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丹参多酚酸盐联合前列地尔治疗糖尿病肾病的效果*

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摘要 目的:探讨丹参多酚酸盐联合前列地尔治疗糖尿病肾病的效果。**方法:**选取 2015 年 11 月~2018 年 11 月我院收治的糖尿病肾病患者 114 例,采用随机数字表法将患者分为两组。对照组在常规治疗的基础上给予前列地尔注射液,观察组在对照组的基础上给予丹参多酚酸盐注射液。比较两组患者的临床治疗效果、治疗前后肾功能、血糖水平、血清可溶性细胞间粘附分子 1 (sICAM-1)及内皮素(ET-1)水平的变化及不良反应的发生情况。**结果:**治疗后,观察组治疗的总有效率为 91.23%,显著高于对照组(73.68%, $P < 0.05$)。两组患者治疗后的血肌酐(Scr)、尿素氮(BUN)、 β_2 -微球蛋白(β_2 -MG)、尿蛋白排泄率(UAER)、血清 sICAM-1 及 ET-1 水平均较治疗前显著下降($P < 0.05$),且观察组以上指标均显著低于对照组($P < 0.05$)。两组患者治疗前后及两组间的糖化血红蛋白(HbA1c)及空腹血糖(FPG)水平比较均无统计学差异($P > 0.05$)。两组患者均未发生严重不良反应,轻微不良反应均经对症处理后好转,且不影响治疗。**结论:**丹参多酚酸盐联合前列地尔可显著改善糖尿病肾病患者的肾功能、提高临床治疗效果,且不影响血糖水平,可能与其显著降低患者血清 sICAM-1 及 ET-1 水平有关。

关键词:丹参多酚酸盐;前列地尔;糖尿病肾病;效果;肾功能

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Effect of Salvianolate Combined with Alprostadil on the Diabetic Nephropathy*

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ABSTRACT Objective: To investigate the clinical efficacy of salvianolate combined with alprostadil in the treatment of diabetic nephropathy. **Methods:** 114 cases of patients with diabetic nephropathy admitted to our hospital from November 2015 to November 2018 were selected. The patients were divided into two groups by random number table method. The control group was given alprostadil injection on the basis of conventional treatment, and the observation group was given salvianolate injection on the basis of the control group. The clinical treatment effect, changes of renal function, blood glucose level, serum sICAM-1 and ET-1 before and after treatment, and occurrence of adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rate in the observation group was 91.23%, which was significantly higher than that in the control group (73.68%, $P < 0.05$). After treatment, the levels of Scr, BUN, β_2 -MG, UAER, serum sICAM-1 and ET-1 of both groups were significantly lower than those before treatment, and the above indexes in the observation group were significantly lower than those in the control group ($P < 0.05$). There was no significant difference in the HbA1c and FPG levels between the two groups before and after treatment ($P > 0.05$). No serious adverse reactions occurred in the two groups, and mild adverse reactions improved after symptomatic treatment without affecting treatment. **Conclusion:** Salvianolate combined with alprostadil can significantly improve the renal function of patients with diabetic nephropathy without affecting the blood glucose level, which may be related to the significant improvement of serum sICAM-1 and ET-1 levels.

Key words: Salvianolate; Alprostadil; Diabetic nephropathy; Effect; Renal function

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前言

糖尿病肾病是糖尿病患者常见的微血管并发症之一,在糖尿病患者中的发病率约为 33.6%,是我国终末期肾病发病的主要原因^[1-3]。糖尿病肾病的发病与糖代谢紊乱、遗传因素、炎症因

子、血流动力学改变、细胞因子等多方面因素相关,具体的发病机制较复杂,目前尚未完全阐明^[9,10]。糖代谢紊乱使血管内皮的慢性炎症改变导致血管内皮功能障碍,出现肾小球和肾小管上皮细胞增生,肾小球基底膜增厚等病理改变,最终发展为肾功能衰竭,严重影响患者的生命及健康^[4-6]。糖尿病肾病临床主要

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表现为尿蛋白增多、肾小管和间质纤维化等,但患者早期没有明显的症状^[7,8]。糖尿病肾病的临床治疗以控制血糖、血压和尿蛋白为主,但治疗效果均不够理想^[11,12]。

前列地尔是一种血管活性药物,可降低血清相关炎症因子水平,降低尿蛋白水平^[13-15]。丹参多酚酸盐具有调节血脂代谢、保护血管内皮细胞及抗氧化等作用^[16-18]。本研究主要探讨了丹参多酚酸盐联合前列地尔治疗糖尿病肾病的效果,旨在为糖尿病肾病的临床治疗提供更多的参考。

1 资料与方法

1.1 一般资料

选取 2015 年 11 月~2018 年 11 月我院收治的糖尿病肾病患者 114 例,纳入标准:① 24h 尿蛋白 ≥ 0.5 g,血肌酐 133~264 μ mol/L;② 晨尿白蛋白/肌酐 ≥ 300 μ g/mg;③ 肾小球滤过正常或者高于正常;④ 入组前 3 个月未接受激素和免疫制剂治疗。排除标准:① 合并原发性肾病及其他肾脏疾病者;② 出现糖尿病急性并发症者;③ 合并严重心功能不全者;④ 合并高钾血症及恶性肿瘤者。采用随机数字表法将患者分为两组,对照组 57 例,男 34 例,女 23 例;年龄 40~70 岁,平均 57.25 $\pm$ 3.64 岁;病程 2~8 年,平均 4.85 $\pm$ 1.12 年;糖尿病类型:Ⅰ型 15 例,Ⅱ型 42 例;疾病分期:早期 32 例,临床期 25 例;观察组 57 例,男 33 例,女 24 例;年龄 42~71 岁,平均 58.41 $\pm$ 3.87 岁;病程 2~10 年,平均 4.93 $\pm$ 1.21 年;糖尿病类型:Ⅰ型 16 例,Ⅱ型 41 例;疾病分期:早期 33 例,临床期 24 例。两组一般资料比较差异均无统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

所患者均进行健康教育、适当体育锻炼指导,控制血糖、控

制血压、纠正水电解质、钙磷代谢紊乱等常规治疗。对照组患者在常规治疗的基础上给予前列地尔注射液(辽宁格林生物药业集团股份有限公司,国药准字 H20066828),10 μ g 加入 250 mL 生理盐水中静脉滴注,1 次/d。观察组联合应用丹参多酚酸盐注射液 200 mg/次,1 次/d。两组均连续治疗 2 周。

1.3 观察指标及评价标准

① 治疗效果:显效:症状消失或明显改善,尿蛋白明显减少,UAER 下降 $\geq 50\%$;有效:症状改善,尿蛋白有所减少,UAER 下降 20%~50%;无效:未达到上述标准或加重。② 肾功能:于治疗前和治疗 2 周后采集患者的空腹静脉血 5ml,采用全自动生化分析仪测定 Scr、BUN、 β 2-MG 水平。分别于治疗前和治疗 2 周后收集两组患者的晨尿,采用放射免疫法测定尿蛋白水平,并计算 UAER。③ 血糖水平:采用全自动生化分析仪测定两组患者治疗前后的 HbA1c 及 FPG 水平。④ 血清 sICAM-1 及 ET-1 水平:采用酶联免疫吸附法测定治疗前后两组患者 sICAM-1 和 ET-1 水平,试剂盒均由深圳晶美生物制品有限公司提供。⑤ 不良反应的发生情况。

1.4 统计学分析

采用 SPSS16.0 软件进行统计学分析,计数资料以率(%)表示,组间比较行卡方检验,计量资料以($\bar{x}\pm s$)表示,组间比较行 t 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组治疗效果的比较

治疗后,观察组总有效率为 91.23%,显著高于对照组($P<0.05$),见表 1。

表 1 两组临床治疗效果比较[n(%)]

Table 1 Comparison of the clinical therapeutic effect between two groups

Groups	Cases	Excellent	Valid	Invalid	Total effective rate
Control group	57	27(47.37)	15(26.32)	15(26.32)	42(73.68)
Observation group	57	38(66.67)	14(24.56)	5(8.77)	52(91.23)
χ^2					6.064
P					0.014

2.2 两组治疗前后肾功能的比较

治疗前,两组患者的 Scr、BUN、 β 2-MG 和 UAER 水平比较

均无统计学差异($P>0.05$),治疗后,两组以上指标均较治疗前显著下降,且观察组显著低于对照组($P<0.05$),见表 2。

表 2 两组患者治疗前后肾功能相关指标的比较($\bar{x}\pm s$)

Table 2 Comparison of the renal function index before and after treatment between two groups($\bar{x}\pm s$)

Groups	Control group(n=57)		Observation group(n=57)	
	Before treatment	After treatment	Before treatment	After treatment
Scr(μ mol/L)	148.67 $\pm$ 31.25	115.28 $\pm$ 28.74*	149.71 $\pm$ 32.14	95.33 $\pm$ 21.36*#
BUN(μ mol/L)	7.88 $\pm$ 2.01	6.61 $\pm$ 1.34*	7.92 $\pm$ 2.12	6.01 $\pm$ 1.13*#
β 2-MG(mg/L)	3.68 $\pm$ 1.01	2.16 $\pm$ 0.64*	3.72 $\pm$ 1.12	1.58 $\pm$ 0.41*#
UAER(μ g/min)	115.67 $\pm$ 27.58	88.65 $\pm$ 18.37*	116.33 $\pm$ 28.12	56.41 $\pm$ 15.32*#

注:与治疗前相比,* $P<0.05$;与对照组相比,# $P<0.05$ 。

Note: Compared with before treatment, * $P<0.05$; Compared with control group, # $P<0.05$.

2.3 两组治疗前后血糖水平的比较

两组治疗前后及两组间的 HbA1c 及 FPG 水平比较均无

统计学差异($P>0.05$),见表 3。

表 3 两组患者治疗前后血糖水平比较($\bar{x} \pm s$)Table 3 Comparison of the blood glucose level between two groups($\bar{x} \pm s$)

Groups	Cases	HbA1c(%)		FPG(mmol/L)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	57	6.44 $\pm$ 1.85	6.65 $\pm$ 1.92	6.35 $\pm$ 1.76	6.57 $\pm$ 1.88
Observation group	57	7.65 $\pm$ 2.12	7.72 $\pm$ 2.14	7.58 $\pm$ 2.01	7.63 $\pm$ 2.10
t		-3.247	-2.810	-3.476	-2.839
P		0.002	0.006	0.001	0.005

2.4 两组治疗前后血清 sICAM-1 及 ET-1 水平的比较

治疗前,两组患者的血清 sICAM-1 及 ET-1 水平比较均无

统计学差异($P>0.05$)。治疗后,两组以上指标均较治疗前显著下降,且观察组显著低于对照组($P<0.05$),见表 4。

表 4 两组患者治疗前后血清 sICAM-1 及 ET-1 水平的比较($\bar{x} \pm s$)Table 4 Comparison of the levels of serum sICAM-1 and ET-1 between two groups before and after treatment($\bar{x} \pm s$)

Groups	Cases	sICAM-1(ng/L)		ET-1(ng/L)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	57	554.32 $\pm$ 113.25	328.95 $\pm$ 85.64*	271.25 $\pm$ 55.37	181.27 $\pm$ 35.61*
Observation group	57	561.28 $\pm$ 122.31	241.35 $\pm$ 53.64*	278.37 $\pm$ 56.74	116.74 $\pm$ 27.16*
t		-0.315	-6.545	-0.678	-10.878
P		0.753	<0.001	0.499	<0.001

注:与治疗前相比, * $P<0.05$ 。

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

2.5 两组不良反应发生情况的比较

两组均未发生重大不良反应,仅少数患者出现呕吐、腹泻等轻微症状,未影响患者的治疗,且肝肾功能及尿常规、血常规均未出现异常。

3 讨论

糖尿病肾病是一种慢性进展性疾病,在疾病的早期,肾小球肥大引起血流量及毛细血管壁压力升高,血清蛋白过滤增加^[19-21]。微血管病变表现为微循环障碍,引起血栓形成,使肾小球滤过膜通透性增高,最终出现蛋白尿^[22-23]。有研究显示^[24]糖尿病肾病患者的血清炎症因子水平显著升高,在疾病的进展过程中发挥重要作用。

丹参是典型的活血化瘀类中药,丹参多酚酸盐是丹参的主要成分,可促进 K^+ 通道开放,抑制血管内皮细胞参与炎症反应,还能够降低患者的高凝状态,调节血脂代谢,保护血管内皮功能、改善患者的微循环,还可在一定程度上改善肾小球膜滤过,减少尿蛋白^[29,30]。本研究还发现联合应用丹参多酚酸盐患者的肾功能相关指标得到明显改善,临床治疗效果显著提升,且不影响患者的血糖水平。这与丹参多酚酸盐可增加组织血流量、改善患者的能量代谢、减少尿蛋白、利于肾功能的改善和延缓疾病进展有关。前列地尔能够扩张血管,提高肾血流量,抑制血小板聚集,改善肾小球动脉的高凝状态,减少尿蛋白,保护肾功能^[31]。两者联合应用治疗效果更佳。

ICAM-1 是一种淋巴细胞相关抗原配体,可促进淋巴细胞和血管内皮细胞的粘附力增强,进而促进血管内皮炎症损伤,血清 sICAM-1 与细胞表面 ICAM-1 的数量成正比,血清 sICAM-1 水平可反映血管内皮表面 ICAM-1 水平,也可反映炎

性改变的程度^[25,26]。ET-1 是产生于血管内皮的多肽,具有收缩血管的作用,其水平可反映血管内皮损伤和功能失调的程度^[27,28]。本研究中,治疗后观察组 sICAM-1 和 ET-1 水平显著降低于对照组,说明联合应用丹参多酚酸盐可显著抑制糖尿病肾病患者的炎症因子的表达和分泌,降低血管内皮炎症反应,保护内皮功能,进而减缓疾病进展。在不良反应方面,两组均未发生重大不良反应,发生的轻微不良反应均经对症处理后改善,且不影响患者的治疗。可见,联合应用丹参多酚酸盐治疗糖尿病肾病安全性较高。

综上所述,丹参多酚酸盐联合前列地尔可显著改善糖尿病肾病患者的肾功能、提高临床治疗效果,且不影响血糖水平,可能与其显著降低患者血清 sICAM-1 及 ET-1 水平有关。

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