

肝豆片对 34 例肝豆状核变性患者肝脏声像图及其功能的影响

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摘要 本文对肝豆片治疗的 34 例肝豆状核变性(HLD)患者肝脏声像图、血清白蛋白、球蛋白、血清蛋白电泳、24 小时尿铜的变化进行了观察。结果表明,该药有明显的排铜作用,13 例患者肝脏声像图较疗前改善,治疗后血清白蛋白由 $35.35 \pm 6.48\text{g/L}$ 增高至 $38.76 \pm 6.36\text{g/L}$ ($P < 0.05$),球蛋白由 $30.42 \pm 5.88\text{g/L}$ 减低至 $25.61 \pm 6.13\text{g/L}$ ($P < 0.01$),提示中药驱铜治疗可通过减轻肝细胞的铜中毒,促进 HLD 肝硬变及肝脏功能的恢复。

主题词 肝豆状核变性/中医药疗法 @ 肝豆片 肝/超声检查

肝豆状核变性(hepatolenticular degeneration, HLD)是一种常染色体隐性遗传性疾病。由铜代谢异常引致大量铜在肝脏、脑等组织器官中沉积而发病,临床以肝脏损害及锥体外系症状为主要表现。由于肝脏是铜的主要蓄积器官,无论患者是脑型还是肝型,所有患者均表现有不同程度的肝脏损害,很多患者在青少年期即出现乳腺女性化发育、蜘蛛痣、血白蛋白减低、球蛋白增高、门静脉高压等肝硬变表现。促使肝功能的恢复、肝硬变的改善是影响 HLD 患者疗效及长期预后的重要环节之一。为此我们在 34 例患者中观察了中药肝豆片对 HLD 患者肝脏声像图、血清白蛋白(A)、球蛋白(G)、血清蛋白电泳的影响,证实该方可促进 HLD 肝硬变及肝脏功能的改善。

1 临床资料

34 例 HLD 患者均经临床及铜代谢检查符合 HLD 诊断标准^[1]。其中男 21 例,女 13 例。年龄 10~34 岁,平均 17.7 ± 5.6 岁。根据我所的临床分型标准^[2]。34 例患者中典型肝豆状核变性型 11 例,假性硬化型 13 例,肝型 4 例,舞蹈样手足徐动型 4 例,扭转痉挛型 2 例。

肝脏声像图检查及评判标准:采用 Aloke SSD 256 型声像图仪,探头频率 3.6MHz 行肝脏声像图检查。肝脏声像图特征评判标准依据文献进行,由轻至

重脂肪肝分为脂肪均匀浸润型、脂肪非均匀浸润型,肝硬变期分为光点闪烁型、岩层征型、树枝状光带型和结节型^[3,4]。

实验检查方法:血清总蛋白、白蛋白分别采用双缩脲法及溴甲酚绿法,经 TB224 半自动生化仪检测;血清蛋白电泳采用醋酸纤维膜电泳法;尿铜采用火焰原子吸收分光光度计检测。

2 治疗方法

本组入院检查完毕后,<15 岁的患者,予肝豆片 6 片,每日 3 次; ≥ 15 岁予肝豆片 8 片,每日 3 次。肝豆片由合肥中药总厂依据我所改良的肝豆汤处方加工制成。每片含大黄、黄连、姜黄各 0.25g,金钱草、泽泻各 0.625g,三七 0.042g。连续服药 4 周,治疗结束后复查各检测指标。

3 结果

治疗前后肝脏声像图的变化:治疗前 34 例 HLD 患者均表现为不同程度的肝硬变声像图。治疗后声像图改善 2 级者 2 例,1 级者 11 例,无变化者 21 例。改善率 38.24%。见表 1。

表 1 治疗前后肝脏声像图的比较(例)

分型	疗前	疗后				
		结节型	树枝状光带型	岩层征型	光点闪烁型	脂肪非均匀浸润型
结节型	6	5	1			
树枝状光带型	14		8	4	2	
岩层征型	11			6	5	
光点闪烁型	3				2	1

表 2 治疗前后血清白蛋白球蛋白含量变化($\bar{x} \pm s$)

例数	A(g/L)	G(g/L)	A/G
治疗前 34	35.35 ± 6.48	30.42 ± 5.88	1.23 ± 0.46
治疗后 34	$38.76 \pm 6.36^*$	$25.61 \pm 6.13^{**}$	$1.62 \pm 0.57^{**}$

与治疗前比较,* $P < 0.05$,** $P < 0.01$;下同

血清 A、G 含量变化:本组 34 例,治疗后 A 明显升高($P < 0.05$),G 明显降低($P < 0.01$),A/G 明显升高($P < 0.01$)。见表 2。

血清蛋白电泳组分变化:治疗前后比较,白蛋白(A)及 γ 球蛋白(γ -G)差异存在显著性(P 均 < 0.05)。见表 3。

治疗前后 24 小时尿铜变化:治疗前 24 小时尿铜

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表3 治疗前后血清蛋白电泳组分的变化

	例数	A(%)	G(%)			
			α_1	α_2	β	γ
治疗前	34	47.73±6.45	4.61±1.83	8.52±2.76	12.30±9.41	27.38±7.71
治疗后	31	51.52±8.57*	4.33±1.74	7.65±3.38	13.06±3.54	23.83±7.18*

为 $5.03 \pm 3.06 \mu\text{mol}$, 治疗后增高至 $9.54 \pm 5.47 \mu\text{mol}$, 治疗前后比较差异有显著性 ($P < 0.001$)。

4 讨论

肝脏是人体内铜的主要蓄积器官, Scheinberg 等测定正常人肝铜含量为 $16 \sim 31 \mu\text{g/g}$ 干重, HLD 患者则可高达 $2950 \mu\text{g/g}$ 干重, 而且远高于其它脏器^[5]。Deiss 等 1970 年对 HLD 患者体内铜的异常沉着过程进行了研究, 认为 HLD 患儿自出生起至 5 岁左右, 铜已在肝脏中蓄积, 称肝铜蓄积期, 此期可无任何临床症状。5~10 岁进入肝铜饱和释放期, 游离铜在细胞浆内逐渐饱和, 进入溶酶体内, 引起肝细胞弥漫性坏死和显著的肝纤维组织增生, 临床上表现为代偿性肝硬变或活动性坏死后肝硬变。其后由于肝铜的不断释放而引起脑内铜的蓄积并出现脑症状^[6]。病理研究表明, 早期肝脏呈轻度的类脂质小滴沉着, 随之脂质小滴体积和数量增加而呈脂肪变性, 并逐渐出现门静脉系统周围胶质增生和小叶中心静脉周围纤维化。肝细胞则出现浊肿、胞浆稀疏、坏死及核空泡变等^[7]。

肝脏声像图是检测肝组织病变可靠而直观的标志。由于 HLD 是因铜的沉积而导致肝脏病变, 金属离子有更高的声阻抗值, 因此其声像图与肝脏炎症性病变有较大区域^[3]。病变早期的类脂质沉着, 肝脏声像图呈均匀性或非均匀性脂肪肝。进入肝硬变期则由轻至重表现为光点闪烁型、岩层征型、树枝状光带型和结节型。本组 34 例患者均表现不同程度的肝硬变声像学异常, 经治疗 13 例患者出现改善, 改善率 38.24%。表明肝豆片可促进 HLD 患者肝硬变的逆转与恢复。白蛋白在体内由肝脏合成, 肝脏病变时白蛋白合成减少, 导致 A/G 比值减低。患者治疗后白蛋白及 A/G 比值较疗前明显增高, 球蛋白较疗前降低, 更进一步提示肝脏功能的改善。

HLD 的治疗主要是驱铜治疗。国外普遍采用青霉胺、硫酸锌治疗, 但均有较为明显的副反应^[8]。1974 年, 笔者开始探索中医药治疗 HLD, 根据大多数患者有口苦口干、口中臭秽、苔黄腻、脉弦数或弦滑。其病机为铜毒内蕴, 久则致肝胆湿热。并创立清热解毒、通腑利尿之法, 拟以大黄、黄连、泽泻等为主要药物的肝豆汤(片)治疗。方中大黄为君, 具有通腑利湿、清热解毒之功; 黄连、泽泻去中下焦湿热; 金钱草、姜黄主入肝经,

清肝利胆。现代药理研究也表明, 大黄的主要成分番泻甙元, 能刺激大肠壁, 促进其排空以加速排便, 可减少铜离子在肠道中的吸收。大黄、黄连、姜黄、金钱草均有促进胆汁分泌, 并稀释胆汁, 有利于铜从胆汁经粪便排出。同时泽泻、金钱草的利尿作用有助于尿铜的排泄。多年的应用表明该方有明显的临床疗效及很强的尿排铜作用^[9,10]。本组病例经肝豆片治疗后, 24 小时尿铜由疗前 $5.03 \pm 3.06 \mu\text{mol}$ 增高至 $9.54 \pm 5.47 \mu\text{mol}$, 提示治疗期间患者体内大量铜被排出。肝硬变程度声像图的改善, 可能是肝细胞中铜的大量排出, 使部分尚未完全坏死的肝细胞功能得以恢复, 肝脏声阻抗值发生变化所致。另外, 方中田三七具有活血散结作用, 也有益于肝硬变的改善。

肝脏既是铜蓄积的主要器官, 也是铜中毒的主要解毒器官。本研究通过对肝脏声像图等客观指标的观察证实, HLD 经过治疗, 肝硬变程度可以改善, 因此驱铜治疗的同时, 合用促进肝细胞功能恢复的药物增强机体本身的解毒功能, 发挥中医药的优势, 应是 HLD 驱铜治疗的一个重要补充。而肝脏声像图在判断肝脏受损、临床病情严重程度及疗效方面具有重要价值, 而且简便、快速、无创伤。

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ABSTRACTS FROM ORIGINAL ARTICLES

Clinical Observation on 60 Cases of Chronic Pulmonary Heart Disease at Acute Attack Stage Treated with Fei Xin Ning Mixture Combined with Western Medicine Therapy

Zhou Duanqiu

Sixty cases of chronic pulmonary heart disease at acute attack stage in the treatment group and 60 cases of the control group were treated with oxygen—inspiration, relieving spasm and asthma, anti—infection, and correcting respiratory failure and heart failure as basic treatment. Self—made Chinese drug Fei Xin Ning Mixture was added to the treatment group. In the two groups, 15 days constituted one course. Plasma endothelin—1 (ET—1) level and hemorheologic indices were determined before and after treatment. Results indicated that the markedly effective rate, effective rate and the total effective rate in the treatment group were 73.33%, 20% and 93.34% respectively, and 35%, 33.34% and 68.34% in the control group, with significant difference in the total effective rate between the two groups ($P < 0.01$). Plasma endothelin—1 level after treatment in the treatment group was significantly lower than that in the control group ($P < 0.01$), and the hemorheologic indices in the treatment group decreased significantly as compared with those before treatment or after treatment in the control group ($P < 0.05$ or $P < 0.01$). It is suggested that Fei Xin Ning Mixture can obviously increase the total effective rate and decrease plasma endothelin—1 level and improve blood rheology for chronic pulmonary heart disease at acute attack stage, and it has a better therapeutic effect than that of the simple Western medicine treatment.

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Key words: Pulmonary heart disease/TCM therapy. @Fei Xin Ning Mixture

(Original article on page 89)

Effects of Gan Dou Pian on Ultrasonogram and Functions of Liver in 34 Cases of Hepatolenticular Degeneration

Hong Mingfan, Wang Gongqiang, Yang Renmin, et al

Ultrasonogram of the liver, serum albumin, globulins, electrophoresis of serum proteins and copper in 24h urine were observed in 34 cases of hepatolenticular degeneration (HLD) before and after treatment with Gan Dou Pian. Results indicated that the agent has an obvious action of excreting copper. Among them 13 patients had improvement in ultrasonogram of the liver, with serum albumin content increased from $35.35 \pm 6.48\text{g/L}$ to $38.76 \pm 6.36\text{g/L}$ ($P < 0.05$), and globulin decreased from $30.42 \pm 5.88\text{g/L}$ to $25.61 \pm 6.13\text{g/L}$ ($P < 0.01$), suggesting that the drug can promote recovery of cirrhosis of liver and hepatic functions in the

patient of HLD via excretion of copper, relieving copper poisoning of hepatic cells.

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Key words: hepatolenticular degeneration/TCM therapy. @Gan Dou Pian, Liver/ultrasonography

(Original article on page 93)

Clinical Study on 205 Cases of Female Climacteric Syndrome Treated with Geng Nian Qing Capsule

Chen Darong, Jin Zhe, Zhou Jiaming, et al

Four hundred and five cases of female climacteric syndrome were randomly divided into treatment group (205 cases), control group (100 cases) and open group (100 cases). The treatment group was administrated orally 4 Geng Nian Qing Capsules and 4 analog starch tablets, 3 times each day. The control group, 4 pieces of Geng Nian An and 4 analog starch tablets, 3 times each day. The open group, only 4 Geng Nian Qing Tablets, 3 time daily. The courses in the 3 groups were 30 days. Clinical symptoms and laboratory indexes were observed before and after treatment. Results showed that the total effective rate was 96.10%, the markedly effective rate was 65.36%, estradiol (E_2) increased ($P < 0.001$), follicle—stimulating hormone (FSH), luteotropic hormone (LH) decreased slightly ($P > 0.05$), vaginal scaling cell mature index (MI) increased ($P < 0.01$), and clinical symptom cumulative scores decreased significantly ($P < 0.01$ or $P < 0.001$). Abnormal safty index did not be found in the treatment group. The total effective rate was 86%, the markedly effective rate 40%, E_2 increased ($P < 0.05$), FSH and LH did not change significantly ($P > 0.05$), MI increased ($P < 0.01$), clinical symptom cumulative score decreased significantly ($P < 0.01$) in the control group. The total effective rate was 99%, the markedly effective rate was 66%, E_2 increased ($P < 0.001$), FSH and LH did not have significant change ($P > 0.05$), MI increased ($P < 0.05$), clinical symptom cumulative score decreased significantly ($P < 0.001$) in the open group. There was significantly difference between the treatment group and the control group ($P < 0.01$), and no significant difference between the treatment group and the open group ($P > 0.05$), suggesting that Geng Nian Qing Capsule can increase E_2 level and it is effective and safe for treatment of female climacteric syndrome.

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Key words: climacteric syndrome/TCM therapy. @Geng Nian Qing Capsule

(Original article on page 95)