腹膜透析患者腹膜纤维化与腹透液中转化生长因子 β1、白介素-6 水平相关性研究

湖北医药学院附属东风医院 毛艳 卢丽* 赵黎 杨涛 曾艳 赵韶静,十堰 442000

摘要 目的:探讨腹膜透析(PD)患者腹膜纤维化与腹透液中转化生长因子(TGF-β1)、白介素(IL)-6 水平的相关性。方法:选取终末期肾病患者 72 例,予 PD 治疗,治疗观察时间为 90 d。在治疗前、后分别检测腹透液中 TGF-β1 及 IL-6 水平,检测患者血浆白蛋白(ALB)、甲状旁腺素(PTH)、钙(Ca)、磷(P)等生化指标,计算肌酐透析液与血浓度之比(D/Pcr)、尿素清除指数(KT/V)、肌酐清除率(Ccr)、超滤量,分析 TGF-β1、IL-6 与 D/Pcr、KT/V、Ccr、超滤量的相关性。结果:治疗后期患者的超滤量、KT/V 值高于治疗前期,D/Pcr、Ccr 值、TGF-β1、IL-6 水平低于治疗前期(均 $P<0.05$);治疗后期患者的 ALB、PTH、Ca、P 含量与治疗前无差异(均 $P>0.05$)。Pearson 相关分析显示,治疗前期与后期患者的 TGF-β1、IL-6 与 KT/V 呈正相关,与 D/Pcr、Ccr、超滤量呈负相关(均 $P<0.05$)。结论:PD 患者腹膜纤维化与腹透液中 TGF-β1、IL-6 水平存在明显相关性,抑制 TGF-β1、IL-6 表达可能有利于防治腹膜纤维化。

关键词 腹膜透析; 腹膜纤维化; 转化生长因子-β1; 白介素-6

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Correlation between peritoneal fibrosis in patients given peritoneal dialysis with TGF-β1 and IL-6 levels in peritoneal dialysis

MAO Yan, LU Li, ZHAO Li, YANG Tao, ZENG Yan, ZHAO Shao-Jing. Department of Nephrology, Dongfeng Hospital, Hubei University of Medicine, Shiyan 442000, China*

Abstract Objective: To investigate the correlation between peritoneal fibrosis in patients undergoing peritoneal dialysis with TGF-β1 and IL-6 levels in peritoneal dialysis. Methods: Seventy-two patients with end-stage renal disease in our hospital were selected as the research subjects, and given peritoneal dialysis treatment for 90 days. The TGF-β1 and IL-6 levels in peritoneal dialysis fluid were determined on the day 1 and 90 after treatment. The ultrafiltration volume, KT/V, D/Pcr and Ccr were also detected and were given correlation analysis. Results: The ultrafiltration volume and KT/V value in the later stage of treatment were greater than those of the prophase stage of treatment, and the D/Pcr and Ccr values were lower than those of the later stage of treatment ($P<0.05$). The TGF-β1 and IL-6 levels in the later stage of treatment were lower than those of the prophase stage of treatment ($P<0.05$). The levels of ALB, PTH, Ca and P in the later stage of treatment were not significantly different from those in the prophase stage of treatment ($P>0.05$). Pearson analysis showed that the TGF-β1 and IL-6 levels in the prophase and later stages of treatment were positively correlated with KT/V ($P<0.05$), and negatively with D/Pcr, ultrafiltration volume, Ccr ($P<0.05$). Conclusion: The peritoneal fibrosis in patients with peritoneal dialysis is significantly correlated with TGF-β1 and IL-6 levels in peritoneal dialysis fluid, and inhibiting the expression of TGF-β1 may provide new and effective targets for prevention and treatment of peritoneal fibrosis.

Key words Peritoneal dialysis; Peritoneal fibrosis; TGF-β1; IL-6

腹膜透析(peritoneal dialysis,PD)是治疗终末期肾病的首选方法[1~4]。长期 PD 使得腹膜发生形态学与功能改变,其中 PD 相关腹膜纤维化是透析患者死亡和技术失败的重要原因[5~7]。多种促纤维化细胞因子与腹膜纤维化有密切关系。转化生长因子(TGF)β1、白介素(IL)-6 是参与 PD 患者腹膜纤维化进程的关键分子[8~11]。本研究分析 PD 患者腹膜纤维化与腹透液中 TGF-1、IL-6 水平的相关性,报道如下。

资料与方法

一般资料 回顾性研究 2013 年 8 月~2017 年 2 月在湖北医药学院附属东风医院肾内科诊治的终末期肾病患者 72 例(男 40,女 32),年龄 20~80 岁,平均(48.53±12.23)岁;平均体重指数(20.98±2.48)kg/m^2;平均透析时间(15.82±1.23)月;原发疾病:40 例慢性肾炎,20 例高血压肾动脉硬化,8 例糖尿病肾病以及 4 例其他肾病。

纳入标准 在试验前 3 个月内没有发生过腹膜炎;腹膜活检符合终末期肾病的诊断标准。排除标准:透析龄 <3个月;合并有肿瘤、肝炎、结核、活动

* 通信作者:卢丽,E-mail:llluli91@163.com

性风湿性疾病等;妊娠与哺乳期;透析管路有机械性问题;恶性肿瘤。研究得到医院伦理委员会批准,所有患者均知情并签署同意书。

透析方法 全部患者都给予腹膜透析治疗,透析液为 Dianeal PD-4 腹膜透析液,购自广州百特医疗用品有限公司,葡萄糖含量 1.0% ~2.5%,每天透析量范围 6 000 ~ 10 000 mL,葡萄糖用量 30 ~ 300 kg,治疗观察时间 90 d。

观察指标 记录净超滤量,计算肌酐透析液与血浓度之比(D/Pcr),计算尿素清除指数(KT/V)和肌酐清除率(Ccr),试剂盒购自上海生工公司;在治疗前期(第 1 ~5 天)与治疗后期(第 80 ~90 天)采集患者的夜间透析液 8 ~10 mL,采用酶联免疫法测定 TGF-β1、IL-6 含量;检测患者血浆白蛋白(ALB)、甲状旁腺素(PTH)、钙(Ca)、磷(P)等生化指标。

统计学处理 采用 SPSS 21.0 统计学软件包,计量资料以($\bar{x} \pm s$)表示,采用 t 检验,运用 Pearson 法分析相关性。以 $P<0.05$ 为差异有统计学意义。

结 果

腹膜纤维化指标 治疗后期患者的超滤量、KT/V 值高于治疗前期,D/Pcr、Ccr 值低于治疗前期($P<0.05$),见表 1。

表 1 PD 患者腹膜纤维化指标变化情况 ($\bar{x} \pm s$)

时间点	例	D/Pcr	KT/V	Ccr (L/W)	超滤量 (mL/d)
治疗前期	72	0.7 ±0.1	1.7 ±0.2	62.5 ±12.8	334.3 ±78.3
治疗后期	72	0.6 ±0.2*	1.8 ±0.2*	32.9 ±10.8*	511.5 ±81.4*

注:与治疗前期比较,*$P<0.05$

TGF-β1、IL-6 水平 治疗后期患者的 TGF-β1、IL-6 水平低于治疗前期($P<0.05$),见表 2。

生化指标 治疗后期患者的 ALB、PTH、Ca、P 含量与治疗前期比较,差异无统计学意义($P>0.05$),见表 3。

表 2 PD 患者 TGF-β1、IL-6 水平变化(pg/mL,$\bar{x} \pm s$)

时间点	例	TGF-β1	IL-6
治疗前期	72	325.3 ±103.8	61.4 ±8.2
治疗后期	72	189.5 ±98.1*	24.6 ±9.1*

注:与治疗前期比较,*$P<0.05$

表 3 PD 患者生化指标变化情况 ($\bar{x} \pm s$)

时间点	例	ALB (g/L)	Ca (mmol/L)	P (mmol/L)	iPTH (pg/mL)
治疗前期	72	37.5 ±7.1	1.6 ±0.4	1.7 ±0.8	413.0 ±77.8
治疗后期	72	37.1 ±8.0	1.7 ±0.6	1.7 ±0.6	411.1 ±89.1

相关性分析 Pearson 相关分析显示治疗前期与后期患者的 TGF-β1、IL-6 与 KT/V 呈正相关(均 $P<0.05$),与 D/Pcr、Ccr、超滤量呈负相关(均 $P<0.05$),见表 4。

讨 论

本研究中治疗后期患者的超滤量、KT/V 值高于治疗前期,D/Pcr、Ccr 值低于治疗前期(均 $P<0.05$)。当患者的 KT/V、D/Pcr、Ccr 出现异常波动时,可引起腹膜纤维化,阻碍 PD 长期治疗。

本研究中治疗后期患者 TGF-β1、IL-6 水平低于治疗前期,表明 PD 可导致患者 TGF-β1、IL-6 水平表达量升高,但是随着病情转好,TGF-β1、IL-6 水平逐渐降低。腹膜炎与腹膜纤维化密切相关[12,13]。部分研究表明腹膜纤维化是腹膜间皮细胞经过分化形成成纤维细胞,其中,机体 TGF-β1 信号通路的激活及氧化应激极为关键[14,15]。

长期 PD 可使得腹膜发生形态学与功能改变,导致腹膜溶质转运逐渐增加,形成腹膜纤维化[16]。本研究中治疗后期患者的 ALB、PTH、Ca、P 含量与治疗前期相比无显著差异(均 $P>0.05$);Pearson 相关分析显示治疗前期与后期患者的 TGF-β1、IL-6 与 KT/V 呈正相关(均$P<0.05$),与 D/Pcr、Ccr、超滤量呈负相关(均 $P<0.05$)。

PD 患者腹膜纤维化与腹透液中 TGF-β1、IL-6

表 4 PD 患者腹膜纤维化与腹透液中 TGF-β1、IL-6 水平的相关性分析

指标	例	D/Pcr	KT/V	Ccr	超滤量	ALB	Ca	P	iPTH
TGF-β1									
治疗前期	72	−0.489*	0.563*	−0.564*	−0.451*	0.103	0.089	0.104	0.081
治疗后期	72	−0.510*	0.582*	−0.375*	−0.511*	0.098	0.128	0.083	0.079
IL-6									
治疗前期	72	−0.402*	0.492*	−0.398*	−0.501*	0.167	0.103	0.089	0.111
治疗后期	72	−0.428*	0.602*	−0.419*	−0.482*	0.152	0.091	0.056	0.119

注:*$P<0.05$

水平存在明显的相关性，抑制 TGF-β1、IL-6 的表达可能有利于防治腹膜纤维化。

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(上接第 18 页)

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