类神经递质去甲肾上腺素、肾上腺素、多巴胺、吲哚乙酸、高香草酸和5-羟色胺的含量,并进行组间对比。

结果:实验动物由于自身体质和环境改变等原因死亡9只,最后进入结果分析的实验动物为87只。痴呆对照组大鼠脑组织内去甲肾上腺素含量显著低于正常对照组大鼠[(0.40±0.23),(0.70±0.14) ng/g,t=2.712,$P < 0.01$],而参麻益智胶囊3.2,1.6 g/kg剂量组大鼠脑组织去甲肾上腺素含量明显高于痴呆对照组大鼠[(0.57±0.09),(0.58±0.19),(0.40±0.23) ng/g,t=2.211,$P < 0.05$],尽管其含量仍然低于正常对照组大鼠。参麻益智胶囊0.8 g/kg剂量组的去甲肾上腺素含量明显低于正常对照组[(0.48±0.23) g/kg,t=2.213,$P < 0.05$],但仍略高于痴呆对照组和阳性药对照组大鼠[(0.41±0.19) ng/g]。其他神经递质间差异不明显。

结论:痴呆大鼠脑组织去甲肾上腺素含量明显降低,而参麻益智胶囊具有升高痴呆大鼠脑组织去甲肾上腺素的作用。参麻益智胶囊治疗血管性痴呆可能与其提高脑组织内去甲肾上腺素的含量有关。

主题词:痴呆,血管性/中药疗法;疾病模型,动物;神经递质;去甲肾上腺素
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