

实验研究

活血祛瘀方药预防自发性高血压大鼠
心肌纤维化实验研究

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摘要 为观察活血祛瘀方药预防自发性高血压大鼠心肌纤维化的作用,采用 14 周龄自发性高血压大鼠(SHR),观察活血祛瘀方药治疗前后大鼠血压、左室重/体重(LVM/BW)、左室壁相对厚度(LVWT)以及心肌胶原蛋白的含量和浓度等变化。结果 14 周龄 SHR 已形成左室肥厚,并随着病程的进展而逐渐出现心肌纤维化。经活血祛瘀方药治疗 12 周后,SHR 血压下降,左心室肥厚明显消退,且没有出现心肌胶原蛋白含量和浓度的增加。表明活血祛瘀方药可以逆转高血压左心室肥厚,并能预防心肌纤维化的发生。

主题词 高血压/中医药疗法 @ 心肌纤维化 @ 活血祛瘀方

心肌纤维化是高血压病主要并发症左心室肥厚(LVH)的进一步病理发展,也是导致心力衰竭的常见原因之一。本实验观察了活血祛瘀方药对自发性高血压大鼠(SHR)左心室肥厚及心肌纤维化的影响,并对其治疗作用机理进行初步的探讨。

1 材料与方法

1.1 实验动物及分组:选用 14 周龄 SHR24 只和同龄正常大鼠(WKY)8 只,雌雄各半,由上海市高血压病研究所提供。SHR 在 14 周龄时已形成 LVH。分组情况:对照组随机选用 14 周龄 SHR 和同龄 WKY 各 8 只(分别为 SHR-C14 组和 WKY-C14 组);自然病程对照组(SHR-N26 组)随机另取 14 周龄 SHR8 只,喂至 26 周取材。以上对照组均喂饲蒸馏水和标准鼠食。中药复方治疗组(SHR-C26 组)采用中药灌胃治疗 14 周龄 SHR8 只,疗程为 12 周,饮食同前,喂至 26 周取材。各组大鼠采用尾动脉测压法,记录大鼠清醒状态下收缩压,每 2 周测血压 1 次。

1.2 方药组成:活血祛瘀方药组成:丹参 15g,黄芪 10g,川芎 12g,瓜蒌 15g,桂枝 5g,半夏 12g,毛冬青 10g,薤白 15g,赭石 12g,牛膝 15g。将上述中药制成 100%水煎液(每毫升含生药 1g),2ml/100g 体重灌胃,每日 2 次,连续给药 12 周。

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1.3 心肌肥厚形态学指标:实验大鼠称重,取出心脏,除去大血管残根、心房、右心室和结缔组织,吸干水分,称取左心室重量(LVM)和体重(BW)之比以及左室壁厚度(LVWT),左室壁相对厚度为室间隔、左室游离壁及心尖厚度的均值^[4]。

1.4 左、右心室肌胶原蛋白含量和浓度的测定:取左右室心肌约 100mg 分别匀浆,干燥后加 6N HCl 于 110℃水解 24 小时,把水溶的胶原蛋白转化为氨基酸。羟脯氨酸的含量可以通过 Ehrlich's 试剂的作用,通过分光光度计测定出来^[1]。1g 羟脯氨酸相当于 8.2g 胶原蛋白^[2],所以胶原蛋白的含量相当于羟脯氨酸含量 $\times 8.2$ 。而心肌胶原蛋白浓度则相当于它的含量与心肌重量的比率。

1.5 统计学处理:所有实验结果用 $\bar{x} \pm s$ 表示,采用 t 检验。

2 结果

2.1 各组大鼠血压(BP)、LVM/BW、LVWT 的变化比较:由表 1 可知,SHR14 周龄时,已出现 LVH,但与 SHR-N26 相比差异无显著性($P>0.05$),说明心肌肥厚出现较早,且会稳定持续一段时间。经活血祛瘀中药治疗后,LVH 随血压的下降而明显消退($P<0.01$)。而自然病程组大鼠 LVH 则进一步加重。

2.2 各组大鼠左右心室肌胶原蛋白含量和浓度的变化比较:从表 2 可知,SHR-C14 组的左室胶原蛋白含量显著高于 WKY-C14 组($P<0.05$),但它们的左室胶原蛋白浓度并没有明显区别($P>0.05$)。而 SHR-N26 组的左室胶原蛋白含量和浓度显著高于 SHR-C14 组($P<0.05$),说明心肌肥厚出现较早,而心肌纤维化出现较迟。SHR-C26 组的左室胶原含量和浓度明显小于 SHR-N26 组($P<0.05$),说明活血祛瘀方药有明显预防心肌纤维化的作用。SHR-C14 组的右室胶原含量和浓度与 WKY-C14 组无明显差别,12 周后,SHR-C26 组的右室胶原含量和浓度则无增加。

3 讨论

通过测量心肌羟脯氨酸浓度来作为心肌纤维化的标志,近年来应用较多。有学者认为,心肌羟脯氨酸浓

表1 各组大鼠血压、LVM、LVM/BW、LVWT 变化比较($\bar{x} \pm s$)

组别	鼠数	血压(kPa)	LVM(g)	LVM/BW(mg/g)	LVWT(mm)
WKY-C14组	8	14.86 $\pm$ 0.83	0.51 $\pm$ 0.04	2.62 $\pm$ 0.16	2.58 $\pm$ 0.16
SHR-C14组	8	24.67 $\pm$ 0.67*	0.68 $\pm$ 0.05*	3.66 $\pm$ 0.36*	3.05 $\pm$ 0.22*
SHR-N26组	8	25.81 $\pm$ 0.65	0.95 $\pm$ 0.13	3.52 $\pm$ 0.23	3.32 $\pm$ 0.47
SHR-C26组	8	16.52 $\pm$ 0.41 Δ $\blacktriangle$	0.74 $\pm$ 0.04 Δ $\blacktriangle$	2.71 $\pm$ 0.21 Δ $\blacktriangle$	2.60 $\pm$ 0.21 Δ $\blacktriangle$

与WKY-C14组比较,* $P < 0.01$;与SHR-C14组比较, $\Delta P < 0.01$;与SHR-N26组比较, $\blacktriangle P < 0.01$

表2 各组大鼠左右心室肌胶原蛋白含量和浓度变化比较($\bar{x} \pm s$)

组别	鼠数	左室胶原含量(mg)	左室胶原浓度(mg/g)	右室胶原含量(mg)	右室胶原浓度(mg/g)
WKY-C14组	8	2.71 $\pm$ 0.52	4.76 $\pm$ 0.98	0.69 $\pm$ 0.14	4.58 $\pm$ 0.61
SHR-C14组	8	3.62 $\pm$ 0.46*	4.81 $\pm$ 0.81	0.73 $\pm$ 0.08	4.59 $\pm$ 0.76
SHR-N26组	8	6.52 $\pm$ 0.56 Δ	5.89 $\pm$ 0.52 Δ	1.22 $\pm$ 0.13 Δ	5.24 $\pm$ 0.47
SHR-C26组	8	3.65 $\pm$ 0.49 $\blacktriangle$	4.35 $\pm$ 0.53 $\blacktriangle$	0.98 $\pm$ 0.13 $\blacktriangle$	4.43 $\pm$ 0.42 $\blacktriangle$

与WKY-C14组比较,* $P < 0.01$;与SHR-C14组比较, $\Delta P < 0.01$;与SHR-N26组比较, $\blacktriangle P < 0.01$

度与形态学分析有很好的相关性^[3]。本实验将羟脯氨酸换算成胶原蛋白,用胶原蛋白浓度作为心肌纤维化的标志。本实验结果表明,14周龄的SHR已经出现了LVH,但左、右心室的胶原浓度并没有发生改变,而SHR-N26组的心室胶原浓度则显著增高,说明心肌肥厚出现较早,以后随着病程的进展而逐渐出现心肌纤维化。本研究观察到活血祛瘀治法能降低血压,并使得LVM/BW这一反映LVH的敏感指标的值得明显降低,说明活血祛瘀法能使LVH发生逆转。

目前的一些研究初步证实,Ca²⁺在心肌纤维化的过程中起着重要作用,细胞内Ca²⁺增加,可刺激成纤维细胞的生长,并充当心肌纤维细胞合成胶原蛋白的信使^[4]。活血祛瘀法能降低肥厚心肌中Ca²⁺的含量,具有钙拮抗剂的效应^[5],提示活血祛瘀方药可通过抑制Ca²⁺所调节的细胞过程而产生预防心肌纤维化的

效应。此外,活血祛瘀方药还能改善肥厚心肌的血液供应和氧自由基代谢^[5],这些因素可能参与了预防心肌纤维化的过程。

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ABSTRACTS FROM ORIGINAL ARTICLES

Clinical and Experimental Studies on Ke Chuan Yi Tie Kang for Treatment of 735 Cases of Cough with Dyspnea Caused by Acute Bronchitis

Chen Zhenfu, Zhou Wenqiu, Gao Juxian, et al

According to the theory of "internal disease is treated with external therapy" in TCM, an externally applied medicinal plaster, Ke Chuan Yi Tie Kang was developed for treatment of cough with dyspnea. Clinical observation of 1158 cases (735 cases in treatment group and 423 in control group) indicated it had satisfactory therapeutic effects, with very significant difference between the two groups in cured rate ($P < 0.01$). The cured rate in the wind-cold group was superior to that of the wind-heat group ($P < 0.01$). The experimental study showed that the drug had functions of relieving cough and asthma without stimulating action on skin and obvious side-effect. It is convenient to apply with markedly therapeutic effect.

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Key words: Bronchitis/TCM therapy, @ Ke Chuan Yi Tie Kang

(Original article on page 284)

Clinical Observation on 30 Cases of Cerebrovascular Dementia Treated with Shen Tong Capsule

Lu Hui, Wang Yanyan, Chen Fu, et al

Fifty cases of mild-moderate cerebrovascular dementia selected by referring to the diagnostic criterion DSM-III-R for cerebrovascular dementia (VaD) established by American Society of Psychoneurology issued by WHO were randomly divided into Shen Tong Capsule treatment group (30 cases) and hydergine treatment group (20 cases). Modified Mental State Examination (MMSE) and Blessed Behavior Scale (BBS) were used to calculate changes of marks before and after treatment for assessment of therapeutic effects. Results show that Shen Tong Capsule has therapeutic effect on key symptoms and clinical behaviour of mild-moderate disturbance of intelligence, with the total effective rate of 86.67%. Differences of accumulated marks in both MMSE and BBS before and after treatment in the treatment group are superior to those of the control group respectively.

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Key words: Dementia, Vascular/TCM therapy, @ Shen Tong Capsule

(Original article on page 290)

Studies on Clinical Division of Stages and TCM Syndrome

Differentiation and Treatment for Chronic Myelogenous Leukemia

Ma Mingfei, Gao Zhijie, Li Dongyun, et al

Clinical division of stages in 289 cases of chronic myelogenous leukemia (CML) and reviewing investigating survey analysis were made for its relationship with TCM syndromes. And then relative problems of clinical syndromes, names of diseases and syndromes were researched respectively according to the analytic results. It is indicated that the disease is characterized mainly by clinical changes of the 4 stages, i.e. pathogenic factor falling while body resistance excessive; pathogenic factor accumulating while body resistance prevailing; pathogenic factor advancing while body resistance weakened; pathogenic factor excess while body resistance deficiency. And it is firstly put forward that Sui Du is served as name of disease and syndrome of CML.

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Key words: Leukemia, Granulocytic, Chronic/TCM therapy

(Original article on page 298)

Experimental Study on Prevention of Myocardial Fibrosis by the Prescription of Promoting Blood Circulation and Eliminating phlegm in Spontaneously Hypertensive Rats

Li Jianping, Yan Can, Deng Zhong Yan, et al

Objective: To observe effects of the prescription and drug for promoting blood circulation and eliminating phlegm in prevention of myocardial fibrosis in spontaneously hypertensive rats (SHR). **Methods:** Changes of blood pressure (BP), left ventricular mass/body weight (LVM/BW), left ventricular wall thickness (LVWT) and content of myocardial collagen were investigated before and after treatment with the prescription and drug for promoting blood circulation and eliminating phlegm in SHR of 14 weeks in age. **Results:** SHR of 14 weeks in age has formed left ventricular thickness, and appears gradually myocardial fibrosis with advance of disease course. After treatment with the prescription and drug for activating blood circulation and eliminating phlegm for 12 weeks, BP decreases, left ventricular thickness eliminates obviously, and the content of myocardial collagen does not increase in SHR. **Conclusion:** The prescription drug for promoting blood circulation can reverse the left ventricular thickness due to hypertension, and can prevent myocardial fibrosis.

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Key words: Hypertension/TCM therapy, @ Myocardial fibrosis, @ Prescription for activating blood circulation and eliminating phlegm.

(Original article on page 301)