

消补减肥片对高脂血症影响的临床研究

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内容提要 本研究观察了中药消补减肥片对31例虚实夹杂型高脂血症患者的血液TC, LDL-C, apo(载脂蛋白)B, apoA₁/以及TC/HDL-C和apoA₁/B比值的影响, 并以20例服防风通圣散作比较。结果提示: 消补减肥片在明显改善虚实夹杂证的同时, 具有降低血中TC, LDL-C, apoB的水平和改善TC/HDL-C和apoA₁/B比值的作用, 优于防风通圣散。

关键词 消补减肥片 高脂血症 TC apoB

高脂血症是引起动脉粥样硬化(AS)的主要原因之一, 而高胆固醇血症的致AS作用则已是无可争议的事实^(1,2)。一般认为, 降低血中TC, LDL-C, apoB和升高HDL-C和apoA, 能够预防和治疗AS⁽³⁾。我们于1989年3~6月观察了中药消补减肥片对虚实夹杂证型高脂血症的临床疗效, 现将结果报告如下。

临床资料

一、病例选择: (1)年龄≥40岁; (2)血清≥230mg/dl, 经二次核实; 且最近1月未服降脂药物治疗者; (3)经询问病史, 体检及实验室检查, 除外有明显肝肾功能不全, 糖尿病及甲状腺疾病, 无严重烟酒嗜好及应用避孕药者; (4)临床表现符合虚实夹杂证型。其主证辨证标准是: A: 气短, 疲倦乏力, 头晕, 腰膝酸软, 舌体胖淡。B: 胸闷, 腹胀满, 舌苔腻。具有主证A中3项及B中1项即可入选。

二、一般资料: 51例中, 男30例, 女21例; 年龄40~67岁, 平均52±7.4岁; 单纯血清TC升高37例, 伴血清TG升高14例; 单纯性高脂血症42例, 伴有陈旧性心肌梗塞4例, 伴有高血压病4例, 伴胆石症术后1例。患者被随机分为治疗组和对照组, 治疗组31例, 对照组20例。两组在年龄, 性别, 体重, 症状积分值和各项血脂水平方面的情况均相当。

三、检测方法: 所有病例至少空腹12h采血, apo管用EDTA Na₂抗凝(1mg/ml)。抽血静置1h后离心分离血清或血浆。立即检测或

放置冷藏室, 血脂于1周内成批测定, apo则于1月内检测。

1. TC检测用酶法⁽⁴⁾, 三酶试剂为上海第十八制药厂产品, HDL-C用硫酸葡聚糖和氯化镁沉淀法⁽⁵⁾, 试剂为广东普宁县洪阳化学试剂厂产品, 然后用酶法测定TC。LDL-C用Friedewald公式换算⁽⁶⁾。

2. apoA₁和apoB用单向免疫扩散法⁽⁷⁾, 试剂盒由中日友好医院内分泌研究室提供。脂质测定用北京市质控血清控制, 仪器用美国SBA 300型自动生化仪。apo测定由试剂盒配备的质控血清控制。

3. 体重指数: 按体重(kg)/身高(m)²计算⁽⁸⁾。

治疗方法

采用单盲法, 治疗组服消补减肥片, 每片0.5g, 每次6~8片, 每日3次, 饭前半小时服。对照组服防风通圣散片, 每片含量、用量及用法与消补减肥片相同。疗程均为1个月。治疗期间停用一切影响血脂的药物, 饮食及生活习惯不改变。每1~2周复查一次, 观察用药及症候演变。疗程结束时复查体重、各项血脂及肝功能等。

药物制剂: 消补减肥片: 主要由黄芪、蛇床子、白术、大黄、姜黄、香附等组成。防风通圣散: 按刘完素《宣明论》原方配制。以上两药均由西苑医院药厂生产, 制剂均为片剂。两药形状、气味及包装均非常相似, 难于辨认。

统计方法: 治疗前后血脂数值变化的显著性分析用 t 检验。两组症状的有效率比较用 χ^2 检验。

结 果

一、疗效评定标准

1. 血脂: (1) 血清 TC 水平: 显效: 血清 TC 下降 $\geq 20\%$; 有效: 血清 TC 下降 $20\sim 10\%$; 无效: 血清 TC 下降 $\leq 10\%$ 。(2) 对 LDL-C, apoB 值及 apoA₁/B 和 TC/HDL-C 比值的影响采用自身及组间比较方法进行评价。

2. 症状按积分计算予以评定: 3 分: 症状主动诉说或反复出现, 2 分: 症状时轻时重或间断出现, 1 分: 症状轻或偶尔出现, 0 分: 无明显症状。治疗前治疗组和对照组平均积分值分别为 13.7 ± 5.65 和 13 ± 4.74 。按积分拟定疗

效评定标准: 显效: 积分值下降 ≥ 8 分; 有效: 积分值下降 $5 \sim 7$ 分; 无效: 积分值下降 $0 \sim 4$ 分。

3. 体重指数: 采用自身及组间比较方法进行疗效评价。

二、结果

1. 消补减肥片对血清 TC, LDL-C, HDL-C 和 TC/HDL-C 的影响, 见表 1。消补减肥片能显著地降低血清 TC, LDL-C 的水平 and 降低 TC/HDL-C 比值。对照组也能降 TC, 但不如消补减肥片 ($P < 0.01$) 明显。对照组对 LDL-C 和 TC/HDL-C 无明显作用。两药对 HDL-C 水平平均无明显的影响。另外, 还统计了两药降 TC 的有效率。结果是: 消补减肥片降 TC 的总有效率为 87% ; 防风通圣散组则为 60% , 两者差异有显著性 ($P < 0.05$)。

2. 消补减肥片对 apoA₁, apoB 和 apoA₁/B

表 1 消补减肥片对 TC, LDL-C, HDL-C 和 TC/HDL-C 的影响 ($\bar{x} \pm S$), 下同

组 别		例数	TC (mg/dl)	LDL-C (mg/dl)	HDL-C (mg/dl)	TC/HDL-C
治 疗	前 后	31	270±31.8	176.1±31.8 ⁺	62.7±13.4	4.5±0.9
			201±44△△***	116.4±45.7△△△***	59.7±13.6	3.5±0.9**
对 照	前 后	20	270±39.1	171.1±39.2	62.3± 9.4	4.3±0.6
			243±51 [*]	159.8±51.3	61.0±12.1	4.1±1.25

注: 自身比较: $*P < 0.05$; $**P < 0.01$; $***P < 0.001$; 组间比较: $\Delta \Delta P < 0.01$; $\Delta \Delta \Delta P < 0.001$ 。+ 例数为 29, 因 2 例 TG 值大于 400 mg/dl , 不适于公式求出。

比值的影响, 见表 2。消补减肥片降低 apoB 作用非常显著, 并能明显升高 apoA₁/B 的比值; 防风通圣散则无此作用。

表 2 消补减肥片对血浆 apoA₁, apoB 水平和 apoA₁/B 比值的影响

组 别	例 数	apoA ₁ (mg/dl)	apoB (mg/dl)	apoA ₁ /B ₁	
治 疗	前 后	31	130±18.2	180±33.3	0.775±0.19
			129±21.2	133±34.9 ^{***} ΔΔΔ	1.021±0.29ΔΔ
对 照	前 后	20	138±18.5	178±41.9	0.816±0.25
			125±23.8	174±54	0.770±0.33

注: 自身比较: $***P < 0.001$; 组间比较: $\Delta \Delta P < 0.01$, $\Delta \Delta \Delta P < 0.001$

3. 消补减肥片对症状和体重指数的影响:

(1) 我们采用症状积分法评价两药对症状

的疗效。结果表明两药均有效, 但消补减肥片组的积分值下降幅度 (9.45 ± 4.7 分) 明显大于防风通圣散的下降幅度 (3.75 ± 3.8 分), $P < 0.001$ 。消补减肥片和防风通圣散对症状改善的总有效率分别为 83.9% 和 55% , 两者有统计学差异 ($P < 0.025$)。(2) 消补减肥片尚有降低体重指数的作用。治疗组的体重指数从服药前的 25.87 ± 2.80 下降到服药后的 25.00 ± 2.80 ($P < 0.001$)。而对照组则无此作用。

患者服消补减肥片后, 除个别出现腹痛或大便稀外, 未见其它不良反应, 一般不影响治疗。

讨 论

一、消补减肥片具有较好的脂质调节作用

许多研究结果表明,高脂血症是引起冠心病(CHD)的主要原因之一。TC、LDL-C和apoB与CHD呈正相关,HDL-C和apoA与CHD呈负相关。这些研究进展促使人们重新考虑对高脂血症的治疗方案。一般认为降低TC,LDL-C和apoB,升高HDL-C和apoA的水平;以及调整TC/HDL-C,LDL-C/HDL-C和apoA/B等比值,对预防和治疗CHD是有益的。由于多数降脂西药存在或多或少的副作用而限制了其普遍使用。

根据高脂血症患者的临床表现,本病似应属于中医学的痰浊、湿阻范畴。外因是由于过食膏粱厚味或嗜酒无度,酿痰生湿。内因则由于脾虚失运,水谷肥甘之物无以化生气血精微而生痰生湿,与现代医学认为超热量摄入及脂质代谢失调是引起脂质升高的认识颇为相似。临床症候所见,患者常表现为虚实夹杂证。本研究所用消补减肥片是以补虚去实,针对虚实夹杂证而设。结果观察到本方可使血中TC、LDL-C和apoB明显下降。尽管防风通圣散亦能降TC,但明显不如本方,且后者对LDL-C和apoB并无明显影响。由于以脂质为主的LDL₁和以蛋白质为主的LDL₂的增高均可升高TC。后者可能是apoB分泌过多所致,具有特殊的致AS作用。而通常的降TC药物可能对apoB无治疗作用,是不够理想的;本方具有兼治作用,则是较为理想的药物。此外,本文病例TC/HDL-C大于4.5,apoA₁/B明显低下,有较明显的异常。目前认为这两项更能反映脂质代谢失调情况^(9,10)。经服消补减肥片后,这两项比值得到良好的纠正。表明此药在治疗高脂血症方面,有深入研究的价值。

二、消补减肥片对高脂血症病人症状有较好的治疗作用。

本文观察的高脂血症病人是以头晕,气短乏力,胸闷,腹胀满和腰膝酸软等为主要症状。属于脾肾气虚,浊阻中焦之虚实夹杂证型,服消补减肥片后,虚实夹杂证型高脂血症患者的症状总积分值明显下降,对症状改善的总有效率为83.9%,明显优于防风通圣散的55%。说

明采用补虚泻实法治疗虚实夹杂型高脂血症明显优于单纯的泻实疗法。此外,消补减肥片尚有明显降低体重指数作用。肥胖是多种疾病发病的危险因素。肥胖与TG,LDL-C和apoB呈正相关,与HDL-C和apoA呈负相关。本文病例的体重指数平均在25以上,说明大部分病人已是超重了。服消补减肥片后,体重指数明显降低,这一减肥作用可能与前面谈及的降脂调脂有关。

现代研究表明,消补减肥片所用药物具有提高机体免疫力,调理肠胃,利胆降脂,调节内分泌之效。因而本方在调节脂质代谢及改善中老年高脂血症患者症候方面可以取得一定效果。

参 考 文 献

1. Carlson LA, et al. Ischaemic heart-disease in relation to fasting values of plasma triglycerides and cholesterol. *Lancet* 1972; 1:865.
2. Wilhelmsen L, et al. Multivariate analysis of risk factors for coronary heart disease. *Circulation* 1973; 48:950.
3. Tyroler HA. Lowering plasma cholesterol levels decreases risk of coronary heart disease: An overview of clinical trials. In: Steinberg D & Olefsky JM. Hypercholesterolemia and atherosclerosis pathogenesis and prevention. Churchill Livingstone INC; New York 1987; 99.
4. 韩琴琴,等.应用国产酶试剂测定血清胆固醇和高密度脂蛋白胆固醇(HDL-C)的方法. *上海第一医学院学报* 1984; 11(3):131.
5. 李丹宇,等.血清高密度脂蛋白亚组的分离及其胆固醇含量的测定. *上海第一医学院学报* 1984; 11(4):184.
6. Friedewald WT, et al. Estimation of concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin Chem* 1972; 18:499.
7. 刚勇,等.人血浆载脂蛋白B的单向免疫扩散测定及其临床应用. *中华医学检验杂志* 1987; 10(4):202.
8. 彭孝廉.中老年的肥胖倾向及其后果. *中华老年医学杂志* 1988; 7(3):177.
9. Gotto AJ. Treatment of hyperlipidemia. *AM J Cardiol* 1986; 57(1):11.
10. Avogaro P, et al. Are apolipoproteins better discriminators than lipids for atherosclerosis. *Lancet* 1979; 1:901.

Application of Xin Bao(心宝) in the Treatment of 87 Patients with Sick Sinus Syndrome

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Since 1987, the authors have observed the therapeutic effect of Xin Bao on 87 patients with sick sinus syndrome. Electrophysiological stimulation examination: SNRT > 1900 ms and CSNRT > 600 ms in all patients. Routine ECG and Holter monitoring ECG: (1) Persistent sinus bradycardia or/and atrio-ventricular junction escape rhythms or/and premature beat, heart rate $< 48 \pm 6$ beats/min in 40 patients; (2) sinus standstill (arrest) or secondary degree sinoatrial block in 10 patients; (3) bradycardia-tachycardia syndrome in 30 patients; (4) the heart rate > 60 beats/min in 7 patients. The major symptoms were dizziness, palpitation, chest press, malaise, remission in memory, nocturia, amaurosis and Adams-Stokes syndrome, etc. Self-comparison was taken. Xin Bao was given 2~10 tablets 2 or 3 times a day by oral administration for 2 months. The major symptoms of sick sinus syndrome was greatly improved after treatment. The total effective rate attaining to 85%. The improvement in heart function was also significant, the total effective rate being 80%. After treatment SNRT and CSNRT were shortened ($P < 0.01$), the total heart beats for 24 hours and the average heart beats/min greatly increased ($P < 0.01$), CO and EF increased too ($P < 0.05$). No serious adverse reactions were found during the treatment. It was believed that Xin Bao could stimulate sino-atrial node and increase its excitability. The basic heart rate was increased and the heart function improved with no adverse reactions. It may be administrated in long term. Therefore, Xin Bao may be recommended as appropriate drug for treating sick sinus syndrome.

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Clinical Study on Hyperlipidemia Treated with Xiaobu Jianfei Pian(消补减肥片)

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A total of 51 cases with hyperlipidemia, who were defined deficiency symptom-complex complicated by symptoms of excessiveness in TCM were studied clinically. The patients were divided into two groups at random. One group was treated with Xiaobu Jianfei Pian (XJP) as treated group, another with Fangfeng Tongsheng San (防风通圣散) as a control. It was found that XJP was able to lower total serum cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and apolipoprotein (apo) B significantly ($P < 0.001, 0.001, 0.001$) while it had markedly improved clinical symptoms. It was also observed that XJP had good effects on the ratios of apoA₁/B and TC/HDL-C, and was able to reduce body weight index. All of these were better than those of the control group statistically. These evidences indicate that XJP possesses clinical therapeutic effects on both lipid-lowering and lipid-adjusting, which suggest that XJP may be an effective anti-hyperlipidemia medicine.

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Study on Immune Function of Cancer Patients with Spleen-Deficiency Syndrome

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According to this study, the immunological function was aberrant in cancer patients with Spleen-deficiency syndrome. The T_H cell in normal persons (n=26) was $30.86 \pm 9.70\%$ ($\bar{x} \pm S$) and in these cases (n=43) was $22.62 \pm 9.92\%$, $P < 0.002$. The cytotoxicity of NK cell in patients (n=59) was $17.65 \pm 10.58\%$, in normal controls (n=43) was $25.51 \pm 14.10\%$. The combining ability of NK cell in patients (n=48) was $39.11 \pm 19.43\%$, the normal persons (n=41) was $55.88 \pm 17.94\%$. It showed that the immune function of the cancer patients with Spleen-deficiency syndrome were markedly lower than that of normal persons. The serum IgA in saliva of patients (n=37) was $0.44 \pm 0.17 \mu\text{g/ml}$. It was much higher than that of normals (n=24, $0.30 \pm 0.06 \mu\text{g/ml}$), $P < 0.001$. Some patients' NK cell function and the level of SIgA in saliva were recovered to normal after treatment of Shengxue Tang (升血汤) which could strengthen the Spleen and replenish the Kidney. These studies proved that the TCM played an important role for modulating immune function in treating cancer patients.

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