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丹参酮ⅡA注射液联合前列地尔治疗糖尿病肾病的疗效观察*

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摘要 目的:探究丹参酮ⅡA注射液联合前列地尔治疗糖尿病肾病的临床疗效。**方法:**选取我院于2014年10月至2015年10月期间收治的糖尿病肾病患者100例为研究对象,按照随机数字表法分为研究组和对照组各50例;对照组给予前列地尔,研究组给予前列地尔与丹参酮ⅡA注射液,比较两组患者总胆固醇(TC)、甘油三酯(TG)、高密度脂蛋白胆固醇(HDL-C)和低密度脂蛋白胆固醇(LDL-C)以及血尿素氮(BUN)、24 h尿蛋白定量及肌酐(Cre)的水平。**结果:**治疗前两组患者间各项指标均无显著性差异($P>0.05$);治疗后两组患者TC、TG、LDL-C、Cre、BUN、24 h尿蛋白定量较治疗前均出现明显降低,HDL-C较治疗前明显升高($P<0.05$);研究组患者TC、TG、LDL-C、Cre、BUN、24 h尿蛋白定量均低于对照组,HDL-C高于对照组($P<0.05$);两组患者均未出现严重不良反应。**结论:**丹参酮ⅡA注射液联合前列地尔治疗糖尿病肾病可以改善患者的血脂水平,降低肌酐,尿蛋白,缓解肾脏损伤,具有明显的临床疗效。

关键词:糖尿病肾病;丹参酮ⅡA;前列地尔;疗效

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Clinical Effect of Alprostadil Jointed with Tanshinone II A Injection on Patient with Diabetic Nephropathy*

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ABSTRACT Objective: To explore the clinical effect of alprostadil jointed with tanshinone II A injection on patient with diabetic nephropathy. **Methods:** 100 cases of patients with diabetic nephropathy treated in our hospital from October 2014 to October 2015 were selected as research object, which were divided into research group and control group according to the random number table method, 50 cases in each group. The control group was given alprostadil, while the research group received alprostadil and Tanshinone II A injection. Compared the level of total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), serum creatinine (Cre), blood urea nitrogen (BUN), 24 h urinary albumin between the two groups. **Results:** There was no significant difference on each index between the two groups before treatment ($P>0.05$), and the levels of TC, TG, LDL-C, Cre, BUN, 24 h urinary albumin were significantly declined and the level of HDL-C was significantly increased after treatment in each group ($P<0.05$). Levels of TC, TG, LDL-C, Cre, BUN, 24 h urinary albumin in research group were significant lower than control groups after treatment ($P<0.05$), while the level of HDL-C was higher ($P<0.05$). There were no serious adverse reaction occurred in the two groups. **Conclusion:** Alprostadil jointed with tanshinone II A injection in the treatment of the patients with diabetic nephropathy can improve the blood lipid levels, reduce Cre and 24h urinary albumin, and alleviate renal injury, which has obvious clinical efficacy.

Key words: Diabetic nephropathy; Tanshinone II A; Alprostadil; Effect

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前言

糖尿病肾病是糖尿病常见的并发症,也是导致慢性肾衰竭、肾功能不全的常见原因之一^[1]。由于糖尿病引起的血糖、脂质代谢以及水电解质代谢紊乱和微血管循环严重损害,引发肾脏动脉压升高,肾小球高灌注,增生肥大,基底膜增厚,肾脏功能失代偿导致肾功能不全甚至死亡^[2]。临床上主要表现为大量蛋白尿、水肿、肌酐水平升高及血压升高。有效控制血脂水平及

降低肌酐(creatinine, Cre)可延缓肾脏病变,对于控制糖尿病肾病具有重要意义^[3]。糖尿病肾病的防治已成为被临床医师关注并重视的问题^[4]。目前,临床上主要采取内科药物治疗,其中前列地尔注射液和丹参酮ⅡA是最常用的药物。研究报道表明^[5],前列地尔具有扩张血管、控制炎症反应、增加肾血流和抑制血栓形成的作用,在治疗糖尿病肾病中得到广泛应用。而丹参酮ⅡA注射液作为中药制剂,在改善微血管循环,延缓肾脏损害方面也具有重要功能^[6]。本研究选取我院于2014年10月至

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2015年10月期间收治的100例糖尿病肾病患者,探究丹参酮II A注射液联合前列地尔在治疗糖尿病肾病的临床疗效,现报道如下。

1 对象与方法

1.1 研究对象

选取2014年10月~2015年10月期间,我院收治的糖尿病肾病患者100例为研究对象。纳入标准:(1)符合1999年WHO提出的2型糖尿病的诊断标准^[9];(2)糖尿病肾病采用

Mogensen 诊断标准^[9],且尿蛋白排泄率(Urinary Albumin Excretion Rate, UAER)在20~200 $\mu\text{g}/\text{min}$;(3)患者知情同意,且经医学伦理协会批准。排除标准:(1)合并其他原因引起的肾脏病变;(2)合并心、肝功能障碍者;(3)合并恶性肿瘤、哺乳期妇女及对药物过敏者;(4)存在精神疾病史。按照随机数字表法将患者分成研究组 and 对照组,每组各50例。其中,男性59例,女性41例;年龄33~65岁,平均年龄(55.01 ± 7.38)岁;两组患者间性别、年龄、病程、糖尿病分型及糖尿病肾病分期等一般资料比较,差异均不存在统计学意义($P>0.05$),具有可比性。见表1。

表1 两组患者间一般资料比较

Table 1 Comparison of the general data between the two groups

Groups	N	Gender(M/F)	Age(years)	Duration of disease(years)	Type 2 diabetes mellitus (I/II)	Diabetic nephropathy stage (III/IV)
Control group	50	27/23	54.61 $\pm$ 6.91	7.92 $\pm$ 4.29	3/47	23/27
Research group	50	32/18	55.37 $\pm$ 7.19	8.41 $\pm$ 3.91	4/46	26/24
t/ χ^2		0.753	0.589	0.655	0.058	0.136
P		0.385	0.722	0.743	0.923	0.854

1.2 治疗方法

所有糖尿病患者均经控制饮食及体育锻炼;给予降糖治疗:使空腹血糖(Fasting blood glucose, FBG) <7.0 mmol/L,餐后2 h血糖 <10.0 mmol/L,糖化血红蛋白(Glycosylated hemoglobin, HbA1c) $<7.0\%$;降脂治疗:控制总胆固醇(Total cholesterol, TC) <4.5 mmol/L,甘油三酯(triglyceride, TG) <1.7 mmol/L,控制血压正常范围持续1个月以上。所有患者均静脉滴注前列地尔注射液(武汉爱民制药有限公司,国药准字H42022501,规格:2 mL:10 μg)10 μg +生理盐水250 mL,每天一次;期间无间断,连续滴注4周。研究组在此基础上增加丹参酮II A(多布瑞菲医药有限公司,国药准字H22026719,规格:2 mL:10 mg)注射液20 mL+生理盐水250 mL。滴注均在上午9时进行。

1.3 观察指标

1.3.1 生化指标 所有研究对象纳入研究后抽取空腹肘静脉血5 mL,25 $^{\circ}\text{C}$ 静置半小时后进行离心,取上层血清,并于2 h内使用AU5800系列全自动生化分析仪(购于美国贝克曼库尔特公司)测定患者TC、TG、高密度脂蛋白胆固醇(high density lipoprotein cholesterol, HDL-C)和低密度脂蛋白胆固醇(low density lipoprotein cholesterol, LDL-C)、血尿素氮(Blood urea ni-

trogen, BUN)及24 h尿蛋白定量及Cre;采用全自动HbA1c分析仪利用高效液相色谱法检测HbA1c水平;分析比较两组患者治疗后TCTG、HDL-C、LDL-C等血脂水平的不同,同时比较两组患者治疗后BUN、24 h尿蛋白定量及Cre水平。

1.3.2 不良反应 观察并记录两组患者治疗过程中药物过敏、恶心、头晕、皮疹等药物不良反应的发生情况。

1.4 统计分析

应用SPSS 16.0统计软件进行数据分析,计量资料用均数 $\pm$ 标准差($\bar{x} \pm s$)表示,各组间均数的比较采用t检验,各组间计数资料的比较采用 χ^2 检验,以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组患者治疗前后血脂水平比较

治疗前两组患者间TC、TG、HDL-C、LDL-C比较,差异不存在统计学意义($P>0.05$);治疗后两组患者TC、TG、LDL-C较治疗前均出现明显降低($P<0.05$),HDL-C显著升高($P<0.05$)。治疗后研究组患者TC、TG、LDL-C均低于对照组,HDL-C高于对照组($P<0.05$)。见表2。

表2 两组患者治疗前后各项指标的比较

Table 2 Comparison of various indexes of two groups before and after treatment

Groups	N	TC(mmol/L)		TG(mmol/L)		HDL-C(mmol/L)		LDL-C(mmol/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	50	6.71 $\pm$ 0.59	6.02 $\pm$ 0.20*	3.61 $\pm$ 1.22	3.24 $\pm$ 1.11*	1.11 $\pm$ 0.28	1.36 $\pm$ 0.98*	5.61 $\pm$ 0.69	3.35 $\pm$ 0.33*
Research group	50	6.68 $\pm$ 0.55	4.51 $\pm$ 0.09*	3.59 $\pm$ 1.34	2.01 $\pm$ 1.05*	1.20 $\pm$ 0.19	2.27 $\pm$ 0.45*	5.59 $\pm$ 0.41	1.89 $\pm$ 0.45*
t		0.213	18.210	0.102	7.389	0.431	9.798	0.132	6.349
P		0.783	0.000	0.871	0.001	0.445	0.001	0.801	0.000

Note: Compared with before treatment, * $P<0.05$.

2.2 两组患者治疗前后肾功能变化情况的对比

两组患者治疗前 Cre、BUN、24 h 尿蛋白定量水平比较,差异均不存在统计学意义($P>0.05$)治疗后两组患者 Cre、BUN、24

h 尿蛋白定量较治疗前均出现明显降低($P<0.05$);研究组患者治疗后 Cre、BUN、24 h 尿蛋白定量水平均显著低于对照组($P<0.05$)。见表 3。

表 3 两组患者治疗前后 Cr、BUN、24h 尿蛋白定量的比较

Table 3 Comparison of Cr, BUN and 24h urinary protein in two groups before and after treatment

Groups	N	Cre ($\mu\text{mol/L}$)		BUN(mmol/L)		Urinary protein(g/24 h)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	50	76.23 $\pm$ 20.39	73.38 $\pm$ 24.39*	6.29 $\pm$ 1.37	6.19 $\pm$ 1.16*	1.51 $\pm$ 0.48	1.20 $\pm$ 0.57*
Research group	50	74.37 $\pm$ 19.78	63.29 $\pm$ 22.29*	6.23 $\pm$ 1.28	4.13 $\pm$ 1.09*	1.49 $\pm$ 0.63	0.81 $\pm$ 0.38*
t		-0.507	1.817	-0.248	2.374	-0.099	2.784
P		0.307	0.021	0.402	0.011	0.461	0.008

Note: Compared with before treatment,* $P<0.05$.

2.3 两组患者药物不良反应的发生情况

治疗过程中研究组出现 1 例恶心、1 例头晕;对照组患者出现 2 例头晕,未经治疗均自愈。两组患者均无严重不良反应发生。

3 讨论

糖尿病肾病是糖尿病全身微血管病变的肾脏表现^[9],糖尿病发病过程中的全身糖脂代谢异常、高血压引起的肾脏血流动力学障碍、肾小球高灌注、高滤过、代偿性肾小球基底膜增生、增厚、通透性增加和细胞间质增生是糖尿病肾病发生的主要机理,也是终末期肾病及死亡的主要原因之一^{—[10,11]}。临床上采取积极的治疗可延缓糖尿病肾病的进展,有效降低死亡率^[12,13]。前列地尔在控制肾脏功能恶化方面具有较高的疗效,主要表现为其一方面能够降低血管内血脂水平,舒张血管,增加血管循环血流量,避免肾脏血管缺血缺氧的发生;另一方面,前列地尔能够抑制血管紧张素-肾素-醛固酮系统活性,改善肾血管压力及肾小球滤过率,保护肾脏功能^[14]。而丹参酮 II A 注射液作为中药制剂能够明显改善血管内皮功能,降低凝血因子,预防血栓,从而改善毛细血管血液循环^[15]。因此,本研究探究前列地尔与丹参酮 II A 注射液联合治疗在糖尿病肾病的临床疗效。

研究显示^[16],脂微球包裹的前列地尔通过调节腺苷酸环化酶和磷酸二酯酶活性增加血管平滑肌中 cAMP 含量,抑制血小板凝聚降低血栓发生率,扩张血管改善肾脏血流动力学;除此之外,其还能够调节血脂及抑制血管紧张素活性,抗氧化保护血管内皮细胞等改善肾小球微循环,降低肾小球肾压,减少蛋白尿的产生,缓解肾脏病变^[17]。丹参酮 II A 为超氧化物歧化酶,可以清除细胞内氧自由基,抗氧化从而降低脂质代谢对血管内皮细胞的损伤,同时能够改善血脂,促进抗凝,改善肾脏血液循环^[18-20]。本研究显示治疗后两组患者 TC、TG、LDL-C 较治疗前均出现明显降低($P<0.05$),说明两种治疗措施均能够改善患者血脂水平。Cre、BUN、24 h 尿蛋白定量是衡量患者肾功能最重要指标,当机体肾功能出现障碍时,患者肾小球滤过功能异常,Cre、BUN、24 h 尿蛋白定量均会上升,本研究显示,治疗后两组患者 Cre、BUN、24 h 尿蛋白定量较治疗前均出现明显降低($P<0.05$),说明两种疗法均能够改善血脂水平,缓解肾损伤。但

治疗后研究组患者 TC、TG、LDL-C、Cre、BUN、24 h 尿蛋白定量均低于对照组($P<0.05$),说明前列地尔与丹参酮 II A 联合治疗在糖尿病肾病改善患者病情上明显优于前列地尔单独用药。因此,我们推测联合用药可能在降低血脂,改善肾脏血液循环,增加肾小球血流量,降低血管内皮细胞氧化以及抗凝方面具有协同作用,从而更好地保护肾脏。

综上所述,丹参酮 II A 注射液联合前列地尔在改善糖尿病肾病患者血脂水平、降低尿蛋白及肌酐水平和降低肾脏损伤方面,具有明显的临床疗效。

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(上接第 3113 页)

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