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百令片联合坎地沙坦对糖尿病肾病患者的临床效果分析 *

杨 涛[1] 张 韬[2] 陈华茜[1] 张 任[1] 赵 黎[1] 李正东[1]

（1 湖北医药学院附属东风医院 肾内科 湖北 十堰 442002；2 湖北医药学院附属东风医院 中医内科 湖北 十堰 442000）

摘要 目的：分析百令片联合坎地沙坦对糖尿病肾病患者的临床治疗效果。**方法：**选择我院 2015 年 6 月 ~2016 年 6 月收治的 98 例糖尿病肾病作为研究对象，参照抽签法随机分为对照组与观察组，每组各 49 例。对照组予以坎地沙坦治疗，观察组基于对照组使用百令片治疗，比较两组治疗前后血清胱抑素(Cys-C)、β2 微球蛋白(β2-MG)、尿素氮(BUN)、肌酐(Cr)、白细胞介素 -6(IL-6)、C 反应蛋白(CRP)、肿瘤坏死因子 -α(TNF-α)、血糖、血压水平和不良反应的发生情况。**结果：**治疗后，两组血清 Cys-C、β2-MG、BUN、Cr、IL-6、CRP、TNF-α、血糖和血压水平均较治疗前显著降低，且观察组血清 Cys-C、β2-MG、BUN、Cr、IL-6、CRP、TNF-α 和血压水平显著低于对照组，差异均具有统计学意义(P<0.05)。**结论：**百令片联合坎地沙坦治疗可更有效改善糖尿病肾病患者的肾功能、血压和血糖水平，抑制其炎症反应，且安全性较好。

关键词：糖尿病肾病；百令片；坎地沙坦；胱抑素 C；β2 微球蛋白

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The Influence of Bailing Film Combined Candesartan on Serum Cys - C and β2-MG Level with Diabetic Nephropathy*

YANG Tao[1], ZHANG Tao[2], CHEN Hua-qian[1], ZHANG Ren[1], ZHAO Li[1], LI Zheng-dong[1]

（1 Kidney internal medicine, Dongfeng hospital, Hubei Medical College, Shiyan, Hubei, 4420002, China;

2 Traditional Chinese medicine, Dongfeng hospital, Hubei Medical College, Shiyan, Hubei, 442000, China）

ABSTRACT Objective: To analyze the clinical effect of Bailing film combined candesartan on the diabetic nephropathy. **Methods:** 98 cases of patients with diabetic nephropathy in our hospital from June 2015 to June 2015 were selected and divided into the control group and the observation group according to the method of drawing lots with 49 cases in each group. The control group was treated with candesartan, while the observation group was treated by Bailing tablets based on the control group. The blood index, blood pressure before and after treatment and the incidence of adverse reactions between two groups were compared. **Results:** After treatment, the serum levels of Cystatin-c(Cys-C), β2-microglobulin (β2-MG), BUN, Cr, IL-6, CRP, TNF-α, blood glucose and blood pressure of both groups were lower than those before treatment, and the serum levels of Cys-C, β2-MG, BUN, Cr, IL-6, CRP, TNF-α, blood glucose and blood pressure of observation group were significantly lower than those of the control group (P<0.05). **Conclusion:** Bailing film combined with candesartan could more effectively improve the renal function, blood pressure and blood glucose levels, inhibit the inflammatory response with high safety in the treatment of diabetic nephropathy.

Key words: Diabetic nephropathy; Bailing film; Candesartan; Cystatin-c; β2microglobulin

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前言

糖尿病肾病主要是因糖尿病的糖代谢出现障碍导致肾小球发生硬化，同时伴尿蛋白含量超标，是糖尿病最为严重的慢性并发症，也是导致糖尿病患者死亡的关键因素[1]。糖尿病肾病初期症状不明显，仅有微量蛋白尿出现，且尿常规等无明显改变，随着病情的不断进展，可导致肾脏产生器质性病变，严重威胁患者生命[2]。有关研究显示 β2 微球蛋白(β2-MG)及胱抑素 C(Cys-c)是肾小球率过滤的可靠标志物，能够客观反映机体的肾功能，是评估临床疗效的重要指标[3,4]。百令片及坎地沙坦对糖尿病肾病均可起到一定的临床效果，但关于二者联合用药的报道少见[5,6]。本研究采用糖尿病肾病患者应用百令片联合坎地沙坦治疗，探讨了其对 Cys-C 及β2-MG 水平的影响。

1 资料与方法

1.1 一般资料

选择 98 例糖尿病肾病患者并参照抽签法分为对照组与观察组，每组各 49 例。本研究家属及患者均签署知情同意书且经过医院伦理委员会的许可。入选患者均吻合糖尿病肾病的诊断标准[7,8]：糖尿病史明确；排除其他因素所致的尿蛋白阳性。纳入

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作者简介：杨涛(1978-)，男，硕士，主治医师，研究方向：肾小球疾病、慢性肾衰竭等，电话：13235667881

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糖尿病肾病早期、无其他肾脏疾病、近期未使用影响本研究指标药物。排除原发性肾脏疾病、心脏及肝脏等器官明显病变、恶性肿瘤、血液及内分泌系统病变等。对照组有 26 例男性,23 例女性;年龄 35~70 岁,平均(54.38± 2.67)岁;病程 1~10 年,平均(6.64± 0.78)年。观察组有 21 例男性,28 例女性;年龄 32~73 岁,平均(52.61± 2.13)岁;病程 1~12 年,平均(5.89± 0.41)年。两组基线资料比较差异无统计学意义(P>0.05),具有可比性。

1.2 治疗方法

两组患者均常规口服降糖药,保持空腹血糖(FPG)低于 8.0 mmol/L、餐后 2 h 血糖低(2 h PG)低于 9.0 mmol/L,期间均配合健康教育、糖尿病饮食、合理运动等治疗。对照组予以坎地沙坦治疗,口服 8 mg 坎地沙坦(广东卫伦生物制药有限公司,8 mg/片,20150523),每日 1 次。观察组基于对照组使用百令片治疗,口服 0.9 g 百令片 (锦州生化制药有限公司,0.45 g/ 片,20150520),早晚各 1 次。两组均持续用药 1 个月,定期检测患者肝肾功能、血尿常规等,记录期间的不良反应。

1.3 观察指标

采集患者治疗前及治疗结束时外周空腹静脉血 4 mL,肝素抗凝后将血清分离,血浆及血清分别保存待检。使用全自动生化分析仪检测 Cys-c、β2-MG、尿素氮(BUN)、肌酐(Cr)等肾功能指标。使用酶联免疫双抗体夹心法检测白细胞介素 -6(IL--6)、C 反应蛋白(CRP)、肿瘤坏死因子 -α(TNF-α)等炎症因子。使用全自动血液分析仪检测纤维蛋白原、红细胞压积、血浆比黏度、全血高切黏度、全血低切黏度等血液流变学指标。使用葡萄糖氧化酶法检测空腹血糖(FPG)、餐后 2 h 血糖低(2h PG)、糖化血红蛋白(HbAlc)等血糖指标。使用水银柱血压计检测患者治疗前后的舒张压及收缩压。

1.4 统计学分析

选择 SPSS18.0 行数据统计, 计量资料用均数± 标准差($\bar{x}$± s)表示,用 t 检验比较,计数资料用[(n)%]表示,用 x^2 检验比较,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组患者治疗前后肾功能比较

治疗前,两组肾功能指标比较差异无统计学意义(P>0.05);治疗后,两组血清 Cys-c、β2-MG、BUN、Cr、UEAR 水平均较治疗前显著降低,且观察组明显低于对照组,差异均具有统计学意义(P<0.05),见表 1。

表 1 两组患者治疗前后肾功能比较($\bar{x}$± s)

Table 1 Comparison the renal function between two groups of diabetic nephropathy patients before and after treatment($\bar{x}$± s)

Groups		Cys-c(mg/L)	β2-MG(mg/L)	BUN(nmol/L)	Cr(μmol /L)
Control group(n=49)	Before treatment	2.71± 0.61	4.06± 0.87	6.64± 1.18	69.97± 9.53
	After treatment	1.73± 0.35[a]	2.83± 0.35[a]	6.10± 0.94[a]	64.80± 8.11[a]
Observation group (n=49)	Before treatment	2.76± 0.64	4.16± 0.72	6.45± 1.24	67.75± 9.32
	After treatment	1.12± 0.24[ab]	1.94± 0.30[ab]	5.31± 0.72[ab]	61.48± 7.65[ab]

Note: Compared with before treatment [a]P<0.05; Compared with control group [b]P<0.05.

2.2 两组患者治疗前后血清 IL-6、TNF-α 和 CRP 水平比较

治疗前,两组血清 IL-6、TNF-α 和 CRP 水平比较差异均无统计学意义(P>0.05);治疗后,两组血清 IL-6、TNF-α 和 CRP 水平均较治疗前显著降低,且观察组明显低于对照组,差异均具有统计学意义(P<0.05),见表 2。

表 2 两组患者治疗前后血清 IL-6、TNF-α 和 CRP 水平比较($\bar{x}$± s)

Table 2 Comparison the serum IL-6, TNF-α and CRP levels between two groups of diabetic nephropathy patients before and after treatment($\bar{x}$± s)

Groups		IL-6(ng/L)	CRP(mg/L)	TNF-α(ng/L)
Control group(n=49)	Before treatment	13.98± 1.87	2.79± 0.61	20.79± 4.35
	After treatment	11.45± 1.40[a]	2.06± 0.42[a]	16.84± 3.20[a]
Observation group(n=49)	Before treatment	13.82± 1.76	2.84± 0.53	19.42± 4.21
	After treatment	9.83± 1.24[ab]	1.63± 0.31[ab]	12.30± 2.51[ab]

Note: Compared with before treatment, [a]P<0.05; Compared with control group, [b]P<0.05.

2.3 两组患者治疗前后血液流变学指标比较

治疗前, 两组血液流变学指标比较差异均无统计学意义(P>0.05);治疗后,两组血液流变学指标如纤维蛋白原、红细胞压积、血浆比黏度、全血高切黏度、全血低切黏度均较治疗前显著降低, 且观察组明显低于对照组, 差异均具有统计学意义(P<0.05),见表 3。

2.4 两组患者治疗前后血糖指标比较

治疗前,两组血糖指标比较差异均无统计学意义(P>0.05);治疗后,两组血糖指标均较治疗前显著降低(P<0.05),但组间比较差异无统计学意义(P>0.05),见表 4。

2.5 两组患者治疗前后血压比较

治疗前,两组血压比较差异无统计学意义(P>0.05);治疗后,两组血压均较治疗前显著降低,且观察组明显低于对照组,差异均具有统计学意义(P<0.05),见表 5。

表 3 比较治疗前后两组患者血液流变学($\bar{x}\pm s$)

Table 3 Comparison of the blood rheology between two groups of diabetic nephropathy patients before and after treatment

Groups		Fibrinogen (g/L)	Red blood cells deposited (%)	Plasma specific viscosity (mPa·s)	Whole blood high shear viscosity(mPa·s)	Whole blood low shear viscosity(mPa·s)
Control group (n=49)	Before treatment	4.81± 0.92	56.47± 4.28	2.76± 0.31	26.89± 1.25	5.91± 0.63
	After treatment	4.12± 0.75[a]	51.40± 3.71[a]	1.71± 0.25[a]	23.97± 1.26[a]	5.02± 0.51[a]
Observation group (n=49)	Before treatment	4.87± 0.83	55.12± 4.19	2.70± 0.28	27.43± 1.31	6.12± 0.58
	After treatment	3.43± 0.60[ab]	45.89± 3.20[ab]	1.46± 0.21[ab]	21.06± 1.20[ab]	4.30± 0.42[ab]

Note: Compared with before treatment [a]P<0.05; Compared with control group [b]P<0.05.

表 4 两组患者治疗前后血糖指标比较($\bar{x}\pm s$)

Table 4 Comparison of the glycemic index between two groups of diabetic nephropathy patients before and after treatment

Groups		FPG(mmol/L)	2hPG(mmo/L)	HbAlc(%)
Control group(n=49)	Before treatment	7.63± 1.50	8.70± 1.21	6.97± 1.02
	After treatment	6.25± 1.12[a]	7.10± 0.96[a]	5.30± 0.81[a]
Observation group(n=49)	Before treatment	7.94± 1.42	8.89± 1.13	6.43± 1.13
	After treatment	5.76± 1.01[a]	6.74± 0.81[a]	5.11± 0.79[a]

Note: Compared with before treatment [a]P<0.05.

表 5 两组患者治疗前后血压比较($\bar{x}\pm s$)

Table 5 Comparison of the blood pressure between the two groups of diabetic nephropathy patients before and after treatment

Groups		Diastolic blood pressure (mmHg)	Systolic blood pressure (mmHg)
Control group(n=49)	Before treatment	78.94± 4.21	135.69± 10.87
	After treatment	65.30± 3.87[a]	112.94± 8.61[a]
Observation group(n=49)	Before treatment	77.30± 4.53	137.84± 11.20
	After treatment	61.42± 3.29[ab]	103.70± 6.35[ab]

Note:Compared with before treatment [a]P<0.05; Compared with control group [b]P<0.05.

2.6 两组不良反应发生情况比较

两组均未见严重不良反应，对照组有 1 例血钾上升,2 例腹泻,两组不良反应的发生率比较差异无统计学意义(P>0.05)。

3 讨论

糖尿病是一种内分泌代谢性疾病,糖尿病肾病是其常见微血管合并症,早期肾功能无明显改变,随着病情的进展,肾功能可呈进行性减弱[8,9]。Cys-c 主要由肾脏所排泄,其稳定性好,肾前性等因素对 Cys-c 无影响,肾小球出现微小病变时其滤过与重吸收可产生异常,导致其浓度上升,可反映早期糖尿病肾病患者的肾功能损伤[10,11]。β2-MG 是小分子球蛋白,主要经肾小球滤过,几乎可于近曲小管处发生重吸收,机体正常生理情况下其血清含量极低,当肾脏受损时能够导致其代谢障碍,从而使血液中的含量上升[12,13]。临床研究显示糖尿病肾病患者若能得到及时有效的干预,可延缓疾病的进展[14]。有研究表明糖尿病肾病发展中肾素 - 血管紧张素系统紊乱可起到关键性作用,血管紧张素Ⅱ分泌增多能够使肾小球内压显著增加,引起蛋白滤过水平上升,积聚过多的基质蛋白,诱导患者肾脏功能产生进行性受损 [15]。坎地沙坦作为血管紧张素Ⅱ受体的一种拮抗药,能够调节肾素系统,可使肾小球内压及滤过膜蛋白的通透性降低,并能调节肾脏的滤过水平及血流灌注等,从而发挥临床效果[16]。

百令片作为一种冬虫夏草的人工制剂,含甘露醇、腺苷、麦角醇、维生素等多种成分,具有多种药物学功效[17]。本研究结果显示其联合百令片治疗后患者肾功能明显优于坎地沙坦治疗,说明百令片能够有效减轻患者的肾损伤,可能与虫草菌丝可使肾小球内压力减轻,导致肾小球的高滤过状态得到改善,并使肾小球的代偿性增大及细胞增殖受到抑制,增加肾小管细胞的稳定性,利于肾小管细胞的修复有关[18]。有关研究显示糖尿病肾病属慢性炎症疾病,炎症反应是其发病的关键环节[19]。IL-6、CRP、TNF-α 等炎症因子能够诱导肾小球的系膜生成并释放氧自由基,使蛋白降解,导致肾损伤,也可参与局部或者全身性的炎症反应,动作微血管出现病变[20,21]。本研究结果显示联合百令片治疗后 IL-6、CRP、TNF-α 水平低于坎地沙坦组,说明百令片能够抑制炎症因子的分泌，减轻炎症反应对机体造成的损伤。而炎症反应能够刺激机体的凝血纤溶系统，增加血浆黏度,导致血液流变学异常,加剧微血管的病变程度[22,23]。本研究结果显示联合百令片治疗后血液流变学指标更低,说明其能够纠正机体血液的高凝状态，可能与百令片可导致血小板聚集受到抑制,促进肾脏的微循环系统改善有关。两组治疗后血糖指标均降低,但二者在血糖控制方面无差异。同时,白令片治疗后患者血压改善更明显,说明其对于血压调节有辅助作用,能够利于

血压的控制[24]。两组用药期间均未见显著不良反应,安全性相当。

综上所述,百令片联合坎地沙坦治疗可更有效改善糖尿病肾病患者的肾功能、血压和血糖水平,抑制其炎症反应,且安全性较好。

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