

自拟健脾化湿汤治疗非酒精性脂肪肝 53 例疗效观察

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摘要 目的:观察自拟健脾化湿汤治疗脾虚湿蕴证非酒精性脂肪肝的疗效。方法:对 106 例脾虚湿蕴证非酒精性脂肪肝患者按就诊顺序 1:1 等分为自拟健脾化湿汤方治疗组、对照组两组,每组病例 53 例。两组患者在强调戒酒、控制饮食、加强运动的基础上,治疗组采用自拟中药健脾化湿汤治疗,对照组选用多烯磷脂酰胆碱胶囊治疗。用药疗程为 3 个月,疗程结束后统计疗效。结果:两组患者症状疗效比较,治疗组明显优于对照组($P<0.01$);两组患者治疗前后肝功能变化比较,治疗组优于对照组($P<0.05$);两组患者治疗前后血脂变化比较,治疗组优于对照组($P<0.05$);两组治疗前后 CT 检查结果比较,治疗组优于对照组($P<0.05$)。结论:自拟健脾化湿汤治疗脾虚湿蕴证非酒精性脂肪肝疗效显著。

关键词 非酒精性脂肪肝 治疗 脾虚湿蕴 中医药疗法

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Curative Effect on the Treatment of 53 Cases of Non-alcoholic Fatty Liver with the Self-prescribed Jianpihuashitang Decoction

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ABSTRACT Objective: To observe the efficacy of Self-prescribed Jianpihuashitang Decoction on Spleen Deficiency, and Damp Retention of Non-alcoholic Fatty Liver. **Methods:** 106 cases of spleen deficiency with damp retention of non-alcoholic fatty liver were allocated equally to group treated with self-prescribed Jianpihuashitang Decoction, and the control group, each group had 53 cases. Two groups were all on the basis of abstinence from alcohol, adherence to a diet and increase of physical activity. Treatment group was given self-prescribed Jianpihuashi Decoction, the control group was given polyene phosphatidyl choline capsules. After 3 months of treatment. **Results:** The symptoms and efficacy of two groups of patients were compared, the effect of the treatment group significantly surpasses the control group ($P<0.01$). The liver function before and after treatment were compared, the effect of the treatment group significantly surpasses the control group ($P<0.05$). The lipid changes before and after treatment were compared, the effect of the treatment group significantly surpasses the control group ($P<0.05$). The CT findings before and after treatment were compared, the effect of the treatment group significantly surpasses the control group ($P<0.05$). **Conclusion:** Self-prescribed Jianpihuashi Decoction shows significant effects on spleen deficiency with damp retention of non-alcoholic fatty liver treatment.

Key words: Non-alcoholic Fatty Liver; Treatment; Spleen Deficiency Damp Retention; Traditional Chinese Medicine

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前言

非酒精性脂肪肝是指一种并非因饮酒过量引起的,以肝实质细胞细胞脂肪变性和脂肪贮积为特征的临床病理综合征。本病属于中医“胁痛”、“积聚”等范畴。近年来,随着人们生活水平的不断提高与人们生活方式的改变,脂肪肝的发病率逐渐升高,非酒精性脂肪肝也已成为最常见的慢性肝病之一。本病的发病率 5%-20%^[1]。自 2008 年 08 月至 2010 年 08 月笔者采用健脾化湿汤治疗非酒精性脂肪肝 53 例,取得了满意的临床疗效。现报告如下:

1 临床资料

1.1 一般资料

选择 2008 年 8 月—2010 年 8 月房山区中医院门诊及住院病例,符合纳入标准的病例共 106 例,其中男性 56 例,女性 50 例,平均(41.5±5.4)岁,病程(5.24±4.36)年。并按就诊顺序 1:1 等分为自拟健脾化湿汤方治疗组、对照组两组。治疗组男性 29 例,女性 24 例,平均(40.9±5.6)岁,病程(5.27±4.28);对照组男性 27 例,女性 26 例;平均(41.9±6.1)岁;病程(5.19±4.41)。经统计学处理,两组性别、年龄、病程、肝功能、血脂及 CT 检查无显著性差异,具有可比性($P>0.05$)。

1.2 诊断标准

1.2.1 西医诊断标准 参照中华医学会脂肪肝和酒精性肝病学组 2006 年制订的《非酒精性脂肪性肝病诊疗指南》^[2],符合非酒精性脂肪肝诊断:①无饮酒史或饮酒折合乙醇量男性每周<140g,女性每周<70g;②除外病毒性肝炎、药物性肝病、全胃肠外营养、肝豆状核变性等可导致脂肪肝的特定疾病;③除原发疾病临床表现外,可有乏力、消化不良、肝区隐痛、肝脾肿大

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等非特异性症状及体征 ④存在代谢综合征或不明原因性血清 ALT 水平升高持续 4 周以上 ；⑤影像学表现符合弥漫性脂肪肝诊断标准。

1.2.2 中医证候诊断标准 中医证候诊断标准 参考《中医消化病诊疗指南》非酒精性脂肪肝中医证候诊断标准^[1]。中医辨证属脾虚湿蕴证。辨证标准及其依据 ⑴主症 ①胸脘痞闷 ；②倦怠乏力 ；③胁肋胀满或疼痛。⑵次症 ①食欲不振 ；②面色萎黄 ；③恶心欲吐 ；④舌淡苔白腻 ；⑤脉细弱。其具备主症中二项 加次症二项者即可诊断。

1.3 入选标准

(1)房山区中医医院门诊及住院病例 符合非酒精性脂肪肝诊断 ；(2)中医符合脾虚湿蕴证 ；(3)患者年龄 18-65 岁 ；(4)实验前 2 周内未接受同类药品治疗者 ；(5)自愿参加本研究 ；签署知情同意书 ；依从性好 ；可随访者。

1.4 排除标准

(1)哺乳、妊娠期或正准备妊娠的妇女 ；(2)过敏体质及对本研究已知成分或其他药物过敏者 ；(3)精神病患者 ；(4)目前参加其他临床实验的患者。

1.5 研究方法

1.5.1 治疗方法 两组患者在强调戒酒、控制饮食、加强运动的基础上。治疗组采用自拟中药健脾化湿汤(成分：太子参 15g、茯苓 10 g、白术 10 g、甘草 10 g、半夏 9 g、陈皮 10 g)，每日 1 剂，水煎服，取汁 300 mL，150 mL/ 次，日两次。

对照组选用多烯磷脂酰胆碱胶囊(北京安万特制药有限公司生产)，3 次 /d，2 粒 / 次。

用药疗程为 3 个月，疗程结束后统计疗效。

1.5.2 观察方法 观察两组患者(1)肝功能：血清丙氨酸氨基转

移酶(ALT)、天冬氨酸转移酶(AST)和谷氨酰转肽酶(GGT) ；(2)血脂：甘油三酯(TG)、总胆固醇(TC)、高密度脂蛋白胆固醇(HDL-C) ；(3)弥漫性肝脏密度降低，肝脏与脾脏的 CT 值之比小于或等于 1。弥漫性肝脏密度降低，肝 / 脾 CT 比值≤ 1.0 但大于 0.7 者为轻度，肝 / 脾 CT 比值≤ 0.7 但大于 0.5 者为中度，肝 / 脾 CT 比值≤ 0.5 者为重度。统计两组患者证候积分、肝功能、血脂及肝脏 CT 检查，并进行比较。

1.6 统计学方法

以 SPSS 13.0 进行数据统计，计量数据以均数± 标准差($\bar{X} \pm S$)表示，计数资料方法使用 χ^2 进行检验， $P < 0.05$ 为有统计学意义。

1.7 疗效观察

1.7.1 疗效评定标准 疗效评定标准参照《中医消化病诊疗指南》非酒精性脂肪肝的标准修订^[1]。临床痊愈：症状、体征消失，影像学检查肝脏形态及实质恢复正常，血脂各项指标及血清转氨酶恢复正常。

显效：症状消失，体征明显减轻，影像学检查重度脂肪肝恢复为轻度或中度、轻度脂肪肝恢复为正常。血脂改善达到以下任意一项：TC(总胆固醇)下降≥ 20%，TG(甘油三酯)下降≥ 40%，HDL-C 上升≥ 0.26 mmol/L。

有效：症状减轻，影像学检查重度脂肪肝恢复为中度或中度脂肪肝恢复为轻度，血清转氨酶好转，血脂改善达到以下任意一项：TC 下降≥ 10%但 <20%，TG 下降≥ 20%但 <40%，HDL-C 上升≥ 0.104 mmol/L 但 0.26 mmol/L。

无效：症状及体征无改善，影像学检查脂肪肝程度及血清转氨酶、血脂无改善。

2 结果

表 1 两组患者症状疗效比较[例(%)]

Table 1 Comparison of the symptoms of Two Groups of patients [Cases(%)]

Group	n	Clinically cured	Significant effect	With effect	No effect	Effective rate
Treatment group	53	15	25	7	6	47(88.68)**
Control group	53	9	12	14	18	35(66.04)

Note: ** $P < 0.01$ Comparison with control group.

表 2 两组患者治疗前后肝功能变化比较($\bar{X} \pm S$, U/L)

Table 2 The comparison of liver function before and after treatment of two groups ($\bar{X} \pm S$, U/L)

Group		ALT	AST	GGT
Treatment group (n = 53)	Before Treatment	53.86± 34.75	34.59± 19.72	64.11± 21.15
	After Treatment	36.56± 15.24*	27.03± 8.08*	45.21± 19.42*
Control group (n = 53)	Before Treatment	55.50 ± 35.71	37.06± 18.31	63.23± 20.91
	After Treatment	45.69 ± 21.72	31.67 ± 9.96	52.20± 18.51

Note: * $P < 0.05$ Comparison with control group before and after treatment.

3 讨论

近年来,由于人们生活水平的提高,非酒精性脂肪肝发病率逐年增加。但其发病机制尚未完全明确,日前认为主要与胰岛素抵抗、游离脂肪酸增加引起的糖脂代谢紊乱(第一次打击)和

氧化应激 / 脂质过氧化因素(第二次打击)有关^[3]。代谢综合征包括肥胖、高脂血症、高血糖、高血压,它们是非酒精性脂肪肝已知的重要危险因素^[4]。21%-61%非酒精性脂肪肝患者存在高脂血症^[5]。脂肪肝病理变化之一为肝细胞膜、细胞器膜受损及膜磷脂的丧失。由于肝细胞膜和线粒体膜的脂质富含多种不饱和

表 3 两组患者治疗前后血脂变化比较($\bar{X} \pm S$, mmol/L)
Table 3 The comparison of lipids before and after treatment of two groups($\bar{X} \pm S$, mmol/L)

Group		TC	TG	HDLc
Treatment group (n = 53)	Before Treatment	4.60 ± 0.71	2.02 ± 0.92	0.88 ± 0.16
	After Treatment	3.95 ± 0.77	1.49 ± 0.87*	0.90 ± 0.23
Control group (n = 53)	Before Treatment	4.53 ± 1.12	2.31 ± 0.96	0.90 ± 0.24
	After Treatment	4.25 ± 1.06	2.06 ± 0.95	0.91 ± 0.36

Note: *P<0.05 Comparison with control group before and after treatment.

表 4 两组治疗前后 CT 检查结果比较($\bar{X} \pm S$)
Table 4 The comparison of CT exam before and after treatment of two groups($\bar{X} \pm S$)

Group		Liver CT value(Hu)	Spleen CT value(Hu)	CT ratio of liver and spleen
Treatment group (n = 53)	Before Treatment	37.51 ± 13.26	51.42 ± 3.31	0.71 ± 0.24
	After Treatment	45.45 ± 8.76*	51.44 ± 3.10	0.90 ± 0.13*
Control group (n = 53)	Before Treatment	37.05 ± 11.24	51.02 ± 2.67	0.72 ± 0.23
	After Treatment	40.24 ± 11.58	51.10 ± 2.78	0.78 ± 0.21

Note: *P<0.05 Comparison with control group before and after treatment.

脂肪酸,且线粒体代谢活跃,因而在致病因素作用下更容易引起生物膜的损伤^[6]。该病并非良性的病理过程,被认为是一种进展性肝病,不仅是隐源性肝硬化的重要病因^[7]。而且,有研究表明肝细胞癌可视为脂肪型肝炎的晚期并发症^[8]。因此,对该病的早期诊断及治疗非常重要。

我国古代医家将脂肪肝归属于“胁痛”、“积聚”等范畴。自拟健脾化湿汤由太子参、茯苓、白术、甘草、半夏、陈皮组成。太子参、茯苓、白术健脾益气,半夏、陈皮化湿,甘草调和诸药,共奏健脾化湿之效。

现代科学研究,Hiroshi Sakugawa 等^[9]对日本 4211 例女性体检的资料分析发现,GGT 独立于脂肪肝,直接与代谢综合征密切相关,Lonardo A^[10]、Yesilova Z^[11]等亦发现 GGT 其水平持续增高可反映胰岛素抵抗(IR),与高 TG 血症及糖尿病的存在有关。最新研究表明,成纤维细胞生长因子 21(FGF21)是一种新的代谢调节因子,具有降糖、降脂、降低胰岛素水平,逆转肝脏脂肪变性,提高胰岛素敏感性的作用^[12,13]。多烯磷脂酰胆碱经口服后,通过淋巴或血液途径最先到达肝脏,并主要聚集于肝脏,其主要活性成分与内源性磷脂相同,能增加肝细胞膜的完整性,流动性和稳定性^[14]。且能通过减少自由基的攻击,降低脂质过氧化损伤,达到保护和修复受损的肝细胞膜。大量的动物实验显示,使用多烯磷脂酰胆碱无中毒的潜在危险,因此被认为是安全无毒的植物类药物之一^[15]。多烯磷脂酰胆碱能提高各种磷脂依赖酶的活性,促使肝内甘油三酯和胆固醇转换成可移动的形式,并得以进行氧化代谢,从而减轻了肝细胞的脂肪变性和坏死,促进了肝细胞的再生。

该研究表明,自拟健脾化湿汤能够改善脾虚湿蕴证非酒精性脂肪肝患者的症状,降低患者血清 TC、TG、ALT、AST 以及 GGT 水平,提高患者肝脏 CT 值及脾脏 CT 比值,具有良好的保肝、降脂的作用,达到了较为理想的治疗脾虚湿蕴证非酒精性脂肪肝的效果。且经比较表明治疗组比多烯磷脂酰胆碱胶囊治疗组疗效更佳。

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(下转第 5260 页)

VEGF^[16]。也有报道认为 CXCL12 与 CXCR4 作用后并没有引起 MMP-9 的增加^[17]。但是尚未见文献报道关于 CXCR4 和 MMP-9 在膀胱移行细胞癌组织中二者的相关性,在膀胱癌浸润过程中是否呈协同作用不得而知。本研究中,采用免疫组化和 RT-PCR 等方法,研究了 CXCR4 和 MMP-9 在膀胱移行细胞癌组织中的表达情况以及相关性,结果表明 CXCR4 和 MMP-9 在膀胱移行细胞癌组织中的表达均高于正常膀胱粘膜,随着浸润深度增加,表达均升高,且二者的表达呈正相关关系($\gamma=0.479$),且 MMP-9 随着肿瘤分级升高而表达增加,而二者均与患者的性别、年龄无关。

因此,我们推测 CXCR4 和 MMP-9 均参与了膀胱癌的浸润与发展,且二者具有协同作用。CXCR4 和 MMP-9 的高表达可以作为判定膀胱癌是否具有高浸润性的一个指标,为临床医生是否采取更加积极的治疗措施提供一种参考,如果能针对 CXCR4 和 MMP-9 这一环节进行靶向治疗,可能会明显改善浸润性膀胱癌的预后。

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(上接第 5338 页)

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