

中药治疗肝豆状核变性 107 例疗效观察

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摘要 应用以清热解毒、通腑利湿之品组成的中药方剂肝豆汤,治疗肝豆状核变性 107 例,取得显效 9 例,总有效率 84.1%的良好疗效。实验室检查证明肝豆汤具有促进尿排铜量的作用。

主题词 肝豆状核变性/中医药疗法

肝豆状核变性(HLD)是一种常染色体隐性遗传性铜代谢障碍疾病。自 1948 年 Mandlebrat 首先在临床上倡用以二巯基丙醇(BAL)驱铜治疗以来,至今国外大都均采用以青霉胺为主治疗该病,但青霉胺有明显的副作用。因此,探求以中药治疗该病具有临床价值。我们自 1974 年 6 月至 1988 年 6 月对 107 例 HLD 住院病人进行了中药肝豆汤治疗,现报告如下:

1 临床资料

本组 107 例 HLD 均符合《临床肝胆病学》关于 HLD 的诊断标准^[1]。其中男 74 例,女 33 例;起病年龄 7~58 岁,平均 22.54 ± 10.8 岁;病程 1 月~9 年,平均为 2.35 ± 5.33 年。本组 107 例 HLD 中,肝豆状核变性型 50 例,假性硬化型 43 例,精神障碍型 5 例,内脏型和脑内脏混合型共 9 例。按 Goldstein 分级法^[2]属 I 级患者 2 例,Ⅱ级 73 例,Ⅲ级 30 例,Ⅳ级 2 例。

2 治疗及观察方法

中药肝豆汤由大黄 6g、黄连 10g、黄芩 10g、鱼腥草 20g、半枝莲 20g、泽泻 20g 组成,加水煎 300ml,每日 1 剂,分 2 次服,4 周 1 疗程。

107 例 HLD 中,86 例入院前未接受任何药物治疗,另 21 例曾用过 BAL、青霉胺、硫酸锌等,均在接受中药治疗前停药 4 周。所有病人入院后一律吃规定的低铜饮食,肝豆汤治疗前均详细记录神经系统阳性征候及做血清铜、血

铜氧化酶及 24 小时尿铜测定,其中 42 例测定了血清锌含量。然后服肝豆汤 4 周,每周检测尿铜 1 次,并于 4 周治疗结束时再复查疗前各项检查作自身对照。

3 疗效分析

3.1 治疗结果:服药 4 周,神经系统症状与体征显著改善,病情改善 2 级(含 2 级)以上,评为显效者 9 例(8.4%);症状与体征有改善,病情改善 1 级,评为好转者 81 例;症状与体征无变化或加重,评为无效者 17 例(15.8%)。总有效率达 84.2%。对于临床症状的改善,以言语不清、流涎、四肢抖动及笨拙疗效最好,肌僵直、扭转痉挛次之,而对四肢挛缩畸形、智能降低及肝脾肿大未见明显变化。

3.2 分型、分级与疗效的关系:同属脑型的肝豆状核变性型、假性硬化型和精神障碍型间疗效无显著差异($P < 0.05$);而脑型与内脏型和脑内脏混合型相比较,疗效显著为优($P < 0.001$)。且病情轻的 I、Ⅱ级患者的疗效明显优于病情重的 Ⅲ、Ⅳ级患者($P < 0.001$)。详见表 1。

表 1 分型分级与临床疗效观察

分型和分级	例数	显效	好转	无效
肝豆状核变性型	50	5	40	5
假性硬化型	43	3	34	6
精神障碍型	5	1	3	1
内脏型与脑内脏型	9		4	5
I~Ⅱ级	75	9	61	5
Ⅲ~Ⅳ级	32		20	12

3.3 尿排铜量治疗前后变化:107 例患者治疗前 24 小时平均排铜量为 $5.710 \pm 3.72 \mu\text{mol/L}$ (均值±标准差,下同),治疗后 4 周的平均量则为 $9.647 \pm 5.169 \mu\text{mol/L}$,治疗前后比较有明显差异($P < 0.01$),其中以疗后第 3 周的排出量增加的最多,为 $10.497 \pm 7.026 \mu\text{mol/L}$,说明中

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药肝豆汤具有明显的促进尿排铜作用。

3.4 治疗前后血清铜氧化酶的变化:治疗前107例患者的血清铜氧化酶均明显低于正常人,平均为0.06779光密度(OD,下同),而治疗后有62例升高,107例的平均值为0.08221OD,治疗前后均差值为 0.014 ± 0.005 OD(均差±标准误),治疗前后比较有明显差异($P < 0.01$)。但无一例达到正常人水平。

3.5 治疗前后血清铜、锌含量的变化:表2示,经4周治疗,血清铜及锌的含量均无明显变化($P > 0.05$)。

表2 治疗前后血清铜、锌含量($\mu\text{mol/L}$)比较

元素	例数	治疗前均值	治疗后均值	治疗后-治疗前均差值±标准误
Cu	107	7.251	7.542	0.291 ± 0.29
Zn	42	18.099	19.033	0.934 ± 0.491

4 讨论

现代医学认为,肝豆状核变性是由于遗传性铜代谢障碍,导致大脑、肝脏和肾脏等人体主要脏器内过量铜的沉积,而引发各种临床表现。目前有关铜代谢异常的发病机制虽尚未完全阐明,但多数学者主张,本病与胆道排铜减少和铜蓝蛋白合成障碍有关。作者曾分别测定20例HLD和22例非HLD患者胆汁内铜、锌含量及铜/锌比值,结果发现HLD胆汁内铜含量和铜/锌比值较非HLD显著减低,而两组胆汁锌含量比较无显著性差异。进一步说明HLD体内铜沉积与肝胆系统排铜减少密切相关^[3]。因此,对该病的治疗目前仍采取以金属络合剂从体内经尿和胆道排除过剩的铜;同是补充锌制剂以求锌能在人体肠腔内与铜离子竞争金属巯基(-SH)组氨酸三甲基内盐(Metallothionein),并阻止胃肠道、器官中内源性分泌铜的重吸收而发挥治疗作用^[4]。

中医古代文献对体病缺乏明确记载。因本病以肢体抖动、肌僵直、口臭流涎、言语不清、性格异常等神经精神症状和黄疸、肝脾肿大、腹水等肝脏症状为主要临床表现。我们曾一度遵“诸风掉眩皆属于肝”“诸暴强直皆属于风”,采用平

肝熄风治法,予以全蝎、僵蚕、地龙、龟板、鳖甲、牡蛎、珍珠母等虫类药物治之,患者症状反趋严重。溯其原因,此类药物铜含量极高,故平肝熄风之法对本病实则有害无益。本组107例患者中80例具备口中臭秽、口苦口腻、舌质红、苔黄或黄腻、脉弦数或弦滑。从中医辨证而言,铜毒内聚、肝胆湿热内蕴为其主要的病机,故苦泄清热、利胆除湿适治本病。故改用清热解毒、通腑利湿之品组成肝豆汤治疗。方中大黄、黄连、黄芩、泽泻解毒利湿,泻肝胆湿热;半枝莲、鱼腥草、泽泻解毒利湿,全方具有解毒清利肝胆湿热之功用。本组107例患者经此法治疗后,神经精神症状明显改善,提示其疾病特点及疗效符合铜毒内聚、肝胆湿热的辨证规律。

现代药理研究也表明,肝豆汤中所选6味药皆属低铜高锌类中草药,其中大黄主要含番泻甙元(Sennidine),它能刺激大肠壁促进大肠排空运动以加速排便,从而减少铜离子在肠道中的吸收;大黄、黄连、黄芩均有促进胆汁分泌、稀释胆液、增进胆汁铜排泄的作用;半枝莲、鱼腥草、泽泻均有利尿解毒的作用^[5]。松田胜彦等对50种生药中微量元素测定表明,每100mg黄连根茎的含锌量高达560ppm,而含铜仅11ppm^[6]。我们的治疗和实验结果也证实,107例HLD经肝豆汤治疗后,在临床症状改善的同时,尿排铜量显著增加,表明肝豆汤能有效地促进体内铜排泄,并可能在此基础上有增加体内锌含量的倾向,提示了此方法治疗HLD可能具备的特殊价值。

5 参考文献

- 1 叶维法主编. 临床肝胆病学. 第一版. 天津科学技术出版社, 1985: 940.
- 2 Goldstein NP, et al. In Clinical Neuropharmacology. Klawans Ed, Raveh Press, New York 1977: 99.
- 3 任明山,等. DMSA治疗肝豆状核变性临床疗效及对胆汁等微量元素的影响. 中国神经精神疾病杂志 1990; (6): 325.
- 4 沈伟敏,等. 近年研究肝豆状核变性的进展. 国外医学儿科分册 1985; (3): 116.
- 5 江苏中医学院主编. 中药大辞典. 第一版. 上海人民出版社, 1975: 207.
- 6 松田胜彦,等. 50种生药と微量元素. 生药杂志 1980; 34: 321.

ABSTRACTS OF ORIGINAL ARTICLES

A Comprehensive Clinical Evaluation of Cholelithiasis Treated by Pellet—pressing to Auriculo—acupoint

Wang Shiming, Wang Hongdu, Zhang Zheping, et al.

One hundred twenty — three hospitalized cases of cholelithiasis wererandomly divided and designed in groups and stratifications and treatedby pellet — pressing to auriculo — acupoints plus taking pig's trotters, simple auricular pressing, placebo, and placebo plus taking pig's trotters respectively for comparative and prospective studies. Resultsrevealed that, in the pellet — pressing plus taking pig's trotters group, the total effective rate was 65.6% and the rate of remission was 25%. In terms of its action of relieving symptoms, preventing occurrence ofcolic pain or recurrent abdominal pain, the pellet — pressing group wassuperior to the other 3 groups. The results of our study al—sodemonstrated that, though pellet — pressing method yielded definiteresults for cholelithiasis, but the effective rates were not as high asthat reported by previous papers.

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Key words: biliary stone/acupoint therapy pellet — pressing to auriculo—acupoints @ biliary stones

(Original article on page 662)

Clinical Observation on Respiratory Infections in AIDS Treated byChinese Materia Medica

Li Guoqin, Lu Weibo, Zhou Zhikuan, et al.

Eighty cases of AIDS patient with coughing were divided into 2 groupson the basis of the severity of the conditions, in which 58 cases weretreated simply by TCM and 22 cases by integrated traditional withwestern medicine. Results showed that in the former group 18 cases (31.03%) were clinically cured, 7 cases (12.07%) effective and 33 cases (56.90%) ineffective, the total effective rate being 43.10%; while forthe latter group, the figures were 6 (27.27%), 2 (9.0%), 14 (63.64%) and 36.36% respectively. The efficacy for integrated medicine group issomewhat inferior to the simple TCM group, which may be related to itsseverer condition or its condition of complication.

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Key Words: Acquired Immune Deficiency Syndrome/TCM therapy Infection of respiratory tract/TCM therapy

(Original article on page 671)

Clinical Study on Chronic B—Hepatitis Treated by B—hepatitis No. 1

ZhangJunfu, Cui Li'an, Yuan Shufang, et al.

On hundred cases of B—hepatitis were treated by self — formulatel B—hepatitis No. 1 granules made of traditional drugs. A control group of100 cases were treated with Jiaosanxian (scorched triple ingredients, consisting of hawthorn, malt, and membrane of chicken gizzard). Resultsshowed that, in the experimented group, the lowering of transaminase, inhibition of virus duplication and improvement of globulin ratio areall — superior to the control group. The results were also verified bylaboratory experiments.

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Key Words: Hepatitis, chronic and acute /TCM therapy. B—hepatitis/TCM @ B—hepatitis No. 1

(Original article on page 673)

107 Cases of Hepatolenticular Degeneration Treated by Chinese MatensMedica

Yang Renmin, Han Yongzhu, Ren Mingshan, et al.

All the cases were treated by Hepatolenticular Drink composing drugs ofclearing heat, detoxifying, dredging hollow — viscera, and eliminating dampness. Nine cases were markedly effective, and the total effective rate was 84.1%. Experiments revealed that HepatolenticularDrinkpossesses the action of improving excretion of copper in urine.

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Key Words: Hepatolenticular degeneration/TCM therapy

(Original article on page 676)