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胰岛素联合百令胶囊对早期糖尿病肾病患者临床疗效的影响*

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摘要 目的:探讨胰岛素联合百令胶囊对早期糖尿病肾病患者临床疗效的影响。**方法:**选取前来我院就诊的已确诊的早期糖尿病肾病患者 70 例,随机分为对照组和治疗组,每组 35 例。对照组给予门冬胰岛素治疗;治疗组在对照组基础上联合百令胶囊。比较治疗前后两组患者的血糖、尿白蛋白排泄率(UAER)、24 h 尿蛋白定量、 β_2 -微球蛋白(β_2 -MG)、血肌酐(SCr)、尿素氮(BUN)、T 淋巴细胞(CD68)水平的变化情况,记录分析两组患者的临床疗效。**结果:**治疗组总有效率明显高于对照组($P < 0.05$)。治疗后,两组患者血糖、UAER、24h 尿蛋白定量、 β_2 -MG、SCr、BUN、CD68 水平均较治疗前显著降低,且治疗组低于对照组($P < 0.05$)。**结论:**胰岛素和百令胶囊的联合应用能有效控制早期糖尿病肾病患者血糖水平,减少肾脏损伤,缓解临床症状,提高临床疗效。

关键词:糖尿病肾病;胰岛素;百令胶囊;尿蛋白;CD68

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Effect of Insulin combined with One Hundred Capsule on the Clinical Effect of Early Diabetic Nephropathy*

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ABSTRACT Objective: To investigate the effect of insulin combined with one hundred Capsule on the clinical effect of early diabetic nephropathy. **Methods:** 70 patients with early diabetic nephropathy in our hospital were selected and randomly divided into the control group and the experiment group with 35 cases in each group. The control group was treated by Insulin aspart and the experiment group was treated on the base of the control group with Corbrin Capsule. The blood glucose, UAER, 24 h urinary protein quantitation, beta 2-MG, SCr, BUN, CD68 levels and clinical curative effect were compared. **Results:** The total effective rate of treatment group was significantly higher than that of the control group ($P < 0.05$). Compared with before treatment, the blood glucose, UAER, 24 h urinary protein quantitation, beta 2-MG, SCr, BUN, CD68 levels were lower ($P < 0.05$), which were lower in the experiment than those of the control group ($P < 0.05$). **Conclusion:** The combination of insulin and one hundred capsule could effectively control the blood glucose level in patients with early diabetic nephropathy, reduce the renal damage, relieve the clinical symptoms and improve the clinical efficacy.

Key words: Diabetic nephropathy; Insulin; Corbrin Capsule; Urinary protein; CD68

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前言

糖尿病性肾病(diabetic nephropathy, DN)是糖尿病患者常见并发症之一^[1],主要是由于机体长时间处于高血糖状态引起肾血流动力学的改变、蛋白非酶糖化加快、多元醇通道活性的增加、葡萄糖转运能力发生功能亢进等,引发微血管病变,促使肾小球硬化,最终导致肾脏结构的改变^[2,3]。流行病学调查显示^[4]糖尿病肾病作为临床最常见的糖尿病微血管并发症,同时也是导致终末期肾病的主要原因之一。近年来,糖尿病及糖尿病肾

病发病率的持续增高^[5]。胰岛素作为由胰岛 β 细胞所分泌的蛋白质激素,参与糖代谢的调控,对蛋白质及脂肪的代谢平衡也有着积极的作用^[6]。虫草菌丝体的干粉作为百令胶囊的主要成分,具有益肺肾、补精髓、止血化痰的作用,能有效改善机体病后虚损、贫血、肺肾两虚等症^[7]。现代研究显示^[8]百令胶囊的有效成分具有抗肿瘤、调血脂、保护肾脏等作用,同时也参与机体免疫、呼吸系统的调节,对于糖尿病肾病患者机体免疫功能的提高、血脂的调控及肾脏的保护有着积极的作用。本研究主要探讨了胰岛素联合百令胶囊对早期糖尿病肾病的疗效及机制。

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1 资料与方法

1.1 临床资料

共收集 70 例于 2010 年 9 月~2012 年 5 月入住我院的早期糖尿病肾病为研究对象。其中,男 42 例,女 28 例,平均年龄(58.32 ± 3.93)岁。将所有患者进行随机分配,两组患者人数相同,各 35 例。对照组平均年龄为(56.37 ± 6.21)岁,治疗组平均年龄(57.14 ± 4.86)岁,两组患者糖尿病病史、平均年龄、病情发展状况等临床资料选择无偏倚性($P > 0.05$)。纳入标准:①符合糖尿病肾病诊断标准,且经过判定病理分期为早期;②年龄 22~75 岁;③无心衰、难治性水肿及恶性高血压等病。排除标准:④剔除患有血液系统、消化道疾病、妊娠期及哺乳期患者;⑤排除精神状态异常患者;⑥尿路感染、酮症酸中毒及心力衰竭患者不预录入;⑦排除有过 ACEI 及 ARB 类药物服用史患者;⑧排除合并其他肾脏疾病及对所用药物过敏患者。

1.2 治疗方法

所有患者均接受糖尿病饮食及运动治疗,两组患者均根据自身情况服用盐酸贝那普利(北京诺华制药有限公司,国药准字:H20030514)起始量为 5 mg/天进行血压控制,并将血压稳定在 140-90 mmHg 之间。对照组:给予门冬胰岛素 50(诺和诺德(中国)制药有限公司,国药准字:J20120011)早、晚餐前 2:1 比例,0.4 U·kg·d 服用,调节血糖;治疗组:在对照组基础上,给予百令胶囊(杭州中美华东制药有限公司,国药准字:Z10910036)1 g/次口服,3 次/d 进行治疗。两组患者均以 14 日为一个疗程,共治疗 4 个疗程。

1.3 观察指标及检测方法

1.3.1 24 h 尿蛋白、尿素氮(BUN)、尿白蛋白排泄率(UAER)检测

通过放射免疫比浊法测定 24h 尿蛋白,采用尿酶偶联速率法测定尿素氮含量,计算患者 24 小时 UAER 水平。

1.3.2 血糖水平检测 动态监测记录患者空腹血糖(FPG)、餐后 2h 血糖及血压的变化,防止低血糖的发生,同时测定患者糖化血红蛋白(HbA1c)水平。

1.3.3 β_2 微球蛋白(β_2 -MG)、血肌酐(SCr)、肾间质 CD68 的阳性率测定 采用放射免疫测定分析法测定 β_2 -MG,全自动生化分析仪进行血肌酐的测定,测定肾间质 CD68 的阳性表达。

1.4 疗效评价标准

显效:患者糖尿病肾病临床症状消失,患者日常生活无障碍,UAER、24 小时尿蛋白定量等指标恢复正常或下降一半及以上,糖化血红蛋白恢复正常或下降 1/3 以上;有效:患者糖尿病肾病临床症状有所改善,日常生活基本无障碍,UAER、24 小时尿蛋白定量、糖化血红蛋白等指标有较明显的下降;无效:患者临床症状改善不明显或加重,各项生化指标无改变或进展。总有效率 = [(显效例数 + 有效例数) / 本组患者例数] × 100%。

1.5 统计学分析

计量数据以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,采用 SPSS17.0 统计软件进行单因素方差分析法,即 one-way ANOVA 进行差异性统计,使用 Turkey 检验进行组间检验、校正。所有数据比较,以 $P < 0.05$ 认为有统计学意义。

2 结果

2.1 两组临床疗效比较

治疗组总有效率(82.86%)高于对照组(60.00%),差异有统计学差异($P < 0.05$)(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	n	Excellence	Effective	Invalid	Clinical effect rate
Control group	35	9(25.71)	12(34.29)	14(40.00)	21(60.00)
Experimental group	35	16(45.71)	10(28.57)	6(17.14)	29(82.86)*

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

2.2 两组患者治疗前后 24 h 尿蛋白定量、BUN、UAER 的比较

经治疗后,两组患者 24 h 尿蛋白定量、BUN、UAER 水平

均有所下降;与治疗组相比,对照组患者 24h 尿蛋白定量、BUN、UAER 水平明显较高,具有统计学意义($P < 0.05$)。

表 2 两组患者治疗前后 24h 尿蛋白定量、BUN、UAER 水平的比较

Table 2 Comparison of the 24h urinary protein quantitation, BUN, UAER levels between two groups before and after treatment

Groups		24 urinary protein quantitation(mg)	BUN(mmol/L)	UAER(μ g/min)
Control group	Before treatment	156.74 $\pm$ 8.81	15.64 $\pm$ 3.21	137.34 $\pm$ 24.51
	After treatment	87.02 $\pm$ 4.33*	8.35 $\pm$ 1.62*	88.76 $\pm$ 17.04*
Experimental group	Before treatment	149.75 $\pm$ 9.86	15.57 $\pm$ 2.98	142.21 $\pm$ 21.57
	After treatment	75.59 $\pm$ 5.78**	7.27 $\pm$ 0.93**	66.96 $\pm$ 13.27**

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

2.3 两组患者治疗前后各项血糖水平相关指标的比较

与治疗前相比,两组患者 FPG、餐后 2 h 血糖、HbA1c 水平

均下降($P < 0.05$);与对照组相比,治疗组患者 FPG、餐后 2h 血糖、HbA1c 水平较低,差异具有统计学意义($P < 0.05$)(表 3)。

表 3 两组患者治疗前后 FPG、餐后 2h 血糖、HbA1c 水平的比较

Table 3 Comparison of the FPG, postprandial 2H blood glucose, HbA1c levels between two groups before and after treatment

Groups		FPG(mmol/L)	postprandial 2H blood glucose(mmol/L)	HbA1c(%)
Control group(n=35)	Before treatment	9.83± 3.51	15.64± 3.21	9.12± 1.04
	After treatment	6.4± 1.72*	8.35± 1.62*	6.83± 0.74*
Experiment group(n=35)	Before treatment	9.34± 3.73	15.57± 2.98	8.93± 1.18
	After treatment	5.68± 0.93**	7.47± 0.93**	6.76± 0.62**

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

2.4 两组患者治疗前后 β_2 -MG、SCr、CD68 水平的比较

两组患者治疗后血清 β_2 -MG、SCr 水平及肾间质 CD68 阳性率均较治疗前明显降低,差异具有统计学意义(P<0.05);对

照组治疗后 β_2 -MG、SCr 水平及肾间质 CD68 阳性率水平高于治疗组,差异具有统计学意义(P<0.05)。(表 4)

表 4 两组患者治疗前后 β_2 -MG、SCr 水平及肾间质 CD68 阳性率的比较Table 4 Comparison of the β_2 -MG, SCr levels and positive rates of renal interstitial CD68 between two groups before and after treatment

Groups		β_2 -MG(mg/24h)	SCr(μ mol/L)	CD68(%)
Control group (n=35)	Before treatment	1.41± 0.13	111.72± 14.54	0.17± 0.09
	After treatment	0.96± 0.11*	87.26± 8.13*	0.13± 0.07*
Experiment group (n=35)	Before treatment	1.38± 0.19	109.81± 15.67	0.15± 0.11
	After treatment	0.87± 0.06**	83.75± 5.43**	0.09± 0.03**

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

3 讨论

糖尿病血糖控制不佳、蛋白质摄入过高、血压控制效果不明显是导致糖尿病肾病发生的主要原因^[10]。早期糖尿病肾病得到及时有效治疗,肾小球的功能结构可以得到修复^[11]。早期糖尿病肾病的治疗方案主要体现在对患者血糖、血脂及血压的有效控制,延缓糖尿病肾病发展速度。胰岛素是糖尿病患者调控血糖的标准用药,参与机体糖代谢,促进葡萄糖分解并抑制其生成,同时抑制脂肪分解,促进葡萄糖的应用,从而使体内糖含量达到有效平衡^[12,13]。百令胶囊的有效成分是虫草菌丝体的干粉,能通过抑制肾小球高过滤、降低醛糖还原酶活性、提高机体免疫力、促进炎症反应的抑制、平衡脂代谢紊乱有效保护肾脏^[14,15]。有研究显示^[16]胰岛素及百令胶囊的联合应用能有效延缓糖尿病肾病的病情进展,缩短治疗时间。本研究结果也显示胰岛素与百令胶囊的联合应用治疗早期糖尿病肾病的治疗疗效更高。

研究表明^[17]24 h 尿蛋白定量、BUN、UAER 水平是诊断和评估早期糖尿病肾病病情发展的重要指标。24 h 尿蛋白定量超标及 BUN 水平的升高提示着肾脏损伤的出现。尿白蛋白排泄率(UAER)是区分糖尿病肾病病理分期的常用指标,UAER 的升高标志着肾小球毛细血管基底膜的增厚,肾小球异常及蛋白尿的出现^[18]。本研究结果显示所有患者治疗后 24 h 尿蛋白定量、BUN、UAER 水平与治疗前相比明显降低,且对照组明显高于治疗组(P<0.05),表明胰岛素与百令胶囊的联合应用对早期糖尿病肾病有较好的延缓作用,能有效改善期临床症状。

血糖的有效控制是早期糖尿病肾病治疗的关键^[19]。FPG、餐后 2 h 血糖、HbA1c 水平的降低为早期糖尿病肾病的后续治疗提供了可能。 β_2 -MG 由淋巴细胞所分泌,经肾小球滤过几乎完全吸收,尿液中 β_2 -MG 的升高标志着机体肾小球的病变。尿液中 SCr 的浓度是由肾小球滤过率功能决定的,肾功能受损时,尿液中 SCr 浓度增高,而 CD68 表达的表达式与肾损伤程度呈正相关^[20]。本研究结果显示对照组患者治疗后的各项血糖水平、 β_2 -MG、SCr 水平及肾间质 CD68 阳性率明显高于治疗组,证实胰岛素和百令胶囊的联合应用对改善病情、抑制糖尿病肾病的进一步发展有积极的作用。

综上所述,胰岛素和百令胶囊的联合应用能有效控制早期糖尿病肾病患者的血糖水平,减少肾脏损伤,缓解临床症状,提高临床疗效。

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