doi: 10.13241/j.cnki.pmb.2017.15.034

血府逐瘀丸治疗老年2型糖尿病伴失眠的临床疗效及其对认知功能的影响*

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摘要 目的：探究血府逐瘀丸治疗老年2型糖尿病伴失眠患者的临床疗效及其对认知功能影响。**方法：**选取43例我院收治的老年2型糖尿病伴失眠患者，将其随机分为实验组及对照组。对照组21例予地西泮治疗，实验组22予血府逐瘀丸治疗。观察两组治疗前后失眠症状及认知功能的变化情况。**结果：**治疗后，实验组总有效率(86.4%)高于对照组(61.9%)，其差异经比较有统计学意义(P<0.05)；两组匹兹堡睡眠质量指数量表(PSQI)评分均较治疗前显著降低(P<0.05)，与对照组相比，实验组PSQI评分较低(P<0.05)，空腹血糖水平较低(P<0.05)，蒙特利尔认知评估量表(MoCA)评分较高(P<0.05)。**结论：**血府逐瘀丸可有效降低老年2型糖尿病伴失眠患者的血糖水平，提升睡眠质量，改善失眠及认知功能障碍。

关键词：老年2型糖尿病；失眠；血府逐瘀丸；认知功能

中图分类号：R587.2 **文献标识码：**A **文章编号：**1673-6273(2017)15-2930-04

Clinical Efficacy of Xuefu Zhuyu Pill in the Treatment of Senile type 2 Diabetes Mellitus with Insomnia and Its Cognitive Function*

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ABSTRACT Objective: To investigate the clinical efficacy of xuefu zhuyu pill in the treatment of senile type 2 diabetes mellitus with insomnia and its cognitive function. **Methods:** 43 senile patients with type 2 diabetes mellitus and insomnia who were treated in our hospital were selected and randomly divided into the experiment group and control group. 21 cases in the control group were treated with diazepam treatment, 22 cases in the experiment group were treated with xuefu zhuyu pill treatment. After treatment for 28 days, the insomnia and cognitive function changed situations of both groups were observed before and after treatment. **Results:** After treatment, the total effective rate of experiment group(86.4%) was higher than the control group(61.9%) (P<0.05); the Pittsburgh sleep quality index - scale (PSQI) scores of both groups were decreased (P<0.05), compared with the control group, the PSQI score, fasting blood glucose level of the experiment group were lower (P<0.05), the montreal cognitive assessment scale (MoCA) score was higher (P<0.05). **Conclusion:** Xuefu zhuyu pill could effectively decrease the blood glucose, improve the sleep quality, insomnia and cognitive dysfunction of senile type 2 diabetes mellitus patients with insomnia.

Key words: Senile type 2 diabetes mellitus; Insomnia; Xuefu zhuyu pill; Cognitive dysfunction

Chinese Library Classification(CLC): R587.2 Document code: A

Article ID: 1673-6273(2017)15-2930-04

前言

糖尿病是内分泌系统的常见疾病，以2型糖尿病(T2DM)为多见并具有年龄相关性，约有50%的患者在55岁后发病[1]。老年2型糖尿病患者常有典型症状如多饮多食等，且易发生大血管的并发症，如脑微循环障碍及脑组织供血不足等，使患者出现失眠的症状[2]。失眠多因血管及神经被异常的血糖水平影响而导致，发生失眠后会进一步引起血糖的不稳定，加重代谢的紊乱[3]。据统计，2007年2型糖尿病已有2.46亿人患病，估算出2025年全球范围内3.8亿人会遭受糖尿病的困扰，同时伴发的失眠症会造成患者免疫力下降加重患者血糖的紊乱[4]。血府逐瘀丸是具有活血化瘀、抗炎消肿功能的中药，主要由当归、川芎、红花等制成，能够增强人体免疫功能，改善患者血液循环促进血液流通，改善患者的失眠症状及血糖水平[5]。本研究主要探讨了血府逐瘀丸对老年2型糖尿病伴失眠患者的临床疗效及认知功能的影响。

* 基金项目：四川省自然科学基金项目(2011K153)

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(收稿日期：2016-11-16 接受日期：2016-12-12)

1 资料与方法

1.1 临床资料

选取我院老年 2 型糖尿病伴失眠患者 43 例，随机将其分成实验组以及对照组。对照组 21 例,男性 13 例,女性 8 例,年龄 61~78 岁,平均(69.2± 7.5)岁,病程 1~9 年,平均(5.2± 0.6)年;实验组 22 例,男性 12 例,女性 10 例,年龄 62~79 岁,平均(68.7± 8.3)岁,病程 8 个月 ~9 年,平均(4.8± 0.5)年。两组患者的性别、年龄、病程等比较差异不具有统计学意义(P>0.05),具有可比性。患者符合世界卫生组织制定(2013 年)中 T2DM 诊断标准及失眠症诊断标准,年龄在 60 至 80 岁间。排除近期存在感染或者酮症酸中毒等急性并发症的患者;全身性疾病患者及造血系统疾病患者;严重肝肾功能损害患者;心脑血管疾病或胰腺疾病患者;对本研究药物过敏者;依从性不好者。此研究已获取本院伦理委员会批准,患者知情同意并已签署知情同意书。

1.2 治疗方法

对两组患者行糖尿病健康教育，科学进食补充膳食纤维,严格限制酒精及食盐摄入,鼓励患者进行适量运动锻炼,忌食过辣、过油及浓茶等食物,养成良好的生活习惯。对照组:地西泮片(广东南国药业有限公司,国药准字 H44021871),每日 1~2 片,每晚睡前 30 分钟口服,胰岛素注射液(四环药业股份有限公司,国药准字 H11020548),每日 50U 皮下注射;实验组:胰岛素注射液(四环药业股份有限公司,国药准字 H11020548),每日 50U 皮下注射,血府逐瘀丸(葵花药业集团(佳木斯)有限公司),每次 1 丸,每日 2 次,空腹温水送服。疗程 28 天。均在治疗前、后采集两组患者,3 mL 空腹肘静脉血,后放入已有 EDTA 的抗凝采血管,依 3000 r/min 转速离心 10 min,吸取上层血清于 EP 管中,置入 -20℃冰箱中保存备用。

1.3 检测方法

血糖测定使用葡萄糖氧化酶法进行测定;PSQI 评分主要由患者本人进行,对 19 个自我评定问题进行计分,最后相加得出总分;MoCA 评分由专业医师进行评测,从注意力、命名、抽象、定位及语言等方面进行计分。

1.4 疗效评价

依照睡眠质量把临床疗效分成显效、有效及无效三个等级。显效:患者能够达到正常睡眠时间或夜晚睡眠时间≥ 6 h,且醒后精力充沛或者睡眠质量好转，总睡眠时间 <6 h 但时间延长≥ 3 h;有效:患者睡眠情况好转,但增加时间 <3 h;无效:患者睡眠时间没有明显延长甚至减少。计算总有效率 =(显效数 + 有效数)/ 总例数× 100%。详细记录患者治疗期间不良反应并积极给予对症治疗。

1.5 统计学方法

用统计学软件 SPSS 19.0 统计分析所得结果，根据 "$\bar{x}$± s" 表达呈现正态分布的数据,t 检验方法进行检验,计数资料用率(%)表示,检验方式采用卡方检验,P<0.05 时,认为其差异具有统计学意义。

2 结果

2.1 两组疗效比较

实验组总有效率 86.4%,显著高于对照组(61.9%),差异有统计学意义(P<0.05),见表 1。

表 1 两组临床疗效比较【例(%)】

Table 1 Comparison of the clinical curative effect between two groups [n(%)]

Groups	Cases	Excellent	Effective	Invalid	Clinical effect rate
Control group	21	7(33.3)	6(28.6)	8(38.1)	13(61.9)
Experiment group	22	10(45.5)	9(40.9)	3(13.6)	19(86.4)*

Note: Compared with the control group, *P<0.05.

2.2 两组治疗前后 PSQI 评分比较

治疗后,两组 PSQI 评分均较治疗前显著降低(P<0.05),与对照组相比，实验组 PSQI 评分较低，差异存在统计学意义(P<0.05)。见表 2、3。

表 2 两组患者治疗前后 PSQI 评分比较($\bar{x}$± s)

Table 2 Comparison of the PSQI scores before and after treatment between two groups($\bar{x}$± s)

Groups	Sleep quality		Time to fall asleep		Sleep time		Sleep efficiency		Sleep disorder	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	2.2± 0.4	1.9± 0.2*	2.8± 0.4	1.8± 0.2*	1.8± 0.2	1.4± 0.2*	1.6± 0.2	1.3± 0.1*	1.5± 0.2	1.3± 0.1*
Experiment group	2.1± 0.3	1.6± 0.2*#	2.7± 0.4	1.3± 0.2*#	1.7± 0.2	1.2± 0.2*#	1.5± 0.2	1.1± 0.1*#	1.4± 0.2	1.1± 0.1*#

Note: compared with before treatment,*P<0.05; compared with the control group after treatment, #P<0.05.

表 3 两组患者治疗前后 PSQI 评分比较($\bar{x}$± s)

Table 3 Comparison of PSQI scores before and after treatment in two groups($\bar{x}$± s)

Groups	Hypnotic drug		Daytime function		The total score	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
control group	2.4± 0.3	1.7± 0.2*	2.2± 0.2	1.7± 0.2*	11.2± 1.3	9.7± 1.1*
Experiment group	2.3± 0.2	1.3± 0.1*#	2.1± 0.2	1.2± 0.1*#	12.1± 1.4	6.2± 0.8*#

Note: compared with before treatment,*P<0.05; compared with the control group after treatment, #P<0.05.

2.3 两组治疗前后空腹血糖水平比较

治疗后，两组患者空腹血糖水平均较治疗前明显下降，与对照组相比较，实验组空腹血糖水平较低(P<0.05)，差异具有统计学意义。见表 4。

表 4 两组治疗前后空腹血糖水平比较($\bar{x}\pm s$)

Table 4 Comparison of the fasting blood glucose between two groups before and after treatment($\bar{x}\pm s$)

Groups	Cases	(mmol/L)Fasting blood glucose	
		Before treatment	After treatment
Control group	21	12.8± 1.4	10.6± 1.2*
Experiment group	22	12.2± 1.3	7.1± 1.0*#

Note: compared with before treatment,*P<0.05; compared with the control group after treatment, #P<0.05.

2.4 两组治疗前后 MoCA 评分比较

治疗后，两组 MoCA 评分均较治疗前明显升高，与对照组相比，实验组 MoCA 评分较高(P<0.05)，差异具有统计学意义。见表 5、6。

表 5 两组治疗前后 MoCA 评分比较($\bar{x}\pm s$)

Table 5 Comparison of the MoCA scores between two groups before and after treatment($\bar{x}\pm s$)

Groups	Cases	Visual space and execution		Attention		Name		Language	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	21	4.4± 0.5	4.6± 0.5*	4.3± 0.5	4.6± 0.5*	2.6± 0.3	2.8± 0.3*	2.5± 0.3	2.7± 0.3*
Experiment group	22	4.3± 0.5	4.9± 0.4*#	4.2± 0.5	4.8± 0.5*#	2.7± 0.3	3.2± 0.3*#	2.6± 0.3	2.9± 0.2*#

Note: compared with before treatment, *P<0.05; compared with the control group after treatment, #P<0.05.

表 6 两组 MoCA 评分比较($\bar{x}\pm s$)

Table 6 Comparison of the MoCA scores between two groups before and after treatment ($\bar{x}\pm s$)

Groups	Directional		Abstract		Delayed recall		Total score	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	5.6± 0.6	5.8± 0.5*	1.6± 0.2	1.9± 0.2*	4.6± 0.6	4.7± 0.5*	23.2± 2.5	24.5± 2.5*
Experiment group	5.5± 0.6	6.1± 0.5*#	1.7± 0.2	2.2± 0.2*#	4.5± 0.5	4.9± 0.4*#	23.3± 2.5	26.3± 2.7*#

Note: compared with before treatment, *P<0.05; compared with the control group after treatment, #P<0.05.

3 讨论

2 型糖尿病患者由于血糖水平异常、脑部微循环障碍导致组织供血减少，使患者的自主神经功能紊乱，患者出现失眠症状，多表现为入睡困难及醒后难眠等[6-8]。2 型糖尿病患者失眠后体内升高血糖的激素水平增高，使胰岛素抵抗更加严重，因此患者血糖波动较大，老年患者因其各系统机能退化等原因，加大 2 型糖尿病的治疗难度[9]。

血府逐瘀丸属中药制剂，主要包含有当归、川芎、桃仁、柴胡以及赤芍等，有效地抑制血小板聚集，发挥活血化瘀、改善微循环的作用[10]。当归味甘性温，能够抑制血小板聚集降低粘滞性，促进红细胞生成，达到活血、增强机体免疫力的作用[11]。有研究表明[12]当归能够镇静催眠及镇痛，明显改善失眠症状。桃仁属味苦甘而性平，活血化瘀并有抗炎作用，神经衰弱患者服用后效果明显；川芎味辛性温，能够活血止痛祛风开郁，当作用于中枢神经系统时出现明显的镇静作用，抑制大脑活动降低中枢兴奋性，缓解失眠。柴胡属性微寒味苦，能增强免疫力，发挥抗炎解热的作用[12]。赤芍属味苦微寒，能够清热凉血，具有散瘀止痛的功效。血府逐瘀丸通过多种药物的配伍与相互作用发挥镇静改善失眠的作用[13]。

大多数糖尿病患者会出现记忆减退及认知障碍，常出现语言及判断能力减退伴有深情冷漠及反应迟钝等，其中以学习记忆障碍为主要表现[14]。长期高血糖水平极易并发糖尿病微血管病变，而存在糖尿病微血管病变的患者神经系统常有异常表现[15]。对认知功能的损害可能是因为体内血糖浓度的升高改变了血脑屏障，脑组织所需因子含量降低造成缺血缺氧性脑损害，而导致认知功能障碍[16]。同时，高浓度的血糖水平损害线粒体功能，诱使神经细胞凋亡，导致患者认知功能障碍。PSQI 评分表是评价患者睡眠质量的重要量表，通过对 9 个自评项目及 5 个他评项目的评分来评价患者的睡眠情况，所得评分越高说明患者的睡眠质量越差[17]。MoCA 评估表常用于评定轻度认知功能异常患者，通过对注意力、语言等各个方面进行评定，当得分≥ 26 分时，说明患者的认知功能处于正常状态[18,19]。患者治疗后 PSQI 评分下降、MoCA 评分升高，说明患者的失眠状态得到改善，认知功能障碍有所缓解。

本次研究结果示实验组总有效率 (86.4%) 高于对照组 (61.9%)，说明血府逐瘀丸治疗后能够有效改善老年 2 型糖尿病伴失眠患者的睡眠质量并提升认知功能。与对照组相比，实

验组 PSQI 评分较低，空腹血糖水平较低，MoCA 评分较高，各个指标的变化均提示经血府逐瘀丸治疗后，降低血糖水平，使血糖浓度维持在较为平稳的水肿，缓解神经功能异常，提高睡眠质量，使认知功能障碍得到提升[20]。血府逐瘀丸的疗效较西药更显著，睡眠质量提升更迅速，认知功能改善更明显。

综上所述，血府逐瘀丸能够有效降低老年 2 型糖尿病伴失眠患者的空腹血糖，提升睡眠质量，逆转认知功能障碍。

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