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美罗培南联合常规治疗对脓毒症休克合并急性肾功能不全患者炎性因子、肾功能及免疫球蛋白的影响*

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摘要 目的：探讨脓毒症休克合并急性肾功能不全患者在常规治疗的基础上联合美罗培南治疗后对其肾功能、炎性因子及免疫球蛋白的影响。**方法：**选取我院 80 例脓毒症休克合并急性肾功能不全患者，根据随机数字表法分为对照组（n=40）和研究组（n=40），对照组予以常规治疗，研究组在对照组的基础上联合美罗培南治疗，比较两组患者疗效、炎性因子[降钙素原（PCT）、C 反应蛋白（CRP）、白介素 -6（IL-6）]、肾功能[尿素氮（BUN）和血肌酐（Scr）]、免疫球蛋白[免疫球蛋白 G（IgG）、免疫球蛋白 M（IgM）、免疫球蛋白 A（IgA）]及不良反应。**结果：**研究组治疗 1 个疗程后的临床总有效率为 90.00%（36/40），高于对照组的 72.50%（29/40）（*P*<0.05）。两组不良反应发生率比较无差异（*P*>0.05）。两组患者治疗 1 个疗程后 BUN、Scr 和 PCT、CRP、IL-6 均下降，且研究组低于对照组（*P*<0.05）。两组患者治疗 1 个疗程后 IgG、IgM 均升高，且研究组高于对照组（*P*<0.05）；两组患者治疗 1 个疗程后 IgA 组间及组内比较无差异（*P*>0.05）。**结论：**脓毒症休克合并急性肾功能不全患者在常规治疗的基础上联合美罗培南治疗，疗效显著，可有效改善肾功能及免疫功能，减轻炎性反应，且安全性较好。

关键词：炎性因子；常规治疗；肾功能；脓毒症休克；美罗培南；急性肾功能不全；免疫球蛋白

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Effects of Meropenem Combined with Routine Treatment on Inflammatory Factors, Renal Function and Immunoglobulin in Septic Shock Patients with Acute Renal Insufficiency*

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ABSTRACT Objective: To investigate the effect of meropenem combined with routine treatment on inflammatory factors, renal function and immunoglobulin in septic shock patients with acute renal insufficiency. **Methods:** 80 patients with septic shock with acute renal insufficiency were selected, they were divided into control group (n=40) and study group (n=40) according to the random number table. The control group was treated with routine treatment. The study group was treated with meropenem on the basis of the control group. The efficacy, inflammatory factors [procalcitonin (PCT), C-reactive protein (CRP), interleukin-6 (IL-6), renal function [urea nitrogen (BUN), blood creatinine (Scr)], immunoglobulin [immunoglobulin G (IgG), immunoglobulin M (IgM), immunoglobulin A (IGA)], and adverse reactions were compared. **Results:** The total effective rate of the study group 1 course after treatment was 90.00% (36/40), which was higher than 72.50% (29/40) of the control group (*P*<0.05). There was no significant difference in the incidence of adverse reactions between the two groups (*P*>0.05). 1 course after treatment, BUN, SCR and PCT, CRP, IL-6 decreased of both groups, and the study group was lower than the control group (*P*<0.05). 1 course after treatment, the IgG and IgM of the two groups increased, and the study group was higher than the control group (*P*<0.05). There was no significant difference between the two groups in the IgA group and within the group (*P*>0.05). **Conclusion:** Meropenem combined with routine treatment is effective in the treatment of septic shock combined with acute renal insufficiency. It can effectively improve renal function and immune function, reduce inflammatory response, and which has good safety.

Key words: Inflammatory factors; Conventional therapy; Renal function; Septic shock; Meropenem; Acute renal insufficiency; Immunoglobulin

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前言

脓毒症是指临床病危患者由于感染而导致的炎症反应失控紊乱状态,患者多表现为器官低灌注状态或循环系统功能衰竭,严重时可引起脓毒症休克合并急性肾功能不全[1-3]。脓毒症休克合并急性肾功能不全患者病情危重,治疗难度大,多由严重创伤或烧伤等情况引起[4,5]。现临床针对该病的治疗尚无特异性方案,多以抗菌药物治疗为主。然而不少临床实践证实[6,7],常规抗菌治疗效果有限,难以达到理想效果。美罗培南属于二代碳青霉烯类抗生素,既往在致病菌诊断不明确脓毒症危重病患者治疗中应用广泛[8]。本研究通过对部分我院收治的脓毒症休克合并急性肾功能不全患者在常规治疗基础上联合美罗培南治疗,疗效显著,报道如下。

1 资料与方法

1.1 一般资料

选取我院于 2013 年 7 月 ~2018 年 9 月期间接收的 80 例脓毒症休克合并急性肾功能不全患者,纳入标准:(1)诊断标准参考美国重症医学会制定的相关标准[9];(2)患者家属知情本研究且签署同意书;(3)对本次研究用药耐受者;(4)经规范化液体复苏治疗后无明显效果者。排除标准:(1)孕期妇女或哺乳期幼儿;(2)合并心肝肺等脏器功能障碍者;(3)合并自身免疫缺陷者;(4) 死亡或停止生命维持治疗者;(5) 合并恶性肿瘤者;(6) 既往伴炎症内科疾病者。根据随机数字表法分为对照组(n=40)和研究组(n=40),其中对照组男 25 例,女 15 例,年龄 26~57 岁,平均(39.64± 4.52)岁;体质量指数 20.6~25.3 kg/m^2,平均(23.68± 0.65)kg/m^2。研究组男 23 例,女 17 例,年龄 28~60 岁,平均(40.06± 5.41)岁;体质量指数 20.2~26.5 kg/m^2,平均(23.82± 0.73)kg/m^2。两组一般资料对比无差异(P>0.05),均衡可比。此次研究已通过我院伦理学委员会批准进行。

1.2 治疗方法

视患者具体病情行营养支持、感染治疗,呼吸不畅者可使用呼吸机进行辅助呼吸。及时进行血液透析治疗,设置血流量为 210~290 mL/h,首次透析 2.5 h,以后每间隔 1 d 治疗 1 次,透析治疗中使用低分子肝素抗凝。研究组在对照组的基础上联合美罗培南(国药准字 H20093466,上海上药新亚药业有限公司,规格:按 $C_{17}H_{25}N_3O_5S$ 计 0.5 g)治疗,将美罗培南 3 g 加入氯化钠注射液 50 mL 融合后,持续泵入,每日 1 次。1 周为 1 个疗程,两组均治疗 1 个疗程。

1.3 观察指标

(1)观察两组患者治疗 1 个疗程后的疗效。疗效判定标准如下[10]:无效:症状、体征均未发生好转甚至加重;有效:症状及体征有所改善;显效:白细胞计数及血培养显示为正常或基本正常,体温恢复至 38℃以下,心率及呼吸频率恢复至正常。总有效率 = 显效率 + 有效率。(2)记录两组治疗期间不良反应发生状况。(3)于治疗前、治疗 1 个疗程后分别抽取两组患者清晨空腹静脉血 3 mL,经常规离心处理(离心半径 13 cm,3600 r/min 离心 15 min),分离上清液,置于 -40℃冰箱中待测。选用上海沪震实业有限公司试剂盒,按照试剂盒说明书步骤,采用酶联免疫吸附法检测炎性因子指标:降钙素原(Procalcitonin,PCT)、C 反应蛋白(C-reactive protein,CRP)、白介素 -6(Interleukin -6,IL-6)。应用 Olypus II 型全自动生化分析仪(深圳迈瑞生物医疗电子股份有限公司)检测肾功能指标:尿素氮(Urea nitrogen,BUN)和血肌酐(Serum creatinine,Scr)以及免疫球蛋白指标:免疫球蛋白 G (Immunoglobulin G,IgG)、免疫球蛋白 M(Immunoglobulin M,IgM)、免疫球蛋白 A(Immunoglobulin A,IgA)。

1.4 统计学方法

应用 SPSS27.0 软件进行统计学分析, 疗效等计数资料以[n(%)]表示,采用 x^2 检验;肾功能、免疫球蛋白水平等计量资料以($\bar{x}\pm s$)表示,采用 t 检验,P<0.05 为差异具有统计学意义。

2 结果

2.1 两组疗效比较

研究组治疗 1 个疗程后的临床总有效率为 90.00%(36/40),高于对照组的 72.50%(29/40)(P<0.05);详见表 1。

表 1 两组疗效比较 例(%)

Table 1 Comparison of efficacy between the two groups n(%)

Groups	Markedly effective	Valid	Invalid	Total effective rate
Control group(n=40)	9(22.50)	20(50.00)	11(27.50)	29(72.50)
Study group(n=40)	15(37.50)	21(52.50)	4(10.00)	36(90.00)
x^2				4.021
P				0.045

2.2 两组肾功能指标比较

两组治疗前 BUN、Scr 比较无差异 (P>0.05); 两组治疗 1 个疗程后 BUN、Scr 均下降,且研究组低于对照组(P<0.05);详见表 2。

2.3 两组炎症因子水平比较

两组治疗前 PCT、CRP、IL-6 比较无差异(P>0.05);两组治疗 1 个疗程后 CRP、PCT、IL-6 均下降, 且研究组低于对照组(P<0.05);详见表 3。

2.4 两组免疫球蛋白比较

两组患者治疗前 IgG、IgM、IgA 比较差异无统计学意义(P>0.05); 两组治疗 1 个疗程后 IgA 组间及组内比较无差异(P>0.05);两组患者治疗 1 个疗程后 IgG、IgM 均升高,且研究组高于对照组(P<0.05);详见表 4。

2.5 两组不良反应比较

治疗期间,研究组出现胃肠道不适 2 例,皮疹 2 例,呕吐 1 例,不良反应发生率为 12.50%(5/40);对照组出现呕吐 1 例,皮疹 1 例,胃肠道不适 1 例,不良反应发生率为 7.50%(3/40);两组不良反应发生率比较无差异(x^2=0.556,P=0.456)。

表 2 两组肾功能指标比较（$\bar{x}\pm s$）

Table 2 Comparison of renal function indexes between the two groups($\bar{x}\pm s$)

Groups	BUN(mmol/L)		Scr(μmol/L)	
	Before treatment	1 course after treatment	Before treatment	1 course after treatment
Control group(n=40)	53.61± 4.88	46.44± 5.78*	417.69± 24.03	346.12± 16.89*
Study group(n=40)	54.15± 6.92	39.72± 6.21*	416.73± 23.11	227.84± 17.13*
t	0.403	5.010	0.182	31.096
P	0.688	0.000	0.856	0.000

Note: compared with before treatment, *P<0.05.

表 3 两组炎症因子水平比较（$\bar{x}\pm s$）

Table 3 Comparison of inflammatory factors between the two groups($\bar{x}\pm s$)

Groups	PCT(μg/L)		CRP(mg/L)		IL-6(pg/mL)	
	Before treatment	1 course after treatment	Before treatment	1 course after treatment	Before treatment	1 course after treatment
Control group(n=40)	94.37± 8.22	63.79± 9.33*	99.78± 15.23	68.03± 7.32*	54.23± 6.45	38.32± 7.38*
Study group(n=40)	95.16± 10.61	35.02± 8.42*	99.12± 17.16	35.12± 8.82*	53.02± 7.31	22.31± 6.25*
t	0.372	14.478	0.1082	18.159	0.785	10.470
P	0.711	0.000	0.856	0.000	0.435	0.000

Note: compared with before treatment, *P<0.05.

表 4 两组免疫球蛋白比较（$\bar{x}\pm s$）

Table 4 Comparison of immunoglobulins between the two groups($\bar{x}\pm s$)

Groups	IgG(g/L)		IgM(g/L)		IgA(g/L)	
	Before treatment	1 course after treatment	Before treatment	1 course after treatment	Before treatment	1 course after treatment
Control group(n=40)	9.01± 0.85	14.83± 2.05*	1.03± 0.12	1.97± 0.13*	2.31± 0.37	2.38± 0.33
Study group(n=40)	9.13± 0.93	21.09± 2.42*	1.09± 0.18	2.73± 0.17*	2.34± 0.35	2.41± 0.45
t	0.602	12.483	1.754	22.460	0.373	0.340
P	0.549	0.000	0.083	0.000	0.711	0.735

Note: compared with before treatment, *P<0.05.

3 讨论

脓毒症为全身炎症反应综合征，主要由感染引发，是外科大手术或严重创伤后常见的一类并发症[11,12]。脓毒症休克具有病情进展快、病死率高的特点，其中约有 50.6%的患者可并发急性肾功能不全[13]。既往研究报道[14]显示，脓毒症休克合并急性肾功能不全的病死率高达 50%~60%，显著高于五脏器损伤的脓毒症患者。目前有关脓毒症休克合并急性肾功能不全的具体发病机制尚不十分明确，多认为其与炎症因子、内毒素、应激激素、血流动力学的剧烈变化有关，其中炎症反应是疾病发生的主要环节[15,16]。现临床针对该病的治疗尚无统一方案，但认为其治疗核心除了控制感染源外，还应加强对器官的功能性支持及免疫调理，加之此类患者肾功能损伤为不可逆损伤，应及早发现并治疗以防止进一步的肾衰竭，危及患者性命。美罗培南是人工合成的新型碳青霉烯，是一种有非常广泛抗菌性且可供注射的抗生素，临床常用于治疗重症感染或多重感染患者[17]。

本次研究结果显示，脓毒症休克合并急性肾功能不全患者在常规治疗的基础上联合美罗培南，可进一步优化治疗效果。周丽琴等人[18]研究结果也证实了这一点。血液透析治疗可通过透析、滤过以及吸附等方式清除血液中的炎症介质，有助于脓毒症的治疗[19,20]。美罗培南对革兰阴性菌以及包括 B 内酰胺酶菌、铜绿假单胞菌在内的革兰阳性菌均具有广谱抗菌活性，可穿透大多数革兰阴性和阳性细菌的细胞壁，到达其靶点青霉素结合蛋白，发挥杀菌效果，同时对中枢系统和肾脏不良反应小，不会对患者恢复造成明显影响 [21-23]。既往研究结果显示[24,25]，PCT、CRP、IL-6 等炎性因子与脓毒症休克合并急性肾功能不全患者的病情进展、预后关系密切。炎性因子的大量释放可导致机体免疫功能下降，进一步加重患者病情。IgA 对病原体增殖具有抑制作用，当发生感染时人体内 IgA 高消耗；而 IgM 为高效能抗生物抗体，具有防御作用；IgG 则对内外毒素具备中和作用[26,27]。血清 BUN、Scr 为肾小球滤过功能损伤情况的主要判断指标。本研究中的两组患者上述血清指标均有所改善，且美罗培南联合常规治疗者的改善效果更佳。这可能是因为普通抗生素对各种革兰阳性球菌、革兰阴性杆菌作用不显著，而美罗

培南却能发挥作用，同时还有研究发现其对多重耐药的需氧革兰阴性杆菌仍然具有抗菌活性，杀菌作用效果显著，引起全身炎症反应的危险性较小，并且可维持患者有效血容量，缓解因肾脏血流灌注不足引起的肾功能损伤现象，减轻免疫抑制[28-30]。通过比较两组不良反应发生率可知，美罗培南联合常规治疗并不会增加不良反应发生率，安全性较好。本研究尚存在样本量较小及只考察了药物一个疗程内疗效的不足，今后将采取扩大样本量及增加考察时间的措施进行研究，以期获取更精确的数据。

综上所述，脓毒症休克合并急性肾功能不全患者在常规治疗的基础上联合美罗培南，疗效显著，可有效改善肾功能及免疫功能，减轻炎性反应，且安全性较好。

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