

临床 研究

大黄廑虫丸对非胰岛素依赖型Ⅳ期糖尿病肾病患者Ⅷ因子相关抗原及纤维蛋白原的影响

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摘要 目的:探讨大黄廑虫丸对非胰岛素依赖型Ⅳ期糖尿病肾病(DN)患者Ⅷ因子相关抗原(vWF:Ag)、纤维蛋白原(Fbg)的治疗作用。方法:选择Ⅳ期DN患者60例,用自动凝血机检测vWF:Ag、Fbg的变化,并随机分为治疗组和对照组。治疗组用大黄廑虫丸,对照组用潘生丁干预治疗,观察大黄廑虫丸对Ⅳ期DN患者vWF:Ag、Fbg的影响。结果:Ⅳ期DN患者血vWF:Ag、Fbg含量显著增高,与正常对照组比较有极显著差异($P<0.01$)。用大黄廑虫丸治疗后,vWF:Ag、Fbg浓度显著降低($P<0.05$ 或 $P<0.01$),明显优于潘生丁组。结论:大黄廑虫丸能显著降低Ⅳ期DN患者血vWF:Ag、Fbg含量,改善高凝状态。

主题词 糖尿病,非胰岛素依赖型/中医药疗法 大黄廑虫丸/治疗应用 糖尿病肾病/血液

非胰岛素依赖型糖尿病肾病(diabetic nephropathy, DN)存在严重的高凝状态(HCS),易出现血栓。目前,对DN缺乏有效的治疗药物。如果HCS得不到有效的控制,会使DN进展加快。因此,研究对DN患者伴HCS的防治具有重要意义。本研究观察了大黄廑虫丸对Ⅷ因子抗原(vWF:Ag)、纤维蛋白原(Fbg)的影响。

1 临床资料

1.1 诊断标准:非胰岛素依赖型糖尿病(NIDDM)诊断标准参照1997年美国糖尿病协会提出的修改糖尿病诊断标准的建议制定,即空腹血糖(FPG)≥7.0mmol/L,或症状+随机血糖≥11.1mmol/L,并排除急性感染、外伤及其它应激情况引起的暂时性高血糖。非胰岛素依赖型Ⅳ期DN诊断标准:NIDDM在10年以上,24小时尿蛋白定量≥0.5g^[1],并排除原发性急慢性肾小球肾炎、肾病综合征、近期应用肾毒性药物等。

1.2 一般资料:60例非胰岛素依赖型Ⅳ期DN患者随机分为治疗组和对照组。治疗组30例,男18例,女

12例。年龄48~79岁,平均54.3岁。DN病史6个月~5.1年,平均 2.1 ± 1.31 年。24小时尿蛋白定量0.5~2.0g者13例,2.1~3.4g者11例,≥3.5g者6例, FPG为 12.7 ± 5.3 mmol/L,内生肌酐清除率(Ccr)≥80ml/min者17例,50~79ml/min者9例,25~49ml/min者4例。19例做过肾活检,典型Kimmelstrel-wilsom结节4例,弥漫性肾小球硬化15例。对照组30例,男17例,女13例。年龄48~81岁,平均55.7岁。DN病史7个月~6.3年,平均 2.4 ± 1.37 年。24小时尿蛋白定量0.5~2.0g者15例,2.1~3.4g者10例, ≥3.5g者5例, FPG为 12.3 ± 4.9 mmol/L, Ccr≥80ml/min者15例,50~79ml/min者10例,25~49ml/min者5例。20例做过肾活检,典型Kimmelstrel-wilsom结节4例,弥漫性肾小球硬化16例。两组病程、临床表现、病理等差异无显著性($P>0.05$),具有可比性。

2 治疗及观察方法

治疗组用大黄廑虫丸(由大黄、黄芩、水蛭、廑虫、干漆、桃仁、芍药、干地黄、杏仁、甘草、蛭蟾组成,天津达仁堂制药厂生产,批号980119),每日3次,每次3g。对照组服用潘生丁(山西亚宝药业股份有限公司生产,批号980315),每日3次,每次50mg。4周为1个疗程,两组均不用其它抗凝药及其它活血化瘀中药。两组血糖高者用糖适平或胰岛素,血压高者用科素亚或加波依定,有感染者用抗生素治疗。

实验方法:治疗前后晨起空腹采静脉血2.7ml,以3.8%枸橼酸钠抗凝,2000r/min离心10分钟,分离血浆,2小时内用美国IL公司生产ACL-200凝血机检测vWF:Ag、Fbg^[2]。尿素氮(BUN)、FPG、血白蛋白(ALb)、胆固醇(Chol)采用自动生化分析仪检测,24小时尿蛋白(pro)定量采用双缩脲法, Ccr计算公式(ml/min)=尿Cr×24小时尿量/1140/Scr。

统计学方法:采用SPSS统计软件处理,治疗前后及组间比较均用 t 检验。

3 治疗结果

3.1 治疗前vWF:Ag、Fbg检测结果:治疗前非胰岛

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表 1 vWF:Ag、Fbg 与各指标相关性分析

指标	vWF:Ag	Fbg
FPG	0.71	0.68
Pro	0.41	0.43
BUN	0.91	-0.19
Ccr	-0.39	0.21
ALb	-0.38	-0.64
Chol	0.37	0.41

表 2 两组治疗前后 vWF:Ag 比较(%, $\bar{x} \pm s$)

组别	例数	治疗前	治疗后
治疗组	30	199.21 $\pm$ 68.13	147.17 $\pm$ 51.19*
对照组	30	197.31 $\pm$ 66.25	178.68 $\pm$ 57.33

* 与本组治疗前比较, $P < 0.01$

表 3 两组治疗前后 Fbg 比较(g/L, $\bar{x} \pm s$)

组别	例数	治疗前	治疗后
治疗组	30	4.93 $\pm$ 1.57	2.83 $\pm$ 0.98* Δ
对照组	30	4.61 $\pm$ 1.51	3.87 $\pm$ 1.12*

与本组治疗前比较, * $P < 0.05$, * * $P < 0.01$; 与对照组治疗后比较, $\Delta P < 0.01$

素依赖型 IV 期 DN 患者血 vWF:Ag 均值为 198.73 $\pm$ 67.52%, 正常对照组为 116.38 $\pm$ 3.39% (资料略)。IV 期 DN 患者血 vWF:Ag 水平较正常对照组显著增高 ($P < 0.01$)。治疗前 IV 期 DN 患者血 Fbg 平均值为 4.71 $\pm$ 1.69g/L, 正常对照组为 2.47 $\pm$ 0.28g/L, IV 期 DN 患者血 Fbg 水平较正常对照组显著增高 ($P < 0.01$)。

3.2 vWF:Ag、Fbg 与各指标相关性分析: 治疗前 IV 期 DN 患者 vWF:Ag、Fbg 与 BUN、Ccr、FPG、ALb、Chol、Pro 相关性分析发现, vWF:Ag 与 BUN 呈显著性正相关 ($r = 0.91, P < 0.01$), FPG 与 vWF:Ag 呈显著性正相关 ($r = 0.71, P < 0.01$), Fbg 与 ALb 呈显著性负相关 ($r = -0.64, P < 0.01$), 与 FPG 呈显著性正相关 ($r = 0.68, P < 0.01$)。见表 1。

3.3 大黄廑虫丸对 vWF:Ag 的影响: 两组治疗前 vWF:Ag 均明显增高, 组间比较差异无显著性 ($P > 0.05$), 治疗组用大黄廑虫丸治疗后明显降低, 与治疗前比较差异显著 ($P < 0.01$)。对照组用潘生丁治疗后, vWF:Ag 含量有所下降, 但差异无显著性 ($P > 0.05$)。见表 2。

3.4 大黄廑虫丸对 Fbg 的影响: 治疗前 IV 期 DN 患者血 Fbg 含量与正常组比较均明显增高 (资料略), 两组差异无显著性 ($P > 0.05$), 治疗组治疗后 Fbg 含量明显降低, 与治疗前比较有显著差异 ($P < 0.01$)。对照组治疗后也有所降低, 统计学处理差异有显著性 ($P <$

0.05)。两组治疗后比较, 大黄廑虫丸治疗组血 Fbg 显著低于潘生丁对照组 ($P < 0.01$)。见表 3。

4 讨论

DN 引起血管内皮损伤的机理有: (1) 由于胰岛 β 细胞的缺陷, 使胰岛素的分泌绝对或相对不足, 导致糖耐量降低和血糖过高, 损伤内皮细胞; (2) 胰岛素不足时, 脂肪组织的分解代谢亢进, 产生大量游离脂肪酸, 被转化为酮体, 造成酮症酸中毒, 造成内皮的损伤; (3) DN 患者由于长期血糖升高, 使部分血红蛋白 A (HbA) 与糖醛结合形成糖化血红蛋白 (HbA1c), HbA1c 可使组织缺氧引起血管内皮损伤; (4) 血糖升高, 红细胞膜变得僵硬, 加上血粘度增高, 引起局部血流停滞, 组织缺氧, 损伤内皮细胞。vWF:Ag 激活 II 因子, II 因子可进一步激活 Fbg, 使 Fbg 含量增加。另外, 当 DN 出现大量蛋白尿时, 血浆蛋白下降, 肝脏代偿合成蛋白增加, Fbg 合成也明显增加, 但 Fbg 为大分子蛋白, 很少从尿中丢失, 而在血中蓄积。因此, 尿蛋白越多, 血浆蛋白越低, 血中 Fbg 含量越高。血 vWF:Ag 和 Fbg 含量明显增高时, 造成血液 HCS, 使血流缓慢, 肾血流减少, 加重 DN 肾损害, 而且容易出现血栓^[3]。DN 患者血液 HCS 与中医血瘀相关, 故我们用《金匱要略》中治疗干血劳的大黄廑虫丸进行干预治疗。本研究发现大黄廑虫丸能显著降低 DN 患者血中 vWF:Ag、Fbg 的含量, 改善 HCS。现代药理研究认为, 方中的大黄可抑制肾小球系膜细胞增殖, 加强血管内皮损伤的修复, 减少内皮细胞释放 vWF:Ag。水蛭、廑虫、虻虫等有很好的抗凝、抗血栓作用, 特别是水蛭中的水蛭素, 其抗凝作用是肝素的 20 倍, 且与凝血酶亲和力极强, 低浓度就能中和凝血酶。凝血酶在内外原凝血反应中起关键的中间枢纽作用。凝血酶主要作用是催化 Fbg 的分解, 使 Fbg 从 N 端脱下四段小肽变为纤维蛋白单体, 又能激活 VII 因子, 促使纤维蛋白单体相互联结, 形成 HCS 和血栓。水蛭素能有效地抑制凝血酶, 抑制内外原凝血反应, 起到很好的抗凝及抗血栓作用^[4]。

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ABSTRACTS FROM ORIGINAL ARTICLES

Effects of electroacupuncture on learning and memory and the producing system of free radicals in brain tissue in the rat of vascular dementia

Wang Li, Tang Chunzhi

Objective: To observe regulative action of electroacupuncture (EA) on learning and memory and the producing system of free radicals in the rat of experimental vascular dementia (VD). **Methods:** In the 4-VO model rat of vascular dementia (VD), learning and memory were detected by morris's water maze, and nitric oxide (NO), malondialdehyde (MDA) contents, nitric oxide synthase (NOS), superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activities in the brain were determined. **Results:** The model rat had obvious learning and memory disorder, and had significantly longer escape latency in the orientation navigation experiment as compared with that of false operation group; and the running over platform times in the original platform quadrant were not significantly higher than other 3 quadrants in the space exploration test. While in the EA group, the escape latency was shortened; the running over platform times in the original platform quadrant were significantly more than other 3 quadrants, with no significant difference to the false operation group. NOS activity, NO and MDA contents in the brain tissue in the model group increased significantly, SOD, GSH-Px activities decreased significantly with significant differences as compared with that of the false operation group, EA group and Nimotop group ($P < 0.05$ or $P < 0.01$). It is indicated that NO, MDA contents and NOS activity decrease in the EA group and the Nimotop group, and SOD and GSH-Px activities increase in varying degrees in the brain tissue. **Conclusion:** EA can regulate the balance of production and elimination of free radicals, and can relieve lesion of nervous cells of the brain due to ischemia, so as to improve learning and memory in the rat of VD.

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Key words: Dementia, vascular/acup - moxibustion therapy electroacupuncture memory/acup eff

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Clinical study on combination of Dan Zhi Xiao Yao Powder with ear point taping and pressing therapy for treatment of 51 cases of optic nerve atrophy

Yang Haiyan

Objective: To observe clinical therapeutic effect of combination of Dan Zhi Xiao Yao Powder with ear point taping and pressing therapy on optic nerve atrophy. **Methods:** In the treatment group (51 cases, 58 eyes) treated with combination of Dan Zhi

Xiao Yao Powder with ear point taping and pressing therapy, and in the control group treated with simple Western medicine (43 cases, 49 eyes), vision and visual field were observed for 3 therapeutic courses. **Results:** The effective rate for vision was 79.3% in the treatment group, and 44.89% in the control group; and the effective rate for visual field was 59.2% in the treatment group and 22.6% in the control group, the therapeutic effect in the treatment group being superior to that of the control group ($P < 0.05$). **Conclusion:** Combination of Dan Zhi Xiao Yao powder with ear point taping and pressing therapy can increase vision and improve optic function for optic nerve atrophy.

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Key words: Optic nerve atrophy/acupoint therapy optic nerve atrophy/TCM therapy: Dan Zhi Xiao Yao Powder/treatment application

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Effects of Da Huang Zhe Chong Pill on VII factor correlative antigen and fibrinogen in the patient of non-insulin dependent diabetic nephropathy at stage IV

Wei Lianbo, Li Delin, Ye Rengao, et al.

Objective: To probe into the action of Da Huang Zhe Chong Pill on VII factor correlative antigen (vWF:Ag) and fibrinogen (Fbg) in the patient of non-insulin dependent diabetic nephropathy (DN) at stage IV. **Methods:** 60 cases of DN at stage IV were randomly divided into treatment group and control group, and vWF:Ag and Fbg changes were detected with automatic coagulation instrument. The treatment group were treated with Da Huang Zhe Chong Pill and the control group with persantine. The effects of Da Huang Zhe Chong Pill on vWF:Ag and Fbg in the patient of DN at stage IV were investigated. **Results:** The blood vWF:Ag, Fbg contents in the patient of DN at stage IV increased as compared with that of the normal control group ($P < 0.01$); after treatment with Da Huang Zhe Chong Pill, vWF:Ag and Fbg contents decreased significantly ($P < 0.05$ or $P < 0.01$), superior to that of the persantine. **Conclusion:** Da Huang Zhe Chong Pill can significantly decrease blood vWF:Ag and Fbg contents and improve hypercoagulable state in the patient of DN at stage IV.

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Key words: Diabetes, non-insulin dependence/TCM therapy Da Huang Zhe Chong/treatment application diabetic nephropathy/blood

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