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丹蛭降糖胶囊联合胰激肽原酶治疗 2 型糖尿病早期肾病的疗效 及对肾功能、血糖指标的影响 *

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摘要 目的:研究丹蛭降糖胶囊联合胰激肽原酶治疗 2 型糖尿病早期肾病的疗效及对肾功能、血糖指标的影响。**方法:**选择 2021 年 1 月~2022 年 7 月于我院诊治的 60 例 2 型糖尿病早期肾病患者,将其随机分为两组。对照组单用胰激肽原酶治疗,观察组采用丹蛭降糖胶囊联合胰激肽原酶治疗。检测两组的肾功能指标、血糖指标[空腹血糖(FPG)、胰岛素抵抗指数(HOMA-IR)、空腹 C 肽(FCP)、餐后 2 h 血糖(PBG)、糖化血红蛋白(HbA1c)和餐后 2hC 肽(PCP)],且检测两组的超敏 C 反应蛋白(hs-CRP)水平。**结果:**观察组的有效率高于对照组($P<0.05$);治疗后,两组的血清 hs-CRP 水平均降低,且观察组较对照组低($P<0.05$);治疗后,两组的血清肌酐、 β_2 -微球蛋白、尿素和胱抑素 C 水平明显降低($P<0.05$),且观察组的血清肌酐、 β_2 -微球蛋白、尿素和胱抑素 C 水平明显低于对照组($P<0.05$);治疗后,两组的 FPG、HOMA-IR、FCP、PBG、HbA1c 和 PCP 水平均明显降低($P<0.05$),且观察组的 FPG、HOMA-IR、FCP、PBG、HbA1c 和 PCP 水平明显低于对照组($P<0.05$)。**结论:**丹蛭降糖胶囊联合胰激肽原酶对 2 型糖尿病早期肾病有显著的疗效,能明显改善肾功能和血糖指标。

关键词:丹蛭降糖胶囊;胰激肽原酶;2 型糖尿病早期肾病;肾功能;血糖

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Efficacy of Danzhi Jiangtang Capsules Combined with Pancreatic Kininogenase in the Treatment of Early Type 2 Diabetic Nephropathy and Its Effect on Renal Function and Blood Sugar Indexes*

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ABSTRACT Objective: To investigate the effect of Danzhi Jiangtang Capsules combined with pancreatic kininogenase in the treatment of early type 2 diabetic nephropathy and its effect on renal function and blood sugar indexes. **Methods:** A total of 60 patients with type 2 diabetes early nephropathy who were diagnosed and treated in our hospital from January 2021 to July 2022 were selected and randomly divided into two groups. The control group was treated with kallikrein alone, and the observation group was treated with Danzhi Jiangtang capsules combined with kallikrein. The renal function indexes, blood glucose indexes [fasting blood glucose (FPG), insulin resistance index (HOMA-IR), fasting C-peptide (FCP), 2 h postprandial blood glucose (PBG), glycosylated hemoglobin (HbA1c) and postprandial 2hC peptide (PCP)], and detected the level of high-sensitivity C-reactive protein (hs-CRP) in both groups. **Results:** The effective rate in the observation group was higher than that in the matched group ($P<0.05$); after treatment, the serum hs-CRP levels in both groups were decreased ($P<0.05$), and the serum hs-CRP levels in the observation group were lower than those in the matched group ($P<0.05$). After treatment, the levels of serum creatinine, β_2 -microglobulin, urea and cystatin C in the two groups were decreased ($P<0.05$), and the levels of serum creatinine, β_2 -microglobulin, urea and cystatin C in the observation group were decreased ($P<0.05$). The level of cystatin C was significantly lower than that in the matched group ($P<0.05$); After treatment, the levels of FPG, HOMA-IR, FCP, PBG, HbA1c and PCP in the two groups were decreased ($P<0.05$), and the FPG in the observation group was significantly lower ($P<0.05$), HOMA-IR, FCP, PBG, HbA1c and PCP levels were lower than those in the matched group ($P<0.05$). **Conclusion:** Danzhi Jiangtang Capsules combined with pancreatic kininogenase has a significant curative effect on early type 2 diabetes nephropathy, and can significantly improve renal function and blood sugar indicators.

Key words: Danzhi Jiangtang Capsule; Pancreatic Kininogenase; Early Type 2 Diabetes Nephropathy; Renal Function; Blood Sugar

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前言

糖尿病肾病具有持续性以及长期性的特点,患者典型的症状有蛋白尿、食欲减退、慢性高血糖和腹水等。当患者的肾损伤发展为持续性蛋白尿阶段,成为终末期肾脏病而不能进行阻止^[1-3]。糖尿病肾病是糖尿病所导致的危害性以及严重性最大的微血管并发症之一,也是引起患者死亡的一个重要原因。目前的处理措施主要包括个体化饮食控制,积极将糖尿病肾病患者的血脂、血糖和血压控制于理想水平,健康生活方式管理^[4,5]。胰激肽原酶主要由激肽原、激肽和激肽酶等构成,其能有效调节血压、炎症反应和血糖等,具有较好的肾脏保护作用^[6]。但单纯采取西医治疗,仍有部分早期糖尿病肾病患者无法获得满意的效果。中医药治疗糖尿病肾病源远流长,积累了比较丰富的经验,在预防糖尿病肾病的发生、减轻症状、延缓肾功能恶化、减轻尿蛋白、阻断病情的进展方面具有独特的效果。丹蛭降糖胶囊由中医经典的名方六味地黄丸改进而成,通过在原方的基础上辅以益气活血的治疗方法,可以有效治疗糖尿病并发症^[7,8]。但目前尚未见将丹蛭降糖胶囊与胰激肽原酶联用的报道,因此,本研究创新性地将二者联用,分析其对2型糖尿病早期肾病的疗效及对肾功能、血糖指标的影响。

1 资料与方法

1.1 一般资料

选择2021年1月~2022年7月于我院诊治的60例2型糖尿病早期肾病患者,用随机数字表法分为两组。观察组30例,男18例,女12例;年龄37~80岁,平均(59.34±12.27)岁;2型糖尿病病程2~13年,平均(6.27±2.24)年。对照组30例,男19例,女11例;年龄37~80岁,平均(58.14±11.36)岁;2型糖尿病病程2~13年,平均(6.34±2.17)年。两组资料比较无差异($P>0.05$)。

纳入标准:(1)均符合2型糖尿病早期肾病诊断标准^[9];(2)均知情同意;(3)患者的尿白蛋白/肌酐比值范围为:30~300 mg/g。

排除标准:(1)长期使用糖皮质激素、有肾毒性药物和免疫抑制剂,或近1年内有外伤手术史的患者;(2)曾行肾移植手术、肾脏透析治疗的患者;(3)患有精神病和肿瘤的患者;(4)合

并泌尿系统感染、严重心脑血管疾病、风湿类疾病、癌症和甲状腺功能异常、肝功能异常的患者;(5)合并严重感染者;(6)近1个月之内出现过严重的代谢紊乱者。

1.2 治疗方法

两组2型糖尿病早期肾病患者均使用胰岛素与口服降糖药,加强运动,合理饮食等。对照组:服用胰激肽原酶40IU肌注,每天1次。观察组:在胰激肽原酶的基础上,联合服用丹蛭降糖胶囊,每天3次,每次服用4粒。两组均治疗3个月

1.3 观察指标

疗效标准^[10]:(1)临床控制:2型糖尿病早期肾患者的泡沫尿、易疲乏、肾性贫血和浮肿等症状消失,实验室指标恢复正常;(2)显效:2型糖尿病早期肾患者的泡沫尿、易疲乏、肾性贫血和浮肿等症状基本消失,24小时尿蛋白定量下降 $>50\%$,实验室指标明显改善;(3)有效:2型糖尿病早期肾患者的泡沫尿、易疲乏、肾性贫血和浮肿等症状和实验室指标明显改善,30%≤24h尿蛋白定量下降≤50%;(4)无效:2型糖尿病早期肾患者的泡沫尿、易疲乏、肾性贫血和浮肿等症状和实验室指标均没有改善。

治疗前后,两组均于清晨抽取5mL静脉血,采取免疫投射比浊法检测血清β₂-微球蛋白含量;采取肌氨酸氧化酶法检测血清肌酐含量;采取乳胶颗粒增强免疫透射比浊法检测两组的血清胱抑素C含量;采取尿素试剂盒检测血清尿素含量,采用ELISA法检测超敏C反应蛋白(Hypersensitive C-reactive protein, hs-CRP)水平。

治疗前后,检测两组的空腹血糖(Fasting blood glucose, FPG)、胰岛素抵抗指数(HOMA-IR)、空腹C肽(Fasting C-peptide, FCP)、餐后2h血糖(2h postprandial blood glucose, PBG)、糖化血红蛋白(HbA_{1c})和餐后2hC肽(2h C peptide, PCP)水平。

1.4 统计学分析

采用SPSS 21.0,计量资料以均数±标准差表示,组间对比用t检验,计数资料用 χ^2 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 临床疗效对比

与对照组相比,观察组的有效率较高($P<0.05$),见表1。

表1 临床疗效比较[例(%)]

Table 1 Comparison of the clinical effect [n(%)]

Groups	n	Clinical control	Effective	Valid	Invalid	The total effect rate
Matched group	30	10(33.33)	8(26.67)	5(16.67)	7(23.33)	23(76.67)
Observation group	30	13(43.33)	10(33.33)	6(20.00)	1(3.33)	29(96.67)*

Note: Compared with the matched group, * $P<0.05$, the same below.

2.2 血清hs-CRP水平对比

两组血清hs-CRP水平治疗前无差异($P>0.05$),治疗后,两组均降低,且观察组较对照组低($P<0.05$),见表2。

2.3 血清肌酐、β₂-微球蛋白、尿素和胱抑素C水平对比

治疗前,两组的血清肌酐、β₂-微球蛋白、尿素和胱抑素C水平无明显差异($P>0.05$),治疗后,两组的血清肌酐、β₂-微球

蛋白、尿素和胱抑素C水平明显降低,且观察组的血清肌酐、β₂-微球蛋白、尿素和胱抑素C水平低于对照组($P<0.05$),见表3。

2.4 FPG、HOMA-IR、FCP、PBG、HbA_{1c}和PCP水平对比

治疗前,两组的FPG、HOMA-IR、FCP、PBG、HbA_{1c}和PCP水平无明显差异($P>0.05$),治疗后,两组的FPG、HOMA-IR、

FCP、PBG、HbA1c 和 PCP 水平均明显降低,且观察组的 FPG、($P<0.05$),见表 3。
HOMA-IR、FCP、PBG、HbA1c 和 PCP 水平明显低于对照组

表 2 治疗前后的血清 hs-CRP 水平对比(均数± 标准差)

Table 2 Comparison of serum hs-CRP levels between the two groups before and Post-treatment ($\bar{x} \pm s$)

Groups	n		hs-CRP(mg /L)
Matched group	30	Pretherapy	53.72± 10.14
		Post-treatment	29.36± 4.78#
Observation group	30	Pretherapy	52.28± 13.29
		Post-treatment	15.13± 2.64*#

表 3 治疗前后的血清肌酐、β2- 微球蛋白、尿素和胱抑素水平对比(均数± 标准差)

Table 3 Comparison of serum creatinine, β2-microglobulin, urea and cystatin levels between the two groups before and Post-treatment ($\bar{x} \pm s$)

Groups	n		Creatinine (μmol/L)	β2-microglobulin (mg/L)	Urea(mmol/L)	Cystatin C (mg/L)
Matched group	30	Pretherapy	173.24± 15.92	3.59± 0.42	8.79± 1.34	1.25± 0.39
		Post-treatment	142.57± 14.36 [#]	3.02± 0.34 [#]	7.13± 1.05 [#]	0.93± 0.25 [#]
Observation group	30	Pretherapy	172.83± 16.24	3.62± 0.57	8.72± 1.59	1.27± 0.43
		Post-treatment	119.38± 12.15* [#]	2.27± 0.25* [#]	6.34± 0.78* [#]	0.62± 0.14* [#]

Note: Compared with Pretherapy, [#] $P<0.05$.

表 4 FPG、HOMA-IR、FCP、PBG、HbA1c 和 PCP 水平对比(均数± 标准差)

Table 4 Comparison of FPG, HOMA-IR, FCP, PBG, HbA1c, PCP levels between the two groups before and Post-treatment ($\bar{x} \pm s$)

Groups	n		FPG(mmol/L)	HOMA-IR	FCP(pmol/L)	PBG(mmol/L)	HbA1c(%)	PCP(pmol/L)
Matched group	30	Pretherapy	9.65± 1.37	2.34± 0.29	715.39± 36.47	15.32± 1.47	9.75± 0.69	2112.47± 178.35
		Post-treatment	7.29± 0.47 [#]	1.93± 0.16 [#]	694.31± 24.26 [#]	13.59± 1.38 [#]	7.48± 0.53 [#]	1673.39± 145.47 [#]
Observation group	30	Pretherapy	9.62± 1.48	2.35± 0.44	714.57± 29.42	15.42± 1.57	9.72± 0.54	2111.32± 183.52
		Post-treatment	6.48± 0.26* [#]	1.45± 0.12* [#]	659.28± 19.69* [#]	12.33± 1.29* [#]	6.93± 0.31* [#]	1436.13± 128.69* [#]

3 讨论

糖尿病肾病是一种微血管病变并发症,因微血管结构、功能发生变化引起的,若未及时干预,将会逐渐进展成终末期肾病,增加病死和致残风险,严重影响患者生活质量^[11-13]。大量研究报道发现,糖尿病肾病的发生与蛋白激酶 C 活化、生化代谢紊乱、炎性反应机制、肾小球高滤过以及遗传易感性等多重因素息息相关^[14,15]。糖尿病肾病患者早期无明显症状,较为严重时方可被检测出异常,因此,对糖尿病肾病进行早期诊断、早期治疗,可改善病情,逆转进程^[16]。

中医学认为,患者由于禀赋不足、脏腑虚衰、劳作太过,加之多食肥甘,情志不畅,造成水湿潴留,脾失健运,蕴而生热,浊毒内生,湿热血瘀,终而发生糖尿病肾病^[17]。本研究发现,观察组的有效率更高,观察组的血清 hs-CRP 水平明显低于对照组。这一结果与李中南^[18]的结果一致,进一步分析可知:组织损伤、各种急性炎症、心肌梗死、放射性损伤以及手术创伤等疾病发作后数小时,hs-CRP 水平会快速升高,且出现成倍增长之势^[19,20]。胰激肽原酶可通过激活纤溶酶、磷脂酶 A2 途径而抑制血小板聚集,预防肾区血管内微血栓形成,减少尿蛋白表达,显著改善肾脏局部微循环^[21,22]。丹蛭降糖胶囊的成分主要为牡丹皮、太子参、水蛭、泽泻、生地黄和菟丝子。其中,太子参具有补脾益胃的

作用;水蛭和牡丹皮具有清热凉血、退虚热和活血化瘀的作用,可产生炎性介质阻滞效果,且改善肾脏微循环;菟丝子具有固精缩尿、滋补肝肾的作用;泽泻具有清热祛痰的作用,能抑制尿蛋白的排泄,可抑制免疫复合物的产生;生地黄具有凉血补血、滋阴补阳的作用;诸药合用,共奏固精缩尿、滋补肝肾、活血化瘀、益胃养气之效,并抑制炎症反应过程,明显减少炎症因子的表达,缓解肾小球硬化和肾间质纤维化,减轻肾脏损伤^[23,24]。两者联用能明显提高疗效,降低炎症因子的表达。

本研究发现,观察组的血清肌酐、β2- 微球蛋白、尿素和胱抑素 C 水平低于对照组,且观察组的 FPG、HOMA-IR、FCP、PBG、HbA1c 和 PCP 水平低于对照组。表明联用丹蛭降糖胶囊能明显改善肾功能,且能有效控制血糖水平。分析可知:肌酐是小分子物质,可通过肾小球滤过,是肾脏功能的重要指标;β2-微球蛋白可自由地在机体的肾小球中滤过,当患者的肾小球过滤功能受到损伤,该蛋白的浓度会升高,。所以血液中 β2-微球蛋白的高表达能有效反映肾小球功能的受损情况或者肾小球过滤功能负荷的增加^[25,26]。血清胱抑素 C 在生理条件下带正电,由于其具有非常小的分子量小,可较自由地从机体肾小球滤过,进而被肾小管上皮细胞重吸收,且会发生降解,不会回到机体的血液中。当肾功能受到损害时,血清胱抑素 C 水平会随着肾小球过滤率的改变而发生改变^[27,28]。血糖相关指标表达量的

变动可在一定程度上损伤血管内皮细胞,促进细胞凋亡以及DNA氧化损伤,因此监测FPG、HOMA-IR、FCP、PBG、HbA1c和PCP等指标可反映患者机体现状^[9]。丹蛭降糖胶囊中丹皮、水蛭行气活血,化瘀通络;太子参补益脾肾之气,生地滋养脾肾之阴,菟丝子补肾固精;泽泻清热泻痰浊,具有养阴益气活血之功效^[30]。联合胰激肽原酶肠溶片可改善患者肾功能及血糖水平。

综上所述,丹蛭降糖胶囊联合胰激肽原酶对2型糖尿病早期肾病有显著的疗效,能明显改善肾功能和血糖指标。

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