中西医结合杂志 1989 年第 9 卷第 9 期

心虚证患者心钠素水平的初步观察及其临床意义探讨

上海医科大学华山医院内科教研室 俞兵 戴瑞鸿 王勇雄
中西医结合研究所心血管病研究室 王受益 王文健

内容提要 用放射免疫法测定了 24 例心气虚(重证组和轻证组)、单纯心虚和非虚证四组患者的血浆心钠素样免疫活性物质(irANP),发现其含量在上述各组和西医心功能Ⅰ～Ⅳ级组中均呈递减现象,且在相应的中西医四组间无显著差别。irANP 与左室射血分数明显相关(r=−0.87)。故认为irANP 可作为心气虚患者的客观指标之一,并能反映病证的严重度。同时再一次提示中医的虚证分型与心功能是相关的。

心钠素是心脏产生和分泌的多肽类激素,具有强大的排钠利尿、血管舒扩生物活性。它在体内有 α、β、γ 三种肽链形式,后二种高分子形式可能是主要生物活性形式 α 链的前体,各肽链间有交叉的免疫反应性[1]。心钠素在调节心血管系统和内环境稳定等方面起着重要的作用。现认为外周血中心钠素样免疫活性物质(irANP)含量的变化常预示着体内某些病理生理的改变,它对心功能的变化尤为敏感[2~5]。而中医虚证分型与心功能有一定的联系[6,7],本文旨在通过测定不同心脏病基础的心虚证患者irANP,探讨其含量变化与中医虚证分型、心功能的关系。

资料与方法

一、临床资料:在 75 天内连续入院的心脏病患者中,凡符合中国中西医结合虚证专业委员会中医虚证参考标准(1986 年 5 月郑州修订,简称虚证标准)的心虚证者均列为本研究对象,共 18 例,其中男 11 例,女 7 例。另选同期非心虚证的铅吸收病人 4 例,胸闷、室性早搏待查症状消失者各 1 例作为对照组(男 5、女 1)。然后先由中医师根据虚证标准作出辨证,将其分为非虚证组、单纯心虚组和心气虚组。后者根据病证程度再分为轻证和重证两组。轻证:神疲乏力,动则气短心悸,易出汗,面色不华,舌质淡边有齿印,脉细或结代。重证:除上证外有懒言声低,心胸憋闷,气急、甚则咳喘,气逆不得平卧,心悸怔忡,自汗甚至大汗淋漓,尿少或尿闭,便溏或便艰,面色㿠白或晦暗青紫,面浮肿,舌胖、质紫或紫暗,苔腻或滑腻,脉细数、细沉或见结代,甚则微细欲绝。再由西医师根据临床表现、胸片、超声心动图和心机械图等资料作出西医诊断和心功能分级(纽约心脏病协会 NYHA 标准);根据超声心动图左室收缩期和舒张期直径(D_s、D_d)计算左室射血分数(EF)。$EF=\frac{D^3_d-D^3_s}{D^3_d}$。各组情况见表 1。

二、方法:所有对象控制饮食 3 天,统一于上午 8～10 时采血。病人平卧 30min 测心率、血压,然后从前臂抽静脉血 3 ml,立即注入含 EDTA 和抑肽酶的试管中,同时将试管插入冰筒送 4°C 离心,取血浆保存于 −20°C 中。所有标本采完后,一次用心钠素快速放射免疫分析法[8]测定 irANP。

与此同时,非选择性地对部分对象作以下各项检查:(1)11例作血液流变学指标及血小板聚集功能测定。包括全血比粘度(低切率和高切率)、血浆比粘度和肾上腺素、ADP 诱导的血小板聚集力等。(2)19例拍胸片。(3)11例作超声心动图检查。各项检查的操作者均在不知道其它结果的情况下,单独作出评价。

三、统计学处理:对各组年龄、采样时心率、血压的平均值均用方差分析法处理,若 F

表 1　各组平均年龄、心率、血压比较　(M±SD)

分　　组	例数	年　龄(岁)	心率（次/分)	收缩压(mmHg)	舒张压(mmHg)
非 虚 证	6	45.0±20.1	83.7± 5.9	125.0±10.5	78.3± 9.8
单纯心虚证	6	59.3±10.6	84.3± 9.6	129.7±15.3	80.0± 6.6
心气虚轻证	6	53.5±23.1	93.3±11.6	130.3±27.9	68.3±13.5
心气虚重证	5	49.8±11.7	92.0±12.3	111.6±18.0	69.2±10.2
Ⅰ　级	6	40.2±13.0	83.0± 5.2	125.0±13.8	76.7± 8.2
Ⅱ　级	6	66.0± 9.4*	83.3± 9.7	133.6± 8.7	82.4± 5.6
Ⅲ　级	5	62.0±15.1	92.0± 7.3	129.7±12.4	80.3± 7.1
Ⅳ　级	7	46.7±17.6	92.9±13.3	131.2±24.6	70.8±14.3

注：辨证分型时，1 例心阴虚患者未列入；与Ⅰ级组比，*$P<0.05$

值$<F_{0.05}$，再进行均数间比较。对 irANP 值先进行正态纠正(取对数)，再用 t 检验比较。对 EF 和 irANP 的关系用直线相关法分析。其它均数都直接用 t 检验比较。定性数据(胸片表现)用 X^2 试验比较。

结　　果

一、临床情况：心虚证患者（包括单纯心虚组和心气虚组）中有高血压性心脏病伴冠心病 7 例，冠心病 5 例，风湿性瓣膜性心脏病和肺源性心脏病各 3 例。其中严重心衰（Ⅲ～Ⅳ　分级也是一致的(表 2)。

表 2　血浆irANP与中医辨证、心功能的关系

中医辨证	例数	相应的心功能	irANP (pg/ml)	心功能 (NYHA)	例数	irANP (pg/ml)	左室喷血分数 (%，M±SD)
心气虚重证	5	Ⅳ (5)	1069.6△	Ⅳ	7	920.9*	33.05±20.19(4)
心气虚轻证	6	Ⅳ(2)　Ⅲ(4)	534.9△	Ⅲ	5	304.8*	38.89±17.18(2)
心阴虚证	1	Ⅱ (1)	158.5	Ⅱ	6	25.5	50.37± 5.2 (4)
单纯心虚证	6	Ⅲ(1)　Ⅱ(3)　Ⅰ(2)	22.8				
非虚证对照	6	Ⅱ(2)　Ⅰ(4)	16.6	Ⅰ	6	16.7	71.37　(1)

注：与下一组比较　△$P<0.001$；　*$P<0.01$；括号内数据均为例数

二、血浆 irANP 结果：见表 2。心气虚　气虚轻证和重证与 NYHA Ⅰ～Ⅳ分级是有重证组明显高于轻证组($P<0.001$)；后者又明显高于单纯心虚组($P<0.001$)，而 1 例心阴虚者 irANP(158 pg/ml)则介于这两组之间；单纯心虚组的 irANP 虽高于非虚证组，但无统计学意义。同样，根据 NYHA 分级，Ⅳ级组明显高于Ⅲ级组，后者又明显高于Ⅱ级组，P 值均<0.01；Ⅱ级组略高于Ⅰ级组($P>0.05$)。中医辨证组和相对应的心功能组间 irANP 均无显著差别，故提示非虚证、单纯心虚证、心气虚轻证和重证与 NYHA Ⅰ～Ⅳ分级是有一定的内在联系的。另外，EF与 irANP 是呈负相关的 ($r=-0.87$，$P<0.01$)。

三、血液流变学结果：6 例心气虚患者的全血比粘度低切率 (9.97±5.09) 和高切率 (6.54±2.52) 显著高于 5 例非虚证患者（分别为 7.48±1.96 和 5.02±0.70，$P<0.05$)。心气虚患者的血浆比粘度 (1.76±0.19) 略高于非虚证患者(1.74±0.09)，$P>0.05$。其它指标和血小板聚集功能均无显著差别。未发现血液流变

学指标与 irANP 有明显相关。

讨　论

Burnett 等的研究认为，在无症状左室功能减退（EF＝34±4%）患者中，就有irANP的明显升高。心功能不全患者由于右房压、肺动脉楔压、左室舒张末期容积等的升高，造成心房牵张而使其处于心钠素高分泌状态，并且这些患者 irANP 与 EF、心脏指数呈负相关[1,3~5]。Hirata 等[5]还发现，不同部位的血浆 cGMP 与 irANP 含量是平行的，两者循环水平与心功能不全程度直接相关，且随 NYHA 分级的递增而上升，本文结果与此相似。

本文心气虚患者的表现与心功能 III～IV 级时，活动受限、末梢循环差、代偿性水钠潴留等症状是相似的。而单纯心虚、心阴虚患者的心悸、失眠多梦、健忘、五心烦热及盗汗等表现，符合心功能不全早期植物神经功能紊乱，交感神经功能相对亢进而致的症状。因而，无论从临床表现还是从既往的研究[7]来分析，均提示中医的虚证分型和心功能分级是相关的。本文通过 irANP 这一生化指标，进一步揭示了上述两者的内在联系。

我们曾发现心气虚患者有右房压和肺动脉楔压的升高；有心脏指数和 EF 的降低，并且 EF 在心气虚兼阳虚，心气虚兼阴虚及非心气虚患者中呈递减现象[8,9]；陈氏等研究也曾发现，心阳虚心气虚患者的血浆 cGMP 高于正常人 2～3 倍，也显著高于心阴虚患者。这三结果分别提示心气虚患者有促心钠素分泌的因素存在；有与 irANP 负相关因素的降低；有 irANP 升高的间接证据。所以尽管本项研究测定例数有限，但仍表现有心气虚重证及轻证、心阴虚、单纯心虚及非虚证患者的 irANP 含量的递减现象。

在心气虚或 III～IV 级患者中，irANP 虽明显高于其它组，但未表现出血管扩张、血压下降及排钠利尿作用，其原因可能有：（1）心钠素形式的不均一性。心力衰竭患者是处于心钠素的高分泌状态，可能超过了某些酶的加工处理能力，致使无明显生物活性的 β、γ 链释入外周血。（2）长期的高心钠素水平，可能使靶组织的反应性降低。（3）高血压、动脉硬化、慢性心力衰竭等都可造成肾血液动力学的异常，致使肾脏对心钠素的特异性效应降低。（4）心钠素受体本身的变构。

心钠素分泌除受心房牵张影响外，还与年龄、时间、体位、摄钠量及某些药物有关。Ohiashi等认为在大于 65 岁的老人中有心钠素分泌的代偿性升高。但我们II级组患者年龄 66.0±9.4 岁，虽高于 I 级组，但 irANP 却未发现有显著差别。我们注意控制了饮食、采样时间与体位。但由于病情的限制，患者或多或少地服用不同种类药物。尽管 Detz 等[4]认为：异山梨醇、利尿剂、硝酸甘油类药物对 irANP 无明显影响，但皮质激素、钙离子阻滞剂及转换酶抑制剂对心钠素的合成、分泌、代谢两条环节有影响，因而可造成一定的误差，这有待于进一步研究时予以除外。

参 考 文 献

1. Arend RM, et al. Molecular weight heterogeneity of plasma-ANP in cardiovascular disease. Klin Wochenchr 1986; 64 (Suppl VI): 97.
2. Nishiuchi T, et al. Radioimmunoassay for atrial natriuretic peptide; method and results in normal subjects and patients with various diseases. Clinica Chimica Acta 1986; 159: 45.
3. Ogawa K, et al. Plasma atrial natriuretic factor in congestive heart failure. Lancet 1986; 1: 106.
4. Dietz R, et al. Pressure dependent release of atrial natriuretic peptide (ANP) in patients with chronic cardiac disease; Does it reset? Klin Wochenschr 1986; 64 (Suppl VI): 42.
5. Hirata Y, et al. Plasma concentrations of α-human atrial natriuretic polypeptide and cyclic GMP in patients with heart disease. Am Heart J 1987; 113: 1463.
6. 董其美，等. 心脏病的中医虚证分型与心功能关系的探讨. 中西医结合杂志 1985; 5(3): 148.
7. 舒乃华，等. 气虚型心肌梗塞患者的心功能特点及综合治疗的初步探讨. 上海中医药杂志 1984; (4): 11.
8. 陈泮藻，等. 心钠素快速放射免疫分析. 中华核医学杂志 1986; 6(3): 147.
9. 戚瑞鸿，等. 丹参和黄芪治疗气虚血瘀型心力衰竭的作用. 上海医科大学学报 1987; 14(4): 301.

Preliminary Observation of Atrial Natriuretic Peptide in the Patients with Cardiac Deficiency and Discussion of Its Clinical Significance

Yu Bing(俞　兵), Dai Ruihong(戴瑞鸿), et al
Dept. of Internal Medicine, Hua Shan Hospital; Research Unit of Cardiology, the Research Institute of the Integration of Traditional and Western Medicine; Shanghai Medical University, Shanghai

Immunoreactive atrial natriuretic peptide (irANP) has been measured in 24 patients of various cardiac diseases by radioimmunoassay. According to the TCM, these patients were divided into 4 groups: cardiac energy deficiency mild (A) and severe (B) groups; simple cardiac deficiency (C); and the control (D). The New York Heart Association (NYHA) classification of cardiac function in 5 cases of group A were all degree Ⅳ; in 6 cases of group B were 2 of degree Ⅳ and 4 of degree Ⅲ; in 6 cases of group C were 1 of degree Ⅲ, 3 of degree Ⅱ and 2 of degree Ⅰ; and in 6 cases of group D were all degree Ⅰ. The results of chest X-ray and echocardiogram suggested that the classification of cardiac function was objective. The quantity of irANP in group A-D and NYHA Ⅳ～Ⅰ decreased gradually and was correlated with left ventricular ejection fraction ($r=-0.87$, $P<0.01$). The average amounts of irANP in the different TCM groups A-D were at the equavelent levels in the groups NYHA Ⅳ～Ⅰ. Meanwhile it was found that the cardiac energy deficiency patients had abnormality in some parameters of hemorrheology, but no correlation with irANP. it suggested that the diagnosis of cardiac deficiency by TCM was correlated with the different degree of NYHA in the sense of biochemical index of irANP. The irANP might be considered as one of the objective signs of the cardiac energy deficiency, which also might represent the severity of the disease.

(Original article on page 526)

Clinical and Experimental Studies of Yiqi Huoxue Principle (益气活血法) in Treating Ulcerative Colitis

Zhao Hui(赵　辉), Zhou Jiangzhong(周建中)*
The People's Hospital, Beijing Medical University
**Xiyuan Hospital, China Academy of TCM, Beijing*

Yiqi Huoxue principle (YH) was applied to treat 30 cases of ulcerative colitis while Yiqi Jianpi (益气健脾) and Qingre Qushi(清热祛湿) principle (YJQQ), which had been proved its therapeutic effect, was used as the control therapy. The herbal medicines were taken by oral and enema. The course of treatment was 6 weeks. The length, wet and dry weights of thrombus, the platelet adherence and the r, k, Ma, M values of thrombelastogram were measured before and after medications. Before medication, the value mentioned above were all abnormal in both YH and YJQQ group. After medication, with alleviation of the symptoms and signs of the colitis, all these values trended gradually to normal levels ($P<0.01$). The rat models of ulcerative colitis were made by immunological and local stimulation methods. The models were divided into three groups: YH(Ⅰ), YJQQ(Ⅱ) and water group(Ⅲ). Three weeks after medication, the results showed that the lesion degree of the colon, the length and weight both wet and dry thrombus were remarkably lower in group Ⅰ than those in group Ⅲ. It was also showed that there was a positive correlation between the lesion degree of colon and the dry weight of thrombus ($r=0.7941$, $P<0.01$). It suggested that the therapeutic effects of YH was similar to those of YJQQ in treating ulcerative colitis.

(Original article on page 529)

The Efficacy of Electromyographic Biofeedback Treatment on Cardiovascular Disease and the Correlation Between Type A Behavior and TCM Syndrome Differentiation

Yang Juxian(杨菊贤), et al
Dept. of Internal Medicine, the Ninth People's Hospital, Shanghai Second Medical University, Shanghai

Using the method of trilineal relaxation training, electromyographic biofeedback technic (EMGBT) in the treatment of 400 cases of cardiovascular disease was reported. There were 274 (68.5%) cases of hypertension and coronary heart disease, more than other diseases. After treatment, average systolic blood pressure reduced 1.85 Kpa (13.86 mmHg), and average diastolic blood pressure reduced 1.29 Kpa (9.73 mmHg). The treatment was more effective for the type A behavior patients, so was it in the treatment of various extrasystoles (75%). To analyse the correlation between TCM syndrome differentiation and behavior pattern, it was found that there were 90.66% of Heart Yin(阴)