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腹膜透析治疗对先天性心脏病患儿术后血清因子水平及预后的影响 *

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摘要 目的:探讨腹膜透析治疗对先天性心脏病患儿术后血清因子水平及预后的影响。**方法:**选择2013年11月~2016年11月我院收治的96例小儿先天性心脏病,按治疗方式分为对照组与研究组,每组48例,两组均接受手术治疗。对照组于术后采用常规治疗,研究组在常规治疗基础上加以腹膜透析治疗,观察并比较两组治疗前后血清 β_2 微球蛋白、24 h尿蛋白、血尿素氮、血肌酐、白细胞介素-6(IL-6)、白细胞介素-8(IL-8)、肿瘤坏死因子- α (TNF- α)、碳酸氢盐、钙离子、钾离子水平的变化及死亡情况。**结果:**治疗后,两组血清 β_2 微球蛋白、24 h尿蛋白、血尿素氮、血肌酐、IL-6、IL-8、TNF- α 、钾离子水平均较治疗前显著降低,且研究组以上指标均明显低于对照组;两组碳酸氢盐、钙离子水平均较治疗前明显上升,且研究组以上指标明显高于对照组($P<0.05$)。此外,研究组死亡率明显低于对照组($P<0.05$)。**结论:**腹膜透析治疗先天性心脏病患儿术后能够降低病死率,改善肾功能、炎症因子及电解质平衡紊乱。

关键词:小儿;先天性心脏病;术后腹膜透析;临床疗效;血清因子

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Clinical Efficacy of Peritoneal Dialysis in Treatment of Congenital Heart Disease in Children and Influence on Serum Factors*

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ABSTRACT Objective: To research the effect of peritoneal dialysis on the serum factors and prognosis of children with congenital heart diseases. **Methods:** 96 children with congenital heart disease from November 2013 to November 2016 were divided into the control group and the research group according to the treatment mode, with 48 cases in each group. Both groups were treated with surgery, the control group was treated with routine treatment after surgery, while the research group was treated with peritoneal dialysis based on the control group. The serum β_2 -microglobulin, 24 h urine protein, blood urea nitrogen, blood creatinine, interleukin 6 (IL-6), interleukin 8 (IL-8), tumor necrosis factor- α (TNF- α), hydrocarbonate, calcium, potassium levels and mortality were observed and compared between two group. **Results:** After treatment, the serum β_2 -microglobulin, 24 h urine protein, blood urea nitrogen, blood creatinine, IL-6, IL-8, TNF- α , potassium levels of two group were decreased, which were obviously lower in the research group than those of the control group, the bicarbonate, calcium ions of two group were obviously increased, which were significantly higher in the research group than those of the control group($P<0.05$). The mortality rate of research group was lower than that of the control group($P<0.05$). **Conclusion:** Peritoneal dialysis can decrease the mortality of congenital heart disease children after operation, which regulate the serum factors, improve the kidney function, inflammation factor and electrolyte balance disorder.

Key words: Children; Congenital heart disease; Postoperative peritoneal dialysis; Clinical curative effect; Serum factor

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前言

先天性心脏病是一种儿科多发性疾病,与宫内感染、遗传等因素有着密切的联系,可出现发育障碍等临床表现,严重影响患儿的身心健康,未经有效诊治者的临床病死率较高^[1,2]。临床研究显示先天性心脏病难以自行愈合,手术为其主要疗法,但难度较大,年龄较小者全身营养及发育状态相对较差,年龄

较大者心脏容易出现代偿性的增加,多伴不同程度的肺动脉高压,延长术后的恢复时间^[3,4]。此外,先天性心脏病患儿术后由于心脏低排量、肾灌注不足等因素容易诱导急性肾功能不全的发生,导致炎症因子过度生成、水电解质的滞留等血清因子的改变,未经及时处理者能够引起肾脏功能发生进展,加剧病情^[5,6]。既往临床多予以利尿及限制液体吸入治疗,但由于先天性心脏病患儿多伴发育迟缓、营养不良,单纯经内科治疗的效果并不

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理想^[7]。腹膜透析可起到肾脏替代作用,利于机体毒素及水分的排出,从而利于肾、心等功能改善,但临床效果报道不一^[8]。因此,本研究主要探讨了腹膜透析对先天性心脏病患儿血清因子水平及预后的影响。

1 资料与方法

1.1 一般资料

96例先天性心脏病患儿入选标准^[9]:经临床表现、X线、心电图、超声等检查明确诊断为先天性心脏病;ASA分级在Ⅰ~Ⅱ级;术后存在肾功能不全;均未见血液系统病变、活动性感染、风湿热等;近期无免疫抑制剂、激素等使用史。排除心肝等脏器显著不全;腹膜严重破损、粘连、脐突出等腹膜透析禁忌症。对照组年龄2~6岁,平均(4.11±0.68)岁;23例女,25例男;疾病类型:7例动脉导管未闭,15例房间隔缺损,26例室间隔缺损。研究组年龄2~6岁,平均(4.36±0.72)岁;27例女,21例男;疾病类型:6例动脉导管未闭,13例房间隔缺损,29例室间隔缺损。两组一般临床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

对照组接受常规治疗,予以正性肌力、利尿、限制入液、营养支持等常规治疗。研究组基于对照组选用腹膜透析治疗,常规麻醉后在脐下2~3cm进行2cm左右的横向或者纵向切口,将各层组织逐步切开。选择特定的小儿腹膜透析管,并于膀胱直肠窝放置且固定。将切口依次缝合,使三通接头实施Y形连接,纱布覆盖创口。予以10~20mL/kg4.25%腹膜透析液(1000mL,国药准字H12020543,江西金钥药业有限公司)进行透析,

于腹腔内停留2h左右并引流30min,1个循环周期为3h。期间密切关注患儿基本身体状态,待患儿情况稳定后中断透析。对两组患儿治疗期间的死亡情况进行统计。

1.3 观察指标

1.3.1 肾功能指标测定 于治疗前及治疗1周时采集患儿肘部静脉血及尿液,常规处理并保留待检。 β_2 微球蛋白、血尿素氮、血肌酐选用比色法检测,24h尿蛋白选用沉淀法检测,试剂盒分别来自上海江莱生物科技有限公司、上海研域生物科技有限公司、上海江莱生物科技有限公司、上海恒远生物科技有限公司。

1.3.2 血清IL-6、IL-8、TNF- α 水平检测 按酶联免疫法检测,试剂盒分别来自北京百奥莱博科技有限公司、上海拜力生物科技有限公司、厦门慧嘉生物科技有限公司。

1.3.3 电解质测定 碳酸氢盐、钙离子、钾离子选用电解质分析仪进行。

1.4 统计学分析

选用SPSS18.0进行本研究的数据处理,计量资料以($\bar{x}\pm s$)表示,组间比较选用t检验进行,用[(例)%]表示计数资料,比较用 χ^2 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组治疗前后肾功能指标的比较

治疗前,两组 β_2 微球蛋白、24h尿蛋白、血尿素氮、血肌酐比较未见统计学差异($P>0.05$);治疗后,两组 β_2 微球蛋白、24h尿蛋白、血尿素氮、血肌酐均较治疗前显著下降,且研究组以上指标明显低于对照组($P<0.05$),见表1。

表1 两组治疗前后肾功能指标的比较($\bar{x}\pm s$)

Table 1 Comparison of the renal function index between two groups before and after the treatment ($\bar{x}\pm s$)

Groups	n	Time	β_2 -microglobulin (mg/L)	24 h urine protein (g/24 h)	Blood urea nitrogen (mmol/L)	Serum creatinine (μ mol/L)
Control group	48	Before treatment	0.93±0.11	0.33±0.04	21.90±2.62	215.27±26.98
		After treatment	0.75±0.09*	0.25±0.04*	13.28±1.60*	120.68±15.41*
Research group	48	Before treatment	0.94±0.12	0.34±0.03	22.52±2.11	216.84±25.09
		After treatment	0.42±0.05**	0.13±0.01**	7.80±0.92**	75.49±9.26**

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

2.2 两组治疗前后血清炎症因子水平的比较

治疗前,两组血清IL-6、IL-8、TNF- α 水平比较差异无统计学意义($P>0.05$);两组治疗后血清IL-6、IL-8、TNF- α 水

平均较治疗前显著下降,且研究组以上指标均较对照组显著降低($P<0.05$),见表2。

表2 两组治疗前后血清炎症因子水平的比较($\bar{x}\pm s$)

Table 2 Comparison of inflammatory cytokines levels between two groups before and after the treatment ($\bar{x}\pm s$)

Groups	n	Time	IL-6(ng/L)	IL-8(ng/L)	TNF- α (ng/L)
Control group	48	Before treatment	38.99±4.72	41.65±5.12	40.29±4.82
		After treatment	28.75±3.51*	26.10±2.76*	24.12±3.12*
Research group	48	Before treatment	39.21±4.11	42.09±5.70	40.85±4.21
		After treatment	15.40±1.87**	21.64±3.01**	13.26±1.62**

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

2.3 两组治疗前后血电解质水平比较

治疗前, 两组血电解质水平比较差异无统计学意义($P>0.05$); 治疗后, 两组碳酸氢盐、钙离子均较治疗前显著上升, 且研

究组明显高于对照组, 两组钾离子均较治疗前明显下降, 且研究组显著低于对照组($P<0.05$), 见表 3。

表 3 两组治疗前后血电解质水平的比较($\bar{x} \pm s$)

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

Groups	n	Time	Hydrocarbonate (mmol/L)	Calcium ions(mmol/L)	Potassium ions (mmol/L)
Control group	48	Before treatment	12.85± 1.52	2.05± 0.25	5.76± 0.71
		After treatment	15.79± 1.90*	2.33± 0.29*	4.22± 0.62*
Research group	48	Before treatment	12.30± 1.75	2.09± 0.26	5.85± 0.68
		After treatment	20.11± 2.51**	2.56± 0.33**	3.74± 0.47**

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

2.4 两组病死率的比较

研究组 1 例患儿死于多器官功能衰竭, 对照组 6 例患儿死亡, 其中严重感染例, 多器官功能衰竭例, 研究组死亡率较对照组显著降低($P<0.05$)。

3 讨论

先天性心脏病可出现系列并发症, 近年来随着外科诊疗技术的不断提高, 多数患儿均可得到有效治疗^[10]。但由于先天性心脏病患儿肾脏调节能力较弱, 肾小球滤过率较低, 容易出现肾功能不全等并发症, 引起血肌酐增加、尿量下降等表现, 降低手术效果^[11,12]。国外研究显示先天性心脏病患儿术后出现肾功能不全等并发症经常规内科治疗难以达到良好的临床效果^[13]。

早期先天性心脏病患儿术后因心功能尚未得到全部恢复, 导致血流动力学的稳定性较差, 难以建立血管通路, 且机液体量较少, 多不建议实施血液透析^[14]。腹膜透析是临床透析的新型方式, 选用机体腹膜进行透析, 将腹膜对侧毛细血管液体与腹腔透析液中水分及溶质进行交换, 从而使机体稽留的水分及代谢产物清除, 经反复替换的腹透液, 发挥支持治疗或者肾脏替代治疗的作用, 且可为机体补充一定的营养物质^[15]。同时, 腹膜透析无需将血管通路开通, 能够减轻多次穿刺造成的疼痛, 且对心血管功能几乎无影响, 易于小儿接受^[16,17]。本研究结果显示腹膜透析组治疗后 β_2 微球蛋白、24 h 尿蛋白、血尿素氮、血肌酐下降更为明显, 说明其能缓解肾功能。 β_2 -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^[18]。机体正常状态下, 尿中可出现微量蛋白, 但当 24 h 尿蛋白定量超过 1.5 g 时即为尿蛋白阳性, 若机体出现持续性阳性尿蛋白, 则提示肾脏病变^[19,20]。血尿素氮及肌酐是肾功能的常用评估指标, 但结果容易受到年龄等因素的影响。

心脏手术由于创伤应激、内毒素释放、缺血再灌注等可促进炎症因子的表达, 诱导炎症反应, IL-6 的生物活性较强, 是机体内重要的免疫调节因子, 机体处于炎症反应时可生成 IL-6, 局部损伤刺激生成淋巴细胞等炎症细胞时会增加 IL-6 的分泌, 且有研究表明 IL-6 也是一种主要的促炎性反应因子, 能够促进其他炎症因子的生成, 进而加重机体的炎症损伤^[21,22]。IL-8 是多源性的炎症细胞因子, 对 T 淋巴细胞、嗜碱性粒细胞及中

性粒细胞的趋化作用比较强, 能够造成炎症细胞集聚, 并产生大量活性物, IL-8 表达过度时能够导致组织不同程度的受损^[23]。TNF- α 主要经巨噬细胞与单核细胞合成并分泌, 能够诱导胶质细胞及神经细胞合成更多的促炎性因子, 从而使多种神经毒性因子释放, 加剧细胞免疫损伤, 影响预后^[24]。本研究显示两组治疗后血清 IL-6、IL-8、TNF- α 水平均显著下降, 且腹膜透析组下降更为明显, 说明腹膜透析能够有效调节机体的炎症状态, 缓解内环境, 可能与其有效清除机体毒素有关。

有研究证实先天性心脏病患儿手术后因肾功能不全等因素能够导致水电解质产生蓄积, 诱导酸及钾中毒, 导致心脏负荷的增加。碳酸氢盐能够客观反映机体血液状态, 其浓度上升提示碱中毒, 反之则为酸中毒^[25,26]。钙离子为机体生理活动的关键因子, 能够确保细胞膜正常的电位, 且可调节心脏跳动^[27]。生理浓度的钾离子能够确保神经肌肉及心肌功能, 其浓度过高能够抑制心肌。本研究结果显示两组治疗后碳酸氢盐、钙离子均上升, 钾离子也相应降低, 但腹膜透析组变化更为明显, 说明腹膜透析能够利于机体水分及代谢产物的排除, 缓解电解质紊乱, 避免多器官的功能发生衰竭^[28]。同时, 腹膜透析组病死率较常规治疗组低, 说明其临床效果肯定, 能够使患儿病死率降低^[29,30]。我们发现腹膜透析置管时需将腹膜仔细缝合, 避免渗漏, 且应严格掌握无菌操作原则, 适当予以抗生素, 避免切口发生感染, 同时需密切关注电解质及水平衡, 并注意应用支持。

综上所述, 膜透析治疗先天性心脏病患儿术后能够降低病死率, 改善肾功能、炎症因子及电解质平衡紊乱。由于本研究纳入样本量较小, 且观察时间较短, 结果可能存在一定差异, 有待于临床进一步考察。

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