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血液透析、灌流对糖尿病肾病患者血清 TNF-α、CRP、IL-6 水平的影响 *

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摘要 目的: 探讨血液透析辅助血液灌流对终末期糖尿病肾病血清 C 反应蛋白 (C-reactive protein, CRP)、肿瘤坏死因子(tumor necrosis factor, TNF-α)及白细胞介素(Interleukin,IL)-6 水平的影响。**方法:**选取近 3 年收治的 79 例糖尿病肾病患者,将其随机分为研究组(n=40)和对照组(n=39),对照组患者接受血液透析治疗,研究组患者接受血液透析辅助血液灌流治疗,对比两组患者治疗前后血清 TNF-α、CRP、IL-6 水平的变化情况。**结果:**治疗后,研究组患者的治疗总有效率、血红蛋白(haemoglobin,Hb)、转铁蛋白水平(transferring,TRF)、白蛋白(albumin,Alb)及营养不良 - 炎症评分(malnutrition inflammation score,MIS)均明显高于对照组($P<0.05$),而 MIS 评分明显低于对照组($P<0.05$);两组患者治疗后血清 CRP、TNF-α、IL-6 水平均明显低于治疗前($P<0.05$),且研究组患者以上指标明显低于对照组($P<0.05$)。**结论:**血液透析辅助血液灌流治疗糖尿病肾病可显著改善患者的临床症状和营养状态,降低 TNF-α、CRP、IL-6 水平,减轻炎症反应。

关键词:血液透析;血液灌流;糖尿病肾病;TNF-α;CRP;IL-6

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Effect of Hemodialysis and Perfusion on the Serum TNF-α, CRP and IL-6 Levels in the Patients with Diabetic Nephropathy*

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ABSTRACT Objective: To investigate the effect of hemodialysis assisted hemoperfusion on serum TNF-α, CRP, IL-6 levels in end-stage diabetic nephropathy. **Methods:** 79 patients with diabetic nephropathy admitted in the past 3 years were randomly divided into the study group (n=40) and the control group (n=39). The control group received hemodialysis treatment. The study group received hemodialysis assistance blood perfusion. Treatment, comparing the changes of serum TNF-α, CRP and IL-6 levels before and after treatment in the two groups. **Results:** After treatment, the total effective rate of treatment, hemoglobin (Hb), transferrin (TRF), albumin (Alb), and malnutrition inflammation score (MIS) were all in the study group. The MIS score was significantly lower than that of the control group ($P<0.05$). The levels of serum CRP, TNF-α and IL-6 in the two groups were significantly lower than those before treatment ($P<0.05$), and the above indicators of the study group were significantly lower than the control group ($P<0.05$). **Conclusion:** Hemodialysis-assisted blood perfusion for the treatment of diabetic nephropathy can significantly improve the clinical symptoms and nutritional status of patients, reduce TNF-α, CRP, IL-6 levels, reduce inflammation.

Key words: Hemodialysis; Blood perfusion; Diabetic nephropathy; TNF-α; CRP; IL-6

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前言

近年来,随着社会经济的快速发展,人们物质水平的不断提高,生活节奏的日益加快,糖尿病发病率也逐渐升高,若不能有效控制糖尿病病情,会产生多种并发症。糖尿病肾病是糖尿病患者一种常见慢性并发症,早期临床症状不明显,主要表现为微量白蛋白尿,后期主要表现为肾功能下降、大量蛋白尿,机体蓄积多种代谢毒性物质,造成机体各器官系统障碍,严重危及患者生命[1,2]。相关研究表明[3]糖尿病肾病是一种慢性亚临床炎症性疾病,在病情发生及发展过程中,炎症反应在其中起着重要作用。目前,药物治疗糖尿病肾病效果不明显,血液透析是终末期肾脏病肾脏替代治疗的主要治疗方法, 通过半渗透薄膜,净化血液毒性物质,是一种安全治疗方案,但难以达到预期治疗效果[4-6]。血液灌流通过借用体外吸附剂容器净化血液,清除血液毒物。两者联合应用可清除机体炎性物质及内源性毒性物质等。本研究主要探讨了血液透析辅助血液灌流对糖尿病肾病患者血清 TNF-α、CRP、IL-6 水平的影响。

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1 资料与方法

1.1 一般资料

选取近 3 年我院收治的糖尿病肾病患者 79 例，将其随机分为研究组(n=40)和对照组(n=39)。纳入标准：符合糖尿病肾病的诊断标准，患者知情同意。排除标准：原发性肾脏疾病；认知能力缺陷患者；严重心肝肾等疾病患者；血液系统疾病、免疫系统疾病患者；合并感染性疾病患者；合并恶性肿瘤患者；合并正在参加其他临床研究患者。两组患者一般资料对比无统计学差异($P>0.05$)，具有可比性。

表 1 两组患者的一般资料对比

Table 1 Comparison of the general data between the two groups of patients

Groups	n	Gender: Male Female)	Age (years)	Disease duration (years)	Weight (kg)	Combined disease		
						Hypertension	Dyslipidemia	Cardiovascular diseases
Study group	40	21/19	67.4±8.0	8.2±2.3	57.3±2.5	23	6	7
Control group	39	22/17	67.9±8.2	8.3±2.1	57.6±2.7	20	7	7

1.2 治疗方法

1.2.1 基础治疗 两组患者均进行糖尿病肾病基础治疗，积极控制饮食，食低脂肪、低盐、高蛋白食物；结合患者性别、年龄、身体状况等因素，制定不同强度有氧运动；针对患者病情，结合患者自身情况，针对性使用降糖药物，控制血糖水平。

1.2.2 具体治疗方案 采用费森尤斯 4008 S 给予对照组患者进行血液透析，血流量控制速度为 200-250 L/min，每次 4 h，每周 2-3 次。研究组患者接受血液透析辅助血液灌流治疗，串联血液透析、血液灌流，血流量控制速度 200-250 L，肝素初始剂量 1 mg/kg，每小时递增 10-20 mg，每次 2-2.5 h，将灌流器取下，每 3-4 周联合治疗一次。

1.3 评价标准

治疗效果：显效为治疗后患者无透析感染或加重器官功能损害，残余肾功能 >2 mL/(min·1.73 m^2)；有效为器官功能损害有所控制，残余肾功能 >1 mL/(min·1.73 m^2)，无效为患者症状无改善，其余指标未达到上述者。

两组患者在治疗前及治疗后 6 个月均进行相关指标检测，采取酶联免疫吸附测定两组患者治疗前后血清 CRP、TNF-α、IL-6 水平。评价两组患者治疗前后的营养指标，包括 HB、ALB、TP、TRF、MIS 评分。采取 MIS 评估两组患者的营养情况，包括体质指数(body mass index，BMI)、病史、体检及实验室指标等，分值范围 0-30 分，分值越高，代表营养状况越差。

1.4 统计学方法

采取 SPSS19.0 软件进行数据分析，计量资料以平均数±标准差($\bar{x}\pm s$)形式表示，计数资料以百分数(%)形式表示，组间及治疗前后计量资料比较采取 t 检验，组间计数资料的比较采用用卡方检验，以 $P<0.05$ 则表示差异有统计学意义。

2 结果

2.1 两组患者治疗效果对比

治疗后，研究组的总有效率为 75.0%，对照组为 51.3%，研究组治疗总有效率明显高于对照组($P<0.05$)。

表 2 两组患者的治疗效果对比(例,%)

Table 2 Comparison of the treatment effects between the two groups (n,%)

Groups	n	Significant effect	Effective	Invalid	Total efficiency
Study Group	40	14	16	10	30(75.0)#
Control group	39	9	11	19	20(51.3)

Note: #$P<0.05$, compared with the control group.

2.2 两组患者治疗前后营养指标对比

两组患者治疗前 HB、ALB、TP、TRF、BIS 评分对比无统计学差异($P>0.05$)，治疗后，研究组患者 HB、ALB、TP、TRF 明显高于对照组($P<0.05$)，BIS 评分明显低于对照组($P<0.05$)。

表 3 两组患者治疗前后营养指标的比较($\bar{x}\pm s$)

Table 3 Comparison of the nutritional indicators before and after treatment between two groups($\bar{x}\pm s$)

Groups	n	HB (g/L)		ALB (g/L)		TP(g/L)		TRF(g/L)		MIS(score)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study Group	40	93.2±1.91	98.49±4.39#*	30.17±0.28	33.91±0.87#*	59.29±5.48	64.82±3.91#*	2.13±0.52	2.61±0.57#*	12.31±2.62	9.17±4.02#*
Control group	39	90.7±1.87	91.28±3.69*	30.20±0.30	31.28±0.23*	60.31±5.51	61.92±5.28*	2.09±0.56	2.02±0.45*	13.01±42.70	12.12±4.13*

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

2.3 两组患者治疗前后血清炎症因子水平的对比

治疗前，两组患者的血清 CRP、TNF-α、IL-6 水平对比无统计学差异($P>0.05$)。两组患者治疗后血清 CRP、TNF-α、IL-6 水平均明显低于治疗前($P<0.05$)，且研究组患者治疗后以上指标均明显低于对照组($P<0.05$)。如表 4 所示。

表 4 两组患者治疗前后血清炎症因子水平的对比

Table 4 Comparison of the serum inflammatory factors levels before and after treatment between two groups of patients

Groups	n	CRP (mg/L)		TNF-α (ng/L)		IL-6 (ng/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study Group	40	8.91±0.91	6.13±0.69#*	26.72±4.75	11.62±2.08#*	28.39±5.03	13.49±2.65#*
Control group	39	8.90±0.92	7.30±0.74*	26.14±4.71	17.90±3.30*	28.40±5.09	19.75±3.80*

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

3 讨论

糖尿病肾病是一种糖尿病常见并发症，近几年发病率呈逐年上升趋势[7-9]。目前，糖尿病肾病的发病机制尚不明确，相关研究表明[10-12]其和多种因素有关，包括血流动力学障碍、代谢异常等，机体呈慢性微炎症状态，体内炎症因子持续增加，严重影响患者心血管系统。因此，清除机体炎症因子是改善糖尿病肾病病情的关键[13,14]。

血液透析是通过体外模拟肾小球滤过原理，将体内多余的有害物质进行排除，达到净化血液目的，并且维持机体电解质平衡、酸解平衡，是治疗糖尿病肾病的有效方法。但血液透析半透膜孔径约为 3 nm，可通过 1.5×10^3 小分子及中性分子，不能通过 3.5×10^3 分子[15,16]。因此，血液透析基础上辅助血液灌流可有效清除患者血液中的大分子、中分子毒素，尤其是中分子毒素，清除效果更佳明显[17,18]。血液灌流可通过大孔径吸附树脂，吸附清除毒素，减少血液中毒素水平[19]。相比于血液透析，血液灌流具有容量大、表面积大、孔径大、吸附力强等特点，可明显清除机体中分子物质[14,15]。血液透析辅助血液灌流可有效避免血液净化单一治疗的弊端，可清除机体大小分子，降低机体微炎性水平，提高治疗效果[20,21]。

本研究根据血液透析、血液灌流两种治疗方式的优缺点，相互弥补各自治疗局限性，全面、快速清除机体内有害物质，维持机体水电解、酸碱平衡。研究结果显示与对照组相比，研究组的治疗有效率明显较高，提示血液透析辅助血液灌流治疗糖尿病肾病具有显著的临床疗效。血液透析辅助血液灌流的治疗效果较血液透析高，研究组患者治疗后 HB、ALB、TP、TRF 明显高于对照组，且 MIS 评分明显低于对照组，提示血液透析辅助血液灌流更有助于改善患者的营养状况。

相关研究表明[16,17]机体内炎症发生是糖尿病肾病发病及病情进展的重要因素。糖尿病肾病患者的血清 CRP、TNF-α、IL-6 水平均明显高于正常人 [22,23]，TNF-α 异常升高致使肾系膜细胞产生过多氧自由基，增加脂质代谢产物，改变肾小球，损伤肾脏基底膜，促使糖尿病肾病发生及发展[24,25]。研究表明 TNF-α 水平和病情呈正相关[26]。IL-6 是一种细胞炎症因子，可促进其他炎症因子释放，增加血管通透性，直接损伤胰岛 B 细胞，降低胰岛 B 细胞功能，诱发胰岛素抵抗，致使肾小球基底膜损伤，进而产生蛋白尿[27,28]。CRP 是血管炎症反应的敏感指标，参与机体多种免疫应答、炎症反应的反应蛋白，在整个炎症反应过程中起着重要作用。CRP 水平异常升高和糖尿病肾病的病情进展有着直接关系[29,30]。本研究结果显示两组患者治疗后各项炎症因子水平明显低于治疗前，研究组治疗后的各项炎症因子水平较对照组明显降低。因此，血液透析辅助血液灌流治疗糖尿病肾病可显著改善患者的炎症反应，减少其对肾脏的损害，保护肾功能，进而抑制病情进展。

总之，血液透析辅助血液灌流治疗糖尿病肾病可显著改善患者的临床症状和营养状态，降低 TNF-α、CRP、IL-6 水平，减轻炎症反应。

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