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涤毒灌肠方对慢性肾衰竭患者肠源性尿毒症毒素的影响分析 *

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摘要 目的:探讨涤毒灌肠方对慢性肾衰竭患者肠源性尿毒症毒素的影响。**方法:**选择2014年2月到2017年6月在我院肾病科门诊及住院诊治的慢性肾衰竭患者92例,按患者意愿分为研究组与对照组各46例。对照组给予常规治疗措施,研究组在对照组治疗的基础上给予涤毒灌肠方治疗,两组都治疗3个月。记录两组疗效、治疗前后肾功能的变化与肠源性尿毒症毒素的释放情况。**结果:**治疗后,研究组与对照组的总有效率分别为93.5%和78.3%,研究组显著高于对照组(*P<0.05*)。两组治疗后的血肌酐与尿素氮水平都显著低于治疗前(*P<0.05*),且研究组显著低于对照组(*P<0.05*)。研究组治疗后的大肠杆菌、肠球菌值均显著低于对照组(*P<0.05*),双歧杆菌、乳酸杆菌值均显著高于对照组(*P<0.05*)。研究组与对照组治疗后的内毒素含量为0.026± 0.004 EU/mL和0.030± 0.006 EU/mL,研究组显著低于治疗前的,且显著低于对照组(*P<0.05*)。**结论:**涤毒灌肠方用于慢性肾衰竭患者中的辅助治疗能抑制肠源性尿毒症毒素的释放,改善肠道菌群及肾功能,提高治疗效果。

关键词:涤毒灌肠方;慢性肾衰竭;肠源性尿毒症毒素;肠道菌群;肾功能

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Analysis of the Effects of Ditan Enema on the Enteric Uremic Toxin in Patients with Chronic Renal Failure*

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ABSTRACT Objective: To explore the effects of Ditan enema on the enteric uremic toxin in patients with chronic renal failure. **Methods:** 92 cases of patients with chronic renal failure in the department of nephropathy of our hospital from February 2014 to June 2017 were selected as the research object. All the patients were randomly divided into the study group and the control group with 46 patients in each group. The control group was given routine treatment measures, the study group was treated with dydic enema on the basis of treatment in the control group, and both groups were treated for 3 months. The prognosis, renal function and release of enteric uremic toxin were compared between two groups. **Results:** The total effective rate of study group and control group were 93.5% and 78.3%, which was significantly higher in the study group than that of the control group (*P<0.05*). After treatment, the levels of serum creatinine and urea nitrogen were significantly lower in the two groups than before the treatment (*P<0.05*), which were significantly lower in the study group than those of the control group after treatment (*P<0.05*). After treatment, the levels of *E. coli* and *enterococci* in the study group were lower than those in the control group, and the values of Bifidobacterium and lactobacillus were higher than those in the control group (*P<0.05*). After treatment, the endotoxin content in the study group and the control group were 0.026± 0.004 EU/mL and 0.030± 0.006 EU/mL, which was significantly lower in the study group than that before treatment and that in the control group (*P<0.05*). **Conclusions:** The auxiliary application of Ditan enema can inhibit the release of enteral uremic toxin, improve the intestinal flora level, promote the improvement of renal function and improve the therapeutic effect in the treatment of patients with chronic renal failure.

Key words: Dafu enema; Chronic renal failure; Enteric uremia toxin; Intestinal flora; Renal function

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前言

慢性肾衰竭(CRF,chronic renal failure)由多种慢性肾脏病持续进展造成。与糖尿病、高血压患病率逐年升高的趋势一致,其造成的慢性肾衰竭亦发展为影响中国公共健康的重大挑战并且其患病率呈现逐年递增趋势[1-3]。现代研究表明慢性肾衰竭

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患者由于功能肾单位减少，不能充分排泄体内代谢废物，可导致机体病理生理改变，从而引起尿毒症毒素[4]。肌酐、尿素氮为早期所熟知的尿毒症毒素，在临床上已被作为评估肾功能的间接指标 [5,6]。肠源性尿毒症毒素是反映当前肾功能的灵敏性指标，尿毒症脑病、内分泌紊乱、细胞免疫功能低下等慢性肾衰竭远期并发症与肠源性尿毒症毒素的蓄积密切相关[7,8]。血液透析可清除慢性肾衰竭患者体内的代谢性废物，尤其是尿毒症毒素，还可排出原发病产生的感染性炎症介质；但是在临床使用中也存在一定的缺陷[9]。

中医药治疗慢性肾衰竭有很好的疗效，其中中医灌肠疗法具有价格低廉、便于基层推广、不受任何条件限制、无创伤、价格低廉、操作简单等优点，也能避免对患者的肠道刺激[10]。涤毒灌肠方能促进患者排出体内蓄积之水湿、痰浊、瘀血等病理产物，理脏腑功能之紊乱[11]。因此，本研究主要探讨了涤毒灌肠方对慢性肾衰竭患者肠源性尿毒症毒素的影响，现报道如下。

1 对象和方法

1.1 研究对象

本研究选取 2014 年 2 月 -2017 年 6 月在我院肾病科门诊及住院诊治的 92 例慢性肾衰竭患者。纳入标准：符合诊断标准；患者知情并同意参加研究；中医辨证以脾肾气(阳)虚、湿浊(湿热)瘀血为主证者；年龄 18-75 岁；病情暂时稳定，药物可以控制；研究得到医院伦理委员会的批准。排除标准：具有紧急透析指征者；孕妇或哺乳期患者；生命体征不稳定、病情不稳定者；合并有活动期恶性肿瘤等严重原发性疾病患者；不耐受灌肠治疗者。按患者意愿分为研究组与对照组，各 46 例，两组患者的性别、原发疾病、年龄、病程、体重指数、收缩压、舒张压等对比无显著差异($P>0.05$)。见表 1。

表 1 两组一般资料的对比

Table 1 Comparison of the general information between two groups

Groups	Cases (n)	Gender (male/female)	Primary diseases (glomerulonephritis/ hypertensive nephrosclerosis/ diabetic nephropathy)	Age(years)	Disease duration (years)	BMI(kg/m^2)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
Study group	46	26/20	22/10/14	57.58± 4.33	6.53± 1.48	20.98± 2.14	138.10± 14.22	80.29± 5.35
Control group	46	24/22	18/12/16	54.72± 5.13	6.49± 1.32	20.71± 1.87	136.88± 19.48	80.11± 6.73
t or x^2		0.293	0.452	0.313	0.194	0.201	0.311	0.091
P		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

1.2 治疗方法

对照组：给予常规治疗措施，包括控制血压、低盐营养饮食、控制血糖、贫血治疗、纠正钙磷代谢紊乱、调节水 / 电解质和酸碱代谢平衡等。

研究组：在对照组治疗的基础上给予涤毒灌肠方治疗，组方：酒大黄 30 g、煅牡蛎 20 g、丹参 30 g、制附子 10 g、煅龙骨 20 g、蒲公英 30 g，煎煮、过滤、水浴蒸发分别浓缩至每毫升含生药材 1.5 g。患者排清大便后取屈膝侧卧位。应用结肠透析机，经润滑后缓慢插入肛内约 10 cm，先冲洗肠道。温度控制在 38℃，以涤毒灌肠方 200 mL 灌入，撤出导管，嘱患者尽量保留药液 2 h 后排便，2 次 /d。

两组都治疗观察 3 个月。

1.3 观察指标

(1)疗效评价：参考《中药新药临床研究指导原则》，结合患者临床症状及实验室指标进行综合评价，包括显效、有效、稳定、无效四种级别，(显效 + 有效)/ 组内例数× 100.0%= 总有效率。(2)常规肾功能指标：在治疗前后进行血肌酐与尿素氮的检测，使用全自动生化分析仪检测。(3)肠道菌群：治疗后在我院检验科细菌室检测大肠杆菌、肠球菌、双歧杆菌、乳酸杆菌等。(4)内毒素：通过鲎试验法检测治疗前后内毒素。

1.4 统计学分析

采用 SPSS 22.00 进行统计学分析，非正态计量资料以中位数(四分位间距)表示，正态计量资料以($\bar{x}\pm s$)表示，组间比较采用 t 检验，计量数据采用%表示，组间对比采用卡方检测，以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组治疗总有效率的对比

治疗后，研究组与对照组的总有效率为 93.5%和 78.3%，研究组显著高于对照组($P<0.05$)，见表 2。

表 2 两组治疗总有效率的对比(例, %)

Table 2 Comparison of the total effective rate between two groups (n, %)

Groups	Cases(n)	Excellent	Effective	Stable	Invalid	Total effective rate (%)
Study group	46	40	3	2	1	93.5
Control group	46	26	10	6	4	78.3
P						<0.05

2.2 两组治疗前后血肌酐与尿素氮水平的变化比较

治疗后，两组的血肌酐与尿素氮水平都显著低于治疗前（*P*<*0.05*），且研究组显著低于对照组（*P*<*0.05*），见表 3。

表 3 两组治疗前后血肌酐与尿素氮水平的变化对比（$\bar{x}\pm s$）

Table 3 Comparison of the changes of serum creatine and urea nitrogen levels between two groups before and after treatment（$\bar{x}\pm s$）

Groups	Cases(n)	Serum creatinine (μmol/L)		*P*	Urea nitrogen (mmol/L)		*P*
		Before treatment	After treatment		Before treatment	After treatment	
Study group	46	538.22± 98.38	504.29± 87.13	<0.05	24.10± 2.49	20.19± 2.88	<0.05
Control group	46	531.19± 100.29	521.99± 90.01	<0.05	24.00± 3.10	22.14± 2.09	<0.05
P		>0.05	<0.05		>0.05	<0.05	

2.3 两组治疗前后肠道菌群水平的对比

治疗后研究组的大肠杆菌、肠球菌值低于对照组，双歧杆菌与乳酸杆菌值高于对照组，对比差异都有统计学意义（*P*<*0.05*），见表 4。

表 4 两组治疗后肠道菌群水平的对比（$\bar{x}\pm s$, Log 10CFU/g）

Table 4 Comparison of the intestinal flora level between two groups after treatment（$\bar{x}\pm s$, Log 10CFU/g）

Groups	Cases (n)	*Colibacillus*	*Enterococci*	*Bifidobacterium*	*Lactobacillus*
Study group	46	9.02± 1.33	9.14± 0.89	9.17± 1.12	9.04± 1.16
Control group	46	9.89± 1.14	9.48± 1.09	8.22± 0.87	7.25± 1.02
P		<0.05	<0.05	<0.05	<0.05

2.4 两组治疗前后内毒素水平变化的对比

治疗后，研究组与对照组的内毒素含量为 0.026± 0.004 EU/mL 和 0.030± 0.006 EU/mL，研究组显著低于治疗前（*P*<*0.05*），且显著低于对照组（*P*<*0.05*），见表 5。

表 5 两组治疗前后内毒素水平变化的对比（$\bar{x}\pm s$, EU/mL）

Table 5 Comparison of the changes of endotoxin between two groups before and after treatment（$\bar{x}\pm s$, EU/mL）

Groups	Cases(n)	Before treatment	After treatment	*P*
Study group	46	0.033± 0.005	0.026± 0.004	<0.05
Control group	46	0.033± 0.004	0.030± 0.006	>0.05
P		>0.05	<0.05	

3 讨论

慢性肾功能衰竭是由各种原因造成进行性肾实质损害，使肾脏萎缩而不能维持基本功能，临床表现为代谢产物潴留、酸碱平衡失调等症状，会造成全身各系统受累，是肾功能不全的严重阶段，当前因各种原发性肾脏疾病原因使得慢性肾功能衰竭患者数量逐年增长，造成的相关医疗费用给社会和家庭均造成了沉重的负担[12]。

灌肠疗法是中医学传统导法与现代医学灌肠法相结合的给药方法，其中结肠透析疗法是由传统低位保留灌肠发展而来的，具有长时间保留药液、药物与肠道粘膜接触面积较多、操作方便等特点[13,14]。特别是药液在结肠袋内可形成多个小透析池便于进行透析，清除血液中蓄积的毒素及水分尤其是肠源性中分子毒素，且在结肠蠕动过程中药液可与结肠粘膜充分接触，从而发挥药效[15]。在涤毒灌肠方中，酒大黄、煅牡蛎具有泻下攻积、逐瘀通经、凉血解毒、清热泻火、利湿等功效；丹参、制附子具有利湿通便、清热解毒等功效；龙骨龙骨与牡蛎疗效相近，具有吸附肠道内有毒物质，调节钙、磷代谢，增加灌肠液的渗透压等作用；蒲公英具有利湿通淋、清热解毒、消肿散结之功效，具有很好的抗菌消炎作用[16,17]。本研究显示研究组与对照组治疗后的总有效率为 93.5%和 78.3%，研究组显著高于对照组，且研究组治疗后的血肌酐与尿素氮水平都显著低于对照组，表明涤毒灌肠方辅助治疗慢性肾衰竭能有效改善患者的肾功能，提高治疗效果，原因主要在于全文多味中药相配，共奏温阳泄浊、排毒祛瘀、散寒利湿之功效。

慢性肾功能衰竭患者存在明显的肠道菌群紊乱，主要表现为以大肠杆菌、肠球菌等需氧型致病性菌群过度增加，乳杆菌、双歧杆菌等厌氧型益生性菌群明显减少[18]。大量繁殖的细菌能够酵解肠腔内潴留的蛋白质，导致肠源性尿毒症毒素表达量上升，引起肠道黏膜结构和功能异常，细胞间紧密连接被破坏，使得肠道细菌及内毒素移位入血，从而形成肠源性内毒素血症[19]。本研究显示研究组治疗后的大肠杆菌、肠球菌值显著低于对照组，双歧杆菌、乳酸杆菌值显著高于对照组。有研究显示大黄可调节肠道菌群结构，起到抗菌、抑菌作用，促进胃肠道蠕动并保护肠道屏障。涤毒灌肠方能有效控制炎症反应，避免全身性炎症反应的出现，减轻循环负担，达到调节机体稳态[20-22]。本

研究亦显示肠道菌群的改善与中药治疗改善肠道浊毒内蕴状态、清除毒素作用相关。

现代研究已经证实多种尿毒症毒素的来源、转移、生成和体内蓄积与肠道直接相关，与慢性肾功能衰竭患者的临床预后密切相关[23,24]。内毒素可激活单核巨噬细胞系统，促使其释放炎症介质、细胞因子等物质，造成肾脏的损伤。在机体肠壁通透性增加的情况下，利于内毒素进入机体，激活补体、凝血系统后产生白介素 -1、产生血管活性激肽，导致肠源性内毒素血症的发生[25-27]。本研究结果显示两组治疗后内毒素显著降低，且研究组更明显。从机制上分析，涤毒灌肠方通过治疗可使得药液直接刺激肠黏膜，增加毛细血管通透性，使肠道充血，加速粪便排泄，从而减少肠腔内蛋白质的分解，从而对延缓肾功能衰竭起到重要的作用[28-30]。

总之，涤毒灌肠方在慢性肾衰竭患者中的辅助应用能抑制肠源性尿毒症毒素的释放，改善肠道菌群水平及肾功能，提高治疗效果。

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