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"标本配穴"针灸结合甲钴胺对老年糖尿病周围神经病变患者糖脂代谢、炎性细胞因子和受损神经传导速度的影响*

叶 欣 刘晓宇 刘 卫 田雄涛 李 洁△

(空军军医大学西京医院内分泌科 陕西 西安 710054)

摘要 目的:探讨"标本配穴"针灸结合甲钴胺对老年糖尿病周围神经病变(DPN)患者糖脂代谢、炎性细胞因子和受损神经传导速度的影响。**方法:**选取2018年3月~2019年12月期间我院收治的93例老年DPN患者,按照随机数字表法将患者分为研究组(n=47)、对照组(n=46),对照组患者予以甲钴胺治疗,研究组在对照组的基础上联合"标本配穴"针灸治疗,比较两组疗效、糖脂代谢、炎性细胞因子、受损神经传导速度及不良反应。**结果:**研究组治疗4周后的临床总有效率87.23%(41/47)高于对照组69.57%(32/46)(P<0.05)。两组治疗4周后空腹血糖(FPG)、甘油三酯(TG)、总胆固醇(TC)、糖化血红蛋白(HbAlc)均下降,且研究组低于对照组(P<0.05)。两组治疗4周后白介素-6(IL-6)、白介素-1β(IL-1β)、肿瘤坏死因子-α(TNF-α)均下降,且研究组低于对照组(P<0.05)。两组治疗4周后腓总神经运动神经传导速度(MCV)、正中神经MCV、腓总神经感觉神经传导速度(SCV)、正中神经SCV均升高,且研究组高于对照组(P<0.05)。两组均未见明显不良反应发生。**结论:**"标本配穴"针灸结合甲钴胺治疗老年DPN患者疗效确切,可改善患者糖脂代谢、炎性细胞因子和受损神经传导速度,安全可靠。

关键词:"标本配穴"针灸;甲钴胺;老年;糖尿病周围神经病变;糖脂代谢;炎性细胞因子;受损神经传导速度

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The Effect of "Specimen Matching Points" Acupuncture Combine with Mecobalamin on Glycolipid Metabolism, Inflammatory Cytokines and Damaged Nerve Conduction Velocity in Elderly Diabetic Peripheral Neuropathy Patients*

YE Xin, LIU Xiao-yu, LIU Wei, TIAN Xiong-tao, LI Jie△

(Department of Endocrine, Xijing Hospital of Air Force Military Medical University, Xi'an, Shaanxi, 710054, China)

ABSTRACT Objective: To investigate the effect of "specimen matching points" acupuncture combine with Mecobalamin on glycolipid metabolism, inflammatory cytokines and damaged nerve conduction velocity in elderly diabetic peripheral neuropathy (DPN) patients. **Methods:** 93 elderly DPN patients who were admitted to our hospital from March 2018 to December 2019 were selected, the patients were divided into control group (n=46) and study group (n=47) according to the method of random number table. Patients in the control group were treated with Mecobalamin, the study group was treated with "sample matching point" acupuncture on the basis of the control group, the clinical effective, glycolipid metabolism, inflammatory cytokines, damaged nerve conduction velocity and adverse reactions were compared between the two groups. **Results:** The total clinical effective rate of the study group after 4 weeks was 87.23% (41/47) higher than 69.57%(32/46) of the control group (P < 0.05). Fasting blood glucose (FPG), triglyceride (TG), total cholesterol (TC), glycosylated hemoglobin (HbAlc) were all decreased in the two groups at 4weeks after treatment, and the study group were lower than those in the control group (P < 0.05). Interleukin-6 (IL-6), interleukin-1β (IL-1β), tumor necrosis factor -α(TNF -α)were all decreased in the two groups at 4weeks after treatment, and the study group were lower than those in the control group (P < 0.05). Motor nerve conduction velocity of common peroneal nerve (MCV), Median nerve MCV, Sensory nerve conduction velocity of common peroneal nerve (SCV), median nerve SCV of median nerve were all increased in the two groups after 4 weeks of treatment, and those in the study group were higher than those in the control group (P < 0.05). No obvious adverse reactions were found in both groups. **Conclusion:** "specimen matching points" acupuncture combined with Mecobalamin can effectively improve glucose and lipid metabolism, inflammatory cytokines and damaged nerve conduction velocity in elderly DPN patients without increasing the incidence of adverse reactions.

Key words: "Sample matching point" acupuncture; Mecobalamin; Elderly; Diabetic peripheral neuropathy; Glycolipid metabolism;

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作者简介:叶欣(1980-),女,本科,主治医师,研究方向:2型糖尿病发病机制,E-mail:joannaxye@126.com

△ 通讯作者:李洁(1978-),女,硕士研究生,主治医生,研究方向:内分泌及代谢疾病,E-mail:Wangwj1978@126.com

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前言

糖尿病周围神经病变(DPN)是引起糖尿病足以及多种糖尿病危重病变的重要因素[1]。DPN 的早期症状主要表现为四肢麻木、神经传导功能障碍,并伴有刺痛、如触电或蚁行般异样感觉,严重者可出现局部肢体萎缩、坏死,致残率、致死率较高[2,3]。由于老年人身体各项机能减退,基础疾病较多,随着人口老龄化的增加,致使 DPN 的发病率呈逐年递增趋势[4,5]。DPN 的发病与血运、代谢、免疫等多种因素异常均相关,发病机制较为复杂,因而缺乏特异性治疗方案[6,7]。甲钴胺是一种内源性的维生素 b12,常用于治疗多种外周末梢神经代谢功能障碍和自主神经病变[8],虽可在一定程度上改善 DPN 患者症状,但临床疗效一般,对已经受损神经的改善效果不大。" 标本配穴 " 针灸是中医治疗的一种表现形式,具有活血通络、荣养经脉之效[9]。鉴于此,本研究通过探讨 " 标本配穴 " 针灸结合甲钴胺对老年 DPN 患者糖脂代谢、炎性细胞因子和受损神经传导速度的影响,以期为临床治疗提供数据参考。

1 资料与方法

1.1 临床资料

选取 2018 年 3 月 ~2019 年 12 月我院接收的 93 例老年 DPN 患者,纳入标准:(1)患者均为糖尿病所致,糖尿病诊断均符合《中国 2 型糖尿病防治指南》[10];(2)DPN 诊断标准参考《实用内科学》[11];(3)患者及其家属知情本研究且签署同意书;(4)肌电图检查显示运动和感觉神经传导障碍;(5) 年龄≥ 60 岁;(6)神经系统检查膝、跟腱反射减弱或消失。排除标准:(1)因遗传、肿瘤、外伤等原因引起的血管病变者;(2)不接受针灸治疗者;(3)合并心肝肾等脏器功能异常者;(4)合并精神障碍,无法配合治疗者;(5) 对本次研究治疗方案不耐受, 中途退出治疗者;(6)近 1 个月使用可对本实验观察指标产生影响的药物者。按照随机数字表法将患者分为研究组(n=47)、对照组(n=46),其中研究组女 19 例,男 28 例,年龄 60~84 岁,平均(72.13±4.25)岁;平均糖尿病病程(6.94±1.08)年;平均 DPN 病程(3.41±0.69)年;平均体质量指数(23.34±0.88)kg/m^2;合并症:冠心病 8 例,高血压 11 例,高脂血 12 例。对照组女 20 例,男 26 例,年龄 61~82 岁,平均(72.92±3.73)岁;平均糖尿病病程(6.82±1.16)年;平均 DPN 病程(3.46±0.87)年;平均体质量指数(23.51±0.96)kg/m^2;合并症:高血压 8 例,冠心病 7 例,高脂血 11 例。两组一般资料比较无差异(P>0.05),临床资料均衡可比。本次研究已通过我院伦理学委员会批准进行。

1.2 方法

两组患者均给予 DPN 的基础治疗及对症处理, 包括糖尿病的科学饮食、运动治疗,DPN 的健康教育,控制血糖、血脂、血压等,上述基础治疗及对症处理为期 15d。在此基础上,对照组给予甲钴胺 (杭州康恩贝制药有限公司, 国药准字 H20060921,规格:0.5 mg)治疗,500 μg/ 次,1 次 /d,肌肉注射,连续治疗 4 周。研究组在甲钴胺的基础上联合 " 标本配穴 " 针灸处理,主穴选取关元、肾俞穴、胃脘下俞、曲池、三阴交、足三里、合谷。随证增加配穴:痰浊较盛者可增加条口、丰隆;淤血较重者可增加阴陵泉、配膈俞、血海;上肢麻木明显者可增加外关、尺泽、手三里。上述穴位常规消毒,选用不锈钢毫针(苏州医疗器械厂生产,规格:0.35 mm×40 mm),针刺后运用提插捻转手法,以局部酸麻肿胀感为宜。足三里和关元穴位加用艾灸治疗,针灸 10~15 min,以皮肤红晕为度。针灸 1 次 /d,6 次 / 周,连续治疗 4 周。

1.3 观察指标

(1)记录两组治疗 4 周后的临床总有效率。临床治愈:神经系统检查无异常, 异常麻木、疼痛等症状与体征完全消失;显效:神经系统检查好转,异常麻木、疼痛等症状与体征有所改善;无效:神经系统检查、异常麻木、疼痛等症状与体征无改善或恶化。总有效率 = 临床治愈率 + 显效率[12]。(2)记录不良反应。(3)于治疗前、治疗 4 周后采用血糖检测仪(德国宝灵曼公司生产)检测两组患者的空腹血糖(FPG)水平。于治疗前、治疗 4 周后采集清晨空腹静脉血 4 mL,3500 r/min 离心 12min,离心半径 13 cm,取上清液待测。采用全自动生化分析仪(贝克曼 5800)检测血清总胆固醇(TC)、甘油三酯(TG)。采用高效液相离子层析法检测糖化血红蛋白(HbAlc),采用酶联免疫吸附法检测血清白介素 -1β(IL-1β)、白介素 -6(IL-6)、肿瘤坏死因子 -α(TNF-α)水平,均严格遵守试剂盒(上海瓦兰生物科技有限公司)说明书步骤进行。(4)于治疗前、治疗 4 周后采用神经传导速度测量仪(上海诺城科技有限公司生产)检测腓总神经、正中神经的感觉神经传导速度 (SCV) 与运动神经传导速度(MCV)。

1.4 统计学方法

采用 SPSS 20.0 进行数据处理与分析,计量资料采用($\bar{x}\pm s$)表示,实施 t 检验,计数资料采用[n(%)]表示,实施 χ^2 检验,当 P<0.05 时差异有统计学意义。

2 结果

2.1 两组疗效比较

治疗 4 周后,研究组的临床总有效率 87.23%(41/47)高于对照组 69.57%(32/46)(P<0.05);详见表 1。

2.2 两组血脂、血糖比较

两组治疗前 FPG、TG、TC、HbAlc 比较差异无统计学意义(P>0.05);两组治疗 4 周后 FPG、TG、TC、HbAlc 均下降,且研究组低于对照组(P<0.05);详见表 2。

2.3 两组炎性细胞因子比较

两组治疗前 IL-6、IL-1β、TNF-α 比较无差异(P>0.05);两组治疗 4 周后 IL-6、IL-1β、TNF-α 均下降, 且研究组低于对照组(P<0.05);详见表 3。

2.4 两组受损神经传导速度比较

两组治疗前正中神经 MCV、腓总神经 MCV、腓总神经

SCV、正中神经 SCV 比较无差异(P>0.05)；两组治疗 4 周后腓总神经 MCV、腓总神经 SCV、正中神经 MCV、正中神经 SCV 均升高，且研究组高于对照组(P<0.05)；详见表 4。

表 1 两组临床疗效比较[n(%)]

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

Groups	Clinical cure	Effective	Invalid	Total efficiency
Control group(n=46)	9(19.57)	23(50.00)	14(30.43)	32(69.57)
Study group(n=47)	15(31.91)	26(55.32)	6(12.77)	41(87.23)
χ^2				4.299
P				0.038

表 2 两组血脂、血糖比较($\bar{x}\pm s$)

Table 2 Comparison of blood lipid and blood glucose between the two groups($\bar{x}\pm s$)

Groups	FPG(mmol/L)		TG(mmol/L)		TC(mmol/L)		HbAlc(%)	
	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment
Control group (n=46)	10.54±1.09	7.23±0.84*	2.89±0.34	2.16±0.41*	5.45±0.38	3.39±0.31*	8.59±0.71	7.03±0.49*
Study group (n=47)	10.46±0.96	6.51±0.63*	2.85±0.49	1.48±0.33*	5.51±0.42	2.46±0.35*	8.51±0.63	6.15±0.53*
t	0.376	4.683	0.456	8.820	0.722	13.554	0.575	8.310
P	0.708	0.000	0.649	0.000	0.472	0.000	0.565	0.000

Note: compared with before treatment, *P<0.05.

表 3 两组炎性细胞因子比较($\bar{x}\pm s$，pg/mL)

Table 3 Comparison of inflammatory cytokines between the two groups($\bar{x}\pm s$，pg/mL)

Groups	IL-6		IL-1β		TNF-α	
	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment
Control group (n=46)	33.91±4.12	24.17±4.87*	37.13±5.57	27.89±6.98*	45.12±4.86	31.89±6.62*
Study group(n=47)	32.57±4.05	16.34±3.09*	36.69±7.12	20.12±5.87*	44.82±5.67	22.71±4.32*
t	1.582	9.279	0.331	5.815	0.274	7.936
P	0.147	0.000	0.741	0.000	0.785	0.000

Note: compared with before treatment, *P<0.05.

表 4 两组受损神经传导速度比较($\bar{x}\pm s$，m/s)

Table 4 Comparison of damaged nerve conduction velocity between the two groups($\bar{x}\pm s$，m/s)

Groups	Common peroneal nerve MCV		Common peroneal nerve SCV		Median nerve MCV		Median nerve SCV	
	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment
Control group (n=46)	34.92±4.98	39.81±5.78*	35.28±5.31	38.78±5.02*	37.98±5.86	42.78±5.12*	36.09±5.31	41.23±6.47*
Study group (n=47)	34.54±5.07	44.99±5.83*	34.89±6.31	43.23±4.34*	37.34±4.13	46.89±4.32*	35.81±4.41	45.26±5.96*
t	0.365	4.302	0.322	4.576	0.559	4.187	0.277	3.125
P	0.716	0.000	0.748	0.000	0.550	0.000	0.782	0.002

Note: compared with before treatment, *P<0.05.

2.5 不良反应发生情况比较

两组均未见明显不良反应发生。

3 讨论

DPN 的主要病理改变在于神经纤维产生节段性脱髓鞘，致使轴索再生能力受损产生退化，临床表现中以感觉神经、运动神经症状最早出现，以肢体麻木疼痛症状最为突出[13,14]。以往研究证实[15]，部分 DPN 患者可出现肢体烧灼样疼痛、电击样痛或者刀割样锐痛，给患者工作及生活质量带来严重影响。目前，其发病机制尚未完全阐明，近年研究显示[16,17]，代谢紊乱、神经营养缺失、血流微循环损伤等多种因素可导致机体长期处于高血糖及胰岛素抵抗状态，导致基底膜增厚、血管壁等病理性改变，随着病情的进展，血管管腔变窄，血流受阻，引起神经传导速度下降。同时，高血糖还可通过激活 NF-kB 通路，诱导激酶将游离 NF-kB 转移至细胞核，神经纤维产生节段性脱髓鞘，刺激 T 细胞在抗原作用下产生炎性细胞因子 TNF-α，上调免疫应答，从而刺激单核及内皮细胞分泌 IL-6、IL-1β 等炎性细胞因子[18,19]。此外，机体长期处于高血糖状态下，凝血和抗凝因子表达异常，引起血脂异常，加速血管病变，参与着 DPN 的病情进展[20,21]。

甲钴胺是临床治疗 DPN 的第一阶梯用药，其主要作用机制在于参与脑、脊髓等神经元细胞胸腺嘧啶核苷的合成，促进神经细胞中的核酸、蛋白质以及神经髓鞘合成，进而促进轴突再生，恢复轴突运输功能，对神经产生营养和修护作用，促进机体神经传导功能恢复[22-24]。单纯的甲钴胺治疗虽可在一定程度上缓解临床症状，但仍难以达到理想预期要求。鉴于此，本研究在利用甲钴胺控制血糖，修复和养护损伤神经的基础上，辅以 " 标本配穴 " 针灸治疗，此类针灸以 " 双固一通 " 针法为指导，选取固护先天之气的肾俞、关元，固护后天脾胃之气的足三里、三阴交以及驱邪之穴合谷、曲池及胃脘下俞为主穴。其中合谷、曲池既能去除湿热之邪，防止湿热；又能改善上肢血液循环，缓解上肢症状。胃脘下俞则为治疗消渴病之经验效穴。三阴交为足太阴脾经穴，可调脾经之气；足三里为足阳明胃经合穴，可健脾胃，助运化，以治消渴之消谷善饥，且可解肢热身烦。曲池为手阳明大肠经合穴，可调理大肠经所变动所生的疾病[25,26]。诸穴诸经共奏驱邪外出、补益气血之效。本研究结果显示，" 标本配穴 " 针灸结合甲钴胺治疗效果确切，疗效显著。进一步观察发现，" 标本配穴 " 针灸结合甲钴胺治疗还可有效改善患者糖脂代谢、炎性细胞因子和受损神经传导速度。相关研究证实针灸可改善胰岛 β 细胞功能，有辅助降血糖之功，配合甲钴胺治疗有进一步协同降血糖之功效[27,28]。并通过改变血液的浓粘凝聚状态，调理血脂，加快血液微循环，改善局部营养状况，从而减少神经组织因缺血缺氧而引起的功能障碍；同时还可调节和修护周围神经，进而改善肢体麻木疼痛、感觉异常、运动异常等症状[29,30]。另本研究结果显示 " 标本配穴 " 针灸结合甲钴胺治疗安全性较好，这可能与针灸本身即具备安全可靠，无副作用等优点有关。

综上所述，" 标本配穴 " 针灸结合甲钴胺治疗老年 DPN 患者疗效较好，可有效改善患者糖脂代谢、炎性细胞因子和受损神经传导速度，安全可靠。

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