

证 的 研 究

血瘀型脑血管硬化性痴呆症与内皮素、降钙素基因
相关肽及一氧化氮的相关性研究

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摘要 选取无心、肺、肝、肾及其它脏器系统严重病变的脑血管硬化性痴呆症(VD)患者 65 例,根据长谷川痴呆量表评分分为轻度痴呆(VD1)组和重度痴呆(VD2)组,与正常对照组进行血瘀评分、内皮素(ET)、降钙素基因相关肽(CGRP)、一氧化氮(NO)比较。结果:(1)VD 患者血瘀评分显著高于正常对照组,VD2 组血瘀评分高于 VD1 组($P<0.01$);(2)VD 组 ET 显著高于正常对照组,CGRP、NO 显著低于正常对照组($P<0.01$);VD2 组 ET 高于 VD1 组,CGRP、NO 低于 VD1 组($P<0.01$);(3)VD 患者的 ET 与 CGRP、NO 呈负相关性,CGRP 与 NO 呈正相关性($P<0.01$),血瘀评分与 ET 呈正相关,与 CGRP、NO 呈负相关($P<0.01$)。表明 VD 患者存在血瘀标实的病理改变,ET、CGRP、NO 之间平衡制约机制的破坏在 VD 的发病、发展中有重要作用。

主题词 痴呆,血管性/血液 血瘀/血液

脑血管硬化性痴呆症(VD)是老年人痴呆的一个主要原因。在原苏联、日本、中国,脑血管性痴呆症多于老年性痴呆。关于 VD 的发病机制,目前尚不十分明确,可能与脑循环代谢改变,神经递质与神经肽异常,自由基代谢异常等有关^[1]。大量研究表明,内皮素(ET)是具有很强血管收缩效应的多肽,另外它还有神经调节作用,参与脑内多种生理、病理反应^[2]。降钙素基因相关肽(CGRP)是强烈的舒张血管的物质,广泛分布于中枢神经系统和外周组织^[3]。一氧化氮(NO)在血管、免疫和中枢神经系统中具有广泛的生理功能,对脑血管硬化性损害起复杂的作用^[4]。本研究拟通过对 VD 患者 ET、CGRP、NO 及其相关性,以及与中医血瘀证相关性的研究,进一步了解血瘀、ET、CGRP、NO 在脑血管硬化形成中的变化规律和相互关系,探讨 VD 的发病机制,为中西医结合防治 VD 提供依据。

1 材料与方 法

1.1 资料来源:VD 组:65 例按照戴自英主编的第 9 版《实用内科学》VD 诊断标准^[5],并进行长谷川痴呆量表评分,筛选出 VD 患者,男 50 例,女 15 例,年龄 55~79 岁。其中根据长谷川痴呆量表评分标准^[6],痴呆

量表评分在 10~21.5 之间者为轻度痴呆(VD1)组(30 例),评分低于 10 者为重度痴呆(VD2)组(35 例)。全部病例均经病史询问,心电图、胸部 X 线片、脑 CT、肝、肾功能及其它生化检查、排除心、肺、肝、肾及其它脏器系统严重病变,脑血管意外急性期者。正常对照组:30 名,为健康体检者,经系统询问病史、体格检查、各项理化检查,无器质性病变。其中男 22 例,女 8 例,年龄 55~78 岁。以上 2 组性别、年龄、受教育水平经齐同检验差异无显著性($P>0.05$)。

1.2 观察项目和检验方法

1.2.1 血瘀分评定:被测试者安静平卧 5 分钟后,自然光下观察,根据王阶、陈可冀、翁维良等人的血瘀证诊断标准记分^[7]。

1.2.2 血浆 ET 测定:采用放射免疫法^[8],¹²⁵I-ET 放免测定药盒由中国人民解放军总医院东亚免疫技术研究所提供。

1.2.3 血浆 CGRP 测定:采用放射免疫法^[8],¹²⁵I-CGRP 放免测定药盒提供处同 ET。

1.2.4 血浆 NO 测定:采用亚硝酸盐比色法^[9],试剂盒提供同 ET。

1.2.5 统计学方法:计数资料用 χ^2 检验、率差别的显著性检验,计量资料用配对 t 检验或 t' 检验,相关分析采用直线相关分析。以上统计均应用美国 SPSS 统计软件在 IBM-PC 机上进行。

2 结 果

2.1 VD 各组血瘀评分、痴呆评分的变化:表 1 示,VD 各级血瘀评分显著高于正常对照组,痴呆评分显著降低。VD2 组的血瘀评分显著高于 VD1 组($P<0.05$ 或 $P<0.01$)。

表 1 各组血瘀评分、痴呆评分变化比较($\bar{x}\pm s$)

组 别	例数	血瘀评分	痴呆评分
正常对照组	30	15.30±5.774	31.05±1.780
VD1 组	30	44.13±6.268**	13.53±2.488*
VD2 组	35	65.91±9.099***	5.89±2.478**

与正常对照组比较,* $P<0.05$,** $P<0.01$,与 VD1 组比较,## $P<0.05$,### $P<0.01$

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表 2 各组 ET、CGRP、NO 变化比较 (pg/ml, $\bar{x} \pm s$)

组别	例数	ET	CGRP	NO
正常对照组	30	44.17 ± 8.606	128.16 ± 16.567	52.24 ± 16.358
VD 组	65	81.80 ± 14.252*	65.42 ± 22.836*	22.61 ± 6.406*
VD1 组	30	71.53 ± 6.091*	83.11 ± 18.606*	26.48 ± 5.709*
VD2 组	35	90.61 ± 13.328*#	50.27 ± 13.185*#	19.30 ± 4.999*#

与正常对照组比较, * $P < 0.01$; 与 VD1 组比较, # $P < 0.01$

2.2 各组 ET、CGRP、NO 的变化比较: 表 2 示, 与正常对照组比较, VD 组 ET 显著增高, CGRP、NO 显著降低 (P 均 < 0.01)。VD1 组与 VD2 组比较, VD2 组 ET 显著高于 VD1 组, CGRP、NO 则显著降低 (P 均 < 0.01)。

2.3 65 例 VD 组血瘀评分与 ET、CGRP、NO 相关性分析: 经统计学分析可知, 血瘀评分与 ET、CGRP、NO 的相关系数分别为 0.8702、-0.7545、-0.5054, 它们的双侧精确概率均为 $P = 0.001$, 故血瘀评分与 ET 呈显著正相关, 与 CGRP 呈显著负相关, 与 NO 呈显著负相关。

3 讨论

VD 属中医学“文痴”、“善忘”、“郁证”、“癡病”等范畴, 其病位在脑, 病因以内因为主, 病机特点多以虚为本, 以实为标。本虚为诸脏亏损, 特别是与肝、肾、心、脾四脏功能衰退有密切关系。标实则气滞、痰阻、血瘀^[10]。本研究中, 所有 VD 患者的血瘀评分均远远高于正常对照组, 说明 VD 患者存在血瘀; 并且机体血瘀的程度与痴呆的程度有关, 血瘀越严重, 其痴呆程度也越重。证实了 VD 的病理改变为血瘀标实。因此, 针对 VD 患者存在血瘀病理改变的特点, 临床应用活血化瘀、祛瘀通络、益气活血等治疗方法, 应该能改善患者的症状, 达到一定治疗目的。

ET 是血管内皮细胞分泌的内皮源性收缩因子, 是迄今为止最强烈的血管收缩肽。李瑶宣动态观察了 20 例脑梗塞患者血浆 ET 的变化, 结果发现脑梗塞和脑动脉硬化者 ET 均高于正常对照组^[11]。CGRP 是一种强的血管舒张剂。有文献报道, 在高血压、动脉粥样硬化、出血性脑卒中、缺血性脑卒中, CGRP 均明显下降, 不能有效拮抗缩血管物质的过度作用^[12]。NO 结构简单, 易扩散但不稳定, 广泛存在于中枢神经系统, 在脑血流调节中起重要作用。周泉生等人的研究发现, 动脉粥样硬化的血管生成 NO 降低, 对乙酰胆碱的舒张效应丧失, 而对儿茶酚胺类的缩血管反应异常敏感^[13]。本研究也发现, VD 患者 ET 增高, CGRP、NO 降低, 且 ET 与血瘀呈正相关, 与 CGRP、NO 呈负相关, 这与以往研究结果是一致的。因此, VD 与内皮细

胞分泌功能异常, 神经—内分泌因子异常有显著关系。ET、CGRP、NO 相互拮抗, 相互制约, 调节血管舒缩功能的破坏, 既可能是 VD 发病的病因, 也可以是其病理结果。VD 患者血管舒缩功能紊乱、微循环障碍的病理变化, 体现了 VD 血瘀标实的客观存在。ET、CGRP、NO 与血瘀评分之间的相关性, 可以提供为血瘀诊断的客观指标, 有助于中医证型客观化, 也将有益于中西医结合防治 VD 诊疗手段的发展和药物开发。

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新世纪中医药创新学术研讨会征文

中国农村中医药学术研究中心、中国民间中医药科技推广交流中心, 拟于 2000 年 12 月在广西桂林联合举办“新世纪中医药创新学术研讨会”特征稿如下。

1. 征稿对象: 医药院校、医疗单位、乡镇卫生院(所)、厂矿企业医院(医务室、所)中的中医药、中西医结合管理、科研、临床人员, 和民间医生、乡村医生及其他中医药爱好者均可投稿。2. 征文内容: 题材不限, 凡是中医药、中西医结合为内容的管理、科研、临床等方面的创新研究成果、学术创新经验、中医药未来探讨等均可。民间医生、乡村医生有一技之长和单方验方等亦可参加交流。3. 征文要求: 每文限 3000 字以内, 须打印, 另附 600 字以内的论文摘要和 200 字以内作者简介。4. 来稿请在 2000 年 11 月 15 日前寄至湖北省麻城市台湾街 237 号中国民间中医药科技推广交流中心吴玲、郭正超收。信封上请注明是“创新学术会”征文, 邮编 438300。

ABSTRACTS FROM ORIGINAL ARTICLES

Clinical Observation on Treatment 54 Cases of Chronic Uric-acid Nephropathy of Blood Stasis Type with Drugs for Purging Turbid, Resolving Dampness and Dispelling Phlegm

Wu Xinlin, Li Junbiao, Zhou Ying

A self-prescribed recipe of drug for purging turbid, Resolving Dampness and Dispelling Phlegm was employed in the treatment group (N=54) with combination of allopurinol, and compared its effect with that in the control group (N=36) only with allopurinol. The total effective rate in the treatment group (92.59%) was significantly higher ($P<0.01$) than that of the control group (63.89%). The levels of uric acid in the blood, urinary protein, microproteins after treatment demonstrated that renal function, lipid metabolism and hyperviscosity were also significantly improved ($P<0.01$). The authors concluded that this therapeutic principle is effective.

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Key words: nephropathy/TCM treatment retention of damp-turbid@ uric acid

(Original article on page 532)

Clinical Observation of 24 Cases of Coronary Disease with Asymptomatic Myocardial Ischemia Treated by Huang Qi Bao Xin Tang

Shang Yun

A self-prescribed Huang Qi Bao Xin Tang was used in the treatment group (N=24) and its effect was compared with the control group (N=24) in which isosorbide dinitrate was administered in cases of asymptomatic myocardial ischemia. The therapeutic effect of the treatment group was significantly better than that of the control after termination of the treatment and 6 months thereafter ($P<0.01$), including the number of decreased ST segment and its duration. The effective rate in the cardinal symptoms and signs in TCM, namely, lassitude, deficiency of qi and disinclination to talk, spontaneous perspiration and teeth-printed corpulent tongue was 90.34%, while in the control group, 43.8% only ($P<0.01$).

Authors' add: Nanhui County, Guangming TCM Hospital, Shanghai, 201300

Key words: coronary diseases/TCM treatment myocardial ischemia/TCM treatment @Huang Qi Bao Xin Tang

(Original article on page 538)

Treatment of 40 Cases of Hyperhyaluronemia due to Liver Cirrhosis by Combination of Drugs for Heat-reducing,

Purgation, Resolving and Tonification

Yang Hongzhi, Yang Yaowu, Shen Weisheng, et al.

Patients of liver cirrhosis with high blood hyaluronic acid level (>800 ng/L) and elevated NO content were enrolled to study the efficacy of treatment with a combination of drugs for heat-reducing, purgation, resolving and tonification for 6 months to 2 years. The symptoms and signs were markedly ameliorated: the level of GPT, GOT, globulin, albumin and bilirubin contents restored to normal level. In B-ultrasonographic examination, a decrease the width of the portal vein and the spleen was found in 50% of the patients. The authors concluded that the combined use of drugs for heat-reducing, purgation, resolving and tonification was effective in treating hyperhyaluronemia due to liver cirrhosis. The ingredient rhemannia root may play the key role in its actions of expelling toxic materials, normalizing the functions of the viscera and discharge of bile, and removing the stagnated heat.

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Key words: liver cirrhosis/TCM treatment hyaluronic acid/metabolism therapy

(Original article on page 543)

Correlation Study on ET, CGRP and NO Levels in Vascular Dementia of Blood Stasis Type

Cai Jing, Du Jian

Patients of vascular dementia (VD) without severe damage in cardinal organs were divided into group VD 1 (mild dementia) and VD 2 (severe dementia) according to the Kasagawa's dementia scale and compared their blood stasis score, endothelin (ET), calcitonin gene-related peptide (CGRP) and NO content with normal subjects. It was found that the blood stasis score and ET in VD were higher than that of the normal subjects and that in VD2 were higher than in VD 1 ($P<0.01$). In contrary, the content of CGRP and NO were significantly lower (all $P<0.01$). ET in VD was negatively correlated with CGRP and NO; while the CGRP is positively correlated with the NO ($P<0.01$). The blood stasis score was positively correlated with the ET, but negatively with the CGRP and NO ($P<0.01$). The authors concluded that the blood stasis in VD is of excess in superficiality and the imbalance in ET, CGRP and NO is an important factor in occurrence and development of VD.

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Key words: dementia, vascular/blood, blood stasis syndrome/blood

(Original article on page 552)