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血府逐瘀汤对糖尿病视网膜病变患者视神经形态结构的影响 *

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摘要 目的：探讨血府逐瘀汤对糖尿病视网膜病变患者视神经形态结构的影响。**方法：**2017 年 11 月 ~2019 年 12 月选择在本院就诊的糖尿病视网膜病变患者 76 例，根据随机信封抽签原则把患者分为观察组与对照组各 38 例。对照组给予康柏西普治疗，观察组在对照组治疗的基础上给予血府逐瘀汤治疗，两组都治疗观察 2 个月，记录视神经形态结构变化情况。**结果：**治疗后观察组的总有效率为 97.37 %，显著高于对照组的 78.95 %（P<0.05）。两组治疗后行空腹血糖（fasting blood glucose，FBG）与餐后 2 h 血糖（2 h postprandial blood glucose，2hPG），值都低于治疗前，观察组低于对照组（P<0.05）。两组治疗前的视盘周围视网膜神经纤维层（Retinal nerve fiber layer，RNFL）厚度在上象限、下象限、颞象限、鼻象限上对比无差异（P>0.05），两组治疗后各个象限的 RNFL 厚度均显著下降（P<0.05），且观察组各个象限的 RNFL 厚度均低于对照组（P<0.05）。观察组治疗后的红细胞聚集指数与纤维蛋白原低于治疗前，也低于对照组（P<0.05），对照组治疗前后对比无差异（P>0.05）。**结论：**血府逐瘀汤在糖尿病视网膜病变患者中的应用能改善视神经形态结构，促进降低血糖，改善患者的血液流变学状况，从而提高治疗效果。

关键词：血府逐瘀汤；糖尿病视网膜病变；视神经形态结构；血液流变学；血糖
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Effect of Xuefu Zhuyu Decoction on Optic Nerve Morphological Structure in Patients with Diabetic Retinopathy*

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ABSTRACT Objective: To explore the effect of Xuefu Zhuyu Decoction on optic nerve morphology in patients with diabetic retinopathy. **Methods:** From November 2017 to December 2019, 76 cases of patients with diabetic retinopathy treated in our hospital were selected as the research object. All the cases were divided into the observation group and control group of 38 cases in each groups accorded to the principle of random envelope drawing. The control group were treated with Compacept, and the observation group were given Xuefu Zhuyu Decoction based on the treatment of the control group. Both groups were treated and observed for 2 months, and the changes of optic nerve morphology and structure were recorded. **Results:** The total effective rates of the observation group after treatment were 97.37 %, which were significantly higher than 78.95 % of the control group（P<0.05）. The fasting blood glucose (FBG) and 2 h postprandial blood glucose (2hPG) values of the two groups after treatment were lower than before treatment, and the observation group were lower than the control group, and compared the difference were statistically significant（P<0.05）. There was no difference in the thickness of the retinal nerve fiber layer (RNFL) around the optic disc between the upper quadrant, the lower quadrant, the temporal quadrant, and the nasal quadrant before treatment (P>0.05), and the thickness of the RNFL around the optic disc in each quadrant of the two groups after treatment decreased significantly (P<0.05), and the thickness of RNFL around the optic disc in each quadrant of the observation group was lower than that of the control group (P<0.05). The erythrocyte aggregation index and fibrinogen in the observation group after treatment were lower than before treatment and also lower than the control group, and the compared the difference were statistically significant (P<0.05), and there were no statistical difference comapred between before and after treatment in the control group (P>0.05). **Conclusion:** The application of Xuefu Zhuyu Decoction in patients with diabetic retinopathy can improve the morphological structure of the optic nerve, promote the reduction of blood glucose, and improve the blood rheology of patients, thereby improving the therapeutic effect.

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前言

糖尿病视网膜病变(diabetic retinopathy,DR)是糖尿病重要并发症之一,在临床上表现为以视网膜微血管损害为特征的慢性、进行性视力丢失,严重时可致盲,可直接影响到患者的生活质量[1,2]。该病的具体发病机制尚不明确,但病因主要涉及到机体胰岛素及细胞代谢异常,从而引起眼部血管、神经微循环改变,并伴随有视网膜新生血管形成,从而造成视功能损坏[3]。目前,药物为糖尿病视网膜病变的主要治疗方法,其中玻璃体腔内给药克服了血 - 眼屏障,可使得药物长时间直接作用于病变处,从而提高治疗效果[4]。中医治疗糖尿病视网膜病变具有悠久的历史,血府逐瘀汤是活血化瘀方中的代表方,由川芎、柴胡、当归、枳壳、桔梗、牛膝、桃仁、赤芍、红花、生地、甘草等组成,可用于气机郁滞,瘀血内结等病症的治疗,可改善微循环、扩张血管、促进眼内出血的吸收[5,6]。视神经是由视网膜神经节细胞的轴突汇聚而成,也是糖尿病视网膜病变病理进程研究的重要部位[7,8]。光学相干断层扫描技术(Optotical Coherece Tomography,OCT)是一种可以实现实时、高分辨、大深度、非接触、无创伤的图像诊断技术,能够精确的测量视网膜神经纤维层的厚度,其发展为视神经的三维重建提供了可能,其能清晰显示视神经各部分组织结构,并获得断层图像[9,10]。本文具体探讨了血府逐瘀汤对糖尿病视网膜病变患者视神经形态结构的影响,希望为改善患者预后提供参考。

1 资料与方法

1.1 研究对象

2017 年 11 月 ~2019 年 12 月选择在本院就诊的糖尿病视网膜病变患者 76 例作为研究对象,纳入标准:符合单纯型糖尿病视网膜病变诊断;年龄 30~80 岁,双眼发病与治疗;均为增殖性糖尿病视网膜病变;医院伦理委员会批准了此次研究;患者均自愿接受研究本研究;患眼最佳矫正视力(best correct visual acuity,BCVA)在 0.05~0.5,无全盲。排除标准:妊娠期或哺乳期妇女;对本研究药物过敏的患者;合并有心力衰竭、肝肾功能严重不全患者;合并青光眼、严重白内障等疾病患者。

根据随机信封抽签原则分为两组,各 38 例,两组一般资料对比无差异(P>0.05),见表 1。

表 1 两组一般资料对比

Table 1 Comparison of two groups

Groups	n	Course of disease (years)	SBP(mmHg)	DBP(mmHg)	BMI(kg/m^2)	Gender (male/female)	Age (years)
Observation group	38	4.56± 0.15	132.98± 10.22	83.20± 5.15	22.76± 1.44	20/18	58.15± 1.48
Control group	38	4.61± 0.22	133.08± 8.73	83.77± 4.19	22.89± 1.24	21/17	58.19± 1.11

1.2 治疗方法

对照组:给予康柏西普治疗,用注射针头向玻璃体腔内注射康柏西普 0.05 mL(0.5 mg,成都康弘,国药准字 S20130012),每个月 1 次,治疗观察 2 个月。

观察组:在对照组治疗的基础上给予血府逐瘀汤治疗,组方:桃仁 12 g,当归、生地、牛膝、红花各 9 g,柴胡、枳壳、桔梗各 6 g,甘草 3 g,水煎 400 mL,每日口服 1 剂,早晚分服,治疗观察 2 个月。

1.3 观察指标

(1)疗效标准:显效:临床症状明显减轻,视力增加 2 行以上;有效:临床症状有所减轻,视力增加 1~2 行;无效:无达到上述标准甚或恶化。总有效率%=(显效 + 有效)/ 患者例数×100%。(2)在治疗前后进行 FBG 与 2hPG 的测定。(3)在治疗前后进行 RNFL 检查,采用德国 Zeiss 光学相干断层扫描仪测量上象限、下象限、颞象限、鼻象限的 RNFL 厚度。(4)在治疗前后测定并记录患者的血液流变学指标,包括红细胞聚集指数与纤维蛋白原等。

1.4 统计方法

应用 SPSS 20.00,经正态性检验和方差齐性检验,计量资料采用均数± 标准差表示(对比为 t 检验),计数资料采用 n(%)表示(对比为 x^2 检验),P<0.05(双侧)差异具有统计学意义。

2 结果

2.1 总有效率对比

治疗后观察组的总有效率为 97.37 %,显著高于对照组的 78.95 %(P<0.05),见表 2。

表 2 两组总有效率对比(例,%)

Table 2 Comparison of total effective rates between the two groups (n, %)

Groups	n	Effect	Effective	Invalid	Total efficiency
Observation group	38	34	3	1	37(97.37)*
Control group	38	25	5	8	30(78.95)

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

2.2 血糖变化对比

两组治疗后的 FBG、2hPG 值都低于治疗前，观察组低于对照组(P<0.05)，见表 3。

表 3 两组治疗前后血糖变化对比(mmol/L，$\bar{x}\pm s$)

Table 3 Comparison of blood glucose changes between two groups before and after treatment (mmol/L, $\bar{x}\pm s$)

Groups	n	FBG		2hPG	
		Pre-treatment	After treatment	Pre-treatment	After treatment
Observation group	38	8.13± 0.66	5.14± 0.32#*	15.20± 2.11	8.99± 1.10#*
Control group	38	8.24± 0.34	5.99± 0.13#	15.28± 1.48	10.77± 1.42#

Note: compared with the control group, *P<0.05, compared with the pre-treatment, #P<0.05.

2.3 视神经形态结构变化对比

两组治疗前的 RNFL 厚度在上象限、下象限、颞象限、鼻象限上对比无差异(P>0.05)，两组治疗后各个象限的 RNFL 厚度均显著下降(P<0.05)，且观察组低于对照组(P<0.05)，见表 4。

表 4 两组治疗前后视神经形态结构变化对比($\bar{x}\pm s$)

Table 4 Comparison of changes in optic nerve morphology before and after treatment between the two groups ($\bar{x}\pm s$)

Groups	n		RNFL thickness(um)			
			Upper quadrant	Lower quadrant	Temporal quadrant	Nasal quadrant
Observation group	38	Pre-treatment	139.08± 32.22	142.57± 34.25	90.27± 6.36	84.47± 7.21
		After treatment	127.42± 31.26#*	132.46± 32.32#*	82.46± 6.14#*	78.36± 6.23#*
Control group	38	Pre-treatment	139.31± 32.41	142.49± 34.16	90.35± 6.57	85.01± 7.15
		After treatment	135.27± 31.37#	139.36± 33.15#	87.53± 6.23#	83.15± 7.16#

2.4 血液流变学变化对比

观察组治疗后的红细胞聚集指数与纤维蛋白原低于治疗前，也低于对照组(P<0.05)，对照组治疗前后对比无差异(P>0.05)，见表 5。

表 5 两组治疗前后血液流变学变化对比($\bar{x}\pm s$)

Table 5 Comparison of blood rheology changes between two groups before and after treatment ($\bar{x}\pm s$)

Groups	n	Red blood cell aggregation index		Fibrinogen (g/L)	
		Pre-treatment	After treatment	Pre-treatment	After treatment
Observation group	38	8.65± 0.13	4.58± 0.12#*	4.59± 0.17	3.78± 0.10#*
Control group	38	8.67± 0.22	8.44± 0.38	4.61± 0.22	4.56± 0.18

3 讨论

糖尿病视网膜病变是眼科较为常见疾病之一，随着生活水平的提高，糖尿病视网膜病变的发生率呈明显上升趋势[11]。当前该病的发病机制尚不完全清楚，其病因主要涉及免疫系统、神经系统、内分泌系统、生理系统、遗传因素、环境因素等多方面。可反复引起发病区域出现出血、渗出、水肿等临床表现，甚至出现玻璃体积血、视网膜脱离等严重并发症，从而导致患者视力急剧下降[12,13]。康柏西普是用生物工程技术生产的 100 % 人源化重组融合蛋白，能特异性地结合 VEGF，抑制新生血管、减轻黄斑水肿，从而达到治疗糖尿病视网膜病变的目的[14]。糖尿病视网膜病变属祖国医学 " 消渴目病 "、" 视瞻昏渺 " 范畴，血瘀贯穿该病发生、发展的始终。在血府逐瘀汤中，柴胡能疏肝理气，升达清阳[15]；生地黄凉血清瘀热，合当归滋养阴血；牛膝通血脉，引瘀血下行；桔梗开肺气载药上行于心中，合枳壳开胸行气，与柴胡同用，使气行则血行；甘草调和诸药，使痰瘀得化[16]。本研究治疗后观察组的总有效率高于对照组；两组治疗后的 FBG、2hPG 值都低于治疗前，观察组低于对照组，与程艳春[17]的研究类似，采用府逐瘀汤联合丹参饮治疗单纯型糖尿病视网膜病变，结果显示治疗后，治疗组总有效率明显高于对照组，2 组 FBG、2hPG 均显著改善，且治疗组治疗后的变化情况显著优于对照组，表明血府逐瘀汤在糖尿病视网膜病变患者的应用能促进血糖降低，提高治疗效果。

视网膜居于眼球壁的内层，周围密布大量微小血管，糖尿病患者可引起血管内皮细胞功能异常，造成血 - 视网膜屏障受损，从而引起视力严重受损[18,19]。视网膜神经纤维厚度能够反映视神经和视觉传导功能，主要由神经节细胞的轴突及传出纤维、Muller 细胞、神经胶质细胞、以及丰富的血管系统组成[20,21]，在糖尿病视网膜病变的早期改变以视网膜神经节细胞凋亡为主，至中晚期则出现视网膜血管明显病变、纤维增殖等导致视网膜水肿，使得视网膜神经纤维厚度可能增加[22,23]。本研究两组治疗后各个象限的 RNFL 厚度均显著下降，且观察组各个象限的 RNFL 厚度均低于对照组，目前国内外对于血府逐瘀汤治疗糖尿病视网膜病的研究很多，但是对 RNFL 厚度的研究目前缺

乏。从机制上分析，血府逐瘀汤能促进糖尿病患者缺血状态以及血液微循环的改善，能够促进内皮功能改善和缺血区血管新生，减轻病情对其视网膜神经纤维厚度的影响，同时也能抑制视网膜新生血管进一步病变增生、缓解视网膜水肿，使得视网膜神经纤维厚度降低[24]。其也能将脂质过氧化物清除，具有良好的抗氧化作用和抗应激作用，能够调节患者的血脂水平，也能纠正患者的代谢紊乱状况，从而促进患者视神经形态结构的改善[25,26]。

糖尿病视网膜病变的临床表现和病理改变多样，比如微血管瘤、出血、棉绒斑、硬性渗出、无灌注区形成、新生血管等[27]。在中医的临床应用中需要积极进行行气活血治疗，才能减轻视网膜毛细血管渗漏和纤维增殖，有效促进视网膜出血、渗出物的吸收与改善[28,29]。本研究显示观察组治疗后的红细胞聚集指数与纤维蛋白原低于对照组，表明血府逐瘀汤在糖尿病视网膜病变患者的应用能改善患者的血液流变学状况，与程艳春[17]的研究类似，治疗后治疗组全血黏度，红细胞压积，红细胞聚集指数，纤维蛋白原水平显著改善，而对照组变化不明显，两组比较差异有统计学意义。当前也有研究显示，血府逐瘀汤提高了血液成分的代谢速度，能促进机体代谢废物的清理[30,31]。但对血府逐瘀汤的有效性和安全性的评价尚需大样本和长期的观察，特别是该药在糖尿病视网膜病变中的作用机制还有待深入分析。

综上所述，血府逐瘀汤在糖尿病视网膜病变患者中的应用能改善视神经形态结构，促进血糖降低，改善患者的血液流变学状况，从而提高治疗效果。

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