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连续性血液净化及肠内营养治疗重症胰腺炎疗效及对炎症因子影响 *

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摘要 目的:探究连续血液净化及肠内营养治疗重症胰腺炎患者的疗效及对患者炎症因子水平的影响。**方法:**选择 2018 年 1 月至 2019 年 12 月于我院接受治疗的 82 例重症胰腺炎患者为研究对象,按照治疗方式不同将其分为研究组(49 例)与对照组(33 例)。对照组患者仅接受连续血液净化,研究组患者在对照组患者基础上加用肠内营养支持,对比两组患者腹痛缓解时间、感染发生率、住院时间、治疗前后血尿素氮(Blood urea nitrogen,BUN)、血肌酐(creatinine,SCr)、C 反应蛋白(C-reactive protein,CRP)、白细胞介素 -6(interleukin-6,IL-6)、肿瘤坏死因子(tumor necrosis factor,TNF-α)、急性生理与慢性健康评分表评分(acute physiology and chronic health evaluationⅡ,APACHE II)评分的变化。**结果:**研究组患者腹痛缓解时间、感染发生率、住院时间均短于对照组患者(P<0.05)。治疗后,研究组患者 APACHE II 评分、血清 CRP、IL-6、TNF-α、BUN 及 SCr 水平均低于对照组(P<0.05)。**结论:**连续血液净化联合肠内营养支持对重症胰腺炎患者具有较好的治疗效果,能够显著加快重症胰腺炎患者转归,改善患者肾损伤及机体炎症状态。

关键词:连续血液净化;肠内营养;重症胰腺炎;炎症因子

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Clinical Efficacy of Continuous Blood Purification and Enteral Nutrition in the Treatment of Severe Pancreatitis and Its Effect on the Inflammatory Factors*

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ABSTRACT Objective: To explore the clinical efficacy of continuous blood purification and enteral nutrition in the treatment of patients with severe pancreatitis and its effect on the levels of inflammatory factors in patients. **Methods:** Eighty-two patients with severe pancreatitis who were treated in our hospital from January 2018 to December 2019 were selected as the research subjects, and they were divided into the experimental group (49 cases) and the control group (33 cases) according to different treatment methods. Patients in the control group received continuous blood purification only, and the patients in the experimental group were supplemented with enteral nutrition on the basis of the patients in the control group. The changes in abdominal pain relief time, infection rate, length of hospital stay, BUN, SCr, CRP, IL-6, TNF-α, and APACHE II scores before and after treatment were compared between the two groups of patients. **Results:** Abdominal pain relief time, infection rate, and hospital stay were shorter in the experimental group than in the control group (P <0.05). After treatment, the APACHE II score, serum CRP, IL-6, TNF-α, BUN, and SCr levels in the experimental group were lower than those in the control group (P<0.05). **Conclusion:** Continuous blood purification combined with enteral nutrition support had a better therapeutic effect on patients with severe pancreatitis, could significantly accelerate the outcome of patients with severe pancreatitis, and improve patients renal injury and inflammation of the body.

Key words: Continuous blood purification; Enteral nutrition; Severe pancreatitis; Inflammatory factors

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前言

重症胰腺炎是一种临床上较为常见的急腹症,是指在各类因素的作用下,胰酶在胰腺内被激活,对胰腺组织进行自身消化,致使胰腺发生水肿、出血甚至坏死等炎性症状的一类疾病。重症胰腺炎是急性胰腺炎的特殊类型,具有病情险恶、并发症高发、病死率高等特点[1-3]。数据显示重症胰腺炎约占据急性胰腺炎的 10 %~20 %左右,20 世纪 80 年代前,该病患者死亡率趋近 100 %,直至近 10 年,随着重症胰腺炎治疗技术的发展,治愈率才有所提升,但死亡率仍维持于 17 %左右。临床实践表明

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70 %~80 %的重症胰腺炎与胆道疾病、酗酒或暴饮暴食等因素相关[4-6]。

当前，临床上对重症胰腺炎的治疗手段包括对症治疗、内科治疗、外科治疗等，连续血液净化是重症胰腺炎常用治疗手段之一，旨在快速降低机体炎症因子水平，抑制病情发展并保护患者肾脏[7,8]。肠内营养支持是近些年才被应用于重症胰腺炎患者的营养支持手段[9]，关于该治疗方式是否适用于重症胰腺炎患者在临床上尚存在一定争议。本研究结果表明连续血液净化联合肠内营养支持对重症胰腺炎患者具有较好的治疗效果，能够显著加快重症胰腺炎患者转归，改善患者肾损伤及机体炎症状态，具有较高的应用价值，现详述如下。

1 资料与方法

1.1 研究对象

选择 2018 年 1 月至 2019 年 12 月于我院接受治疗的 82 例重症胰腺炎患者为研究对象，按照其选择的治疗方式不同将其分为研究组(49 例)与对照组(33 例)。

纳入标准：(1) 所有患者均符合 2007 年中华医学会外科学分会胰腺外科学组制定的《重症胰腺炎诊治指南》[10]中重症胰腺炎的诊断标准且出现腹痛、恶心呕吐、实验室指标改变等典型临床症状；(2)患者发病至治疗时间 <48 h；(3)患者意识清醒，能够配合进行调研；(4)年龄位于 20~65 岁之间；(5)患者及其家属对本次调研过程、方法、原理清楚明白并签署知情同意书；(6)调研经医院伦理学会批准实施。

排除标准：(1) 合并其他器质性疾病如冠心病、肾衰竭等；(2)合并精神疾患者；(3)妊娠或哺乳期妇女；(4)于院内留观时间 <48 h 的患者；(5)重症胰腺炎并发症需实施手术者，如胰腺感染性坏死或存在胆道梗阻者；(6)对肠内营养成分过敏者。

1.2 治疗方法

两组患者入院后均接受相同的一般治疗，包括禁食、镇痛、纠正水电解质酸碱失衡、充分氧供、抗生素防治感染等，同时对照组患者实施连续性血液净化治疗，具体方式如下：对患者实施麻醉后进行股静脉或颈内静脉置管，建立血管通路，采用费森尤斯 4008s 型血液透析机对患者实施连续血液净化，透析器选择 F60，设置血流量为 250 mL/min，置换液流速设置为 4~6 L/h，同时依据患者实际情况选择是否实施无肝透析治疗，行连续血液净化 24~72 h 后依据患者实际情况实施血液透析滤过治疗，首次透析时间设置为 24 h 或 48 h，待患者病情稳定后改为日间透析 12 h，共进行 72 h；研究组患者在对照组基础上加用肠内营养治疗，具体方式如下：采取鼻肠管的方式当日予以患者葡萄糖氯化钠 500 mL 经鼻肠管缓慢注入，对患者肠道形成初步刺激，第 2 日予以百普力 30 mL/h，连续喂养 24 h，设置能量目标量为(20±2)kcal/kg，设置每日氮量为 0.2 g/kg；两组患者监测时间点分别为入院时和干预 72 h 后。

1.3 观察指标及评测标准

1.3.1 **一般临床指标** 分别记录两组患者住院时间、治疗中感染发生率、腹痛缓解时间以及死亡率，并实施组间对比。

1.3.2 **肾功能指标** 分别采集两组患者入院时以及治疗 72 h 后的血样，离心后留血清，并对 BUN 和 SCr 的水平进行检测，而后实施组间对比以及组内前后水平对比。

1.3.3 **炎症因子指标** 分别采集两组患者入院时以及治疗 72 h 后的血样，离心后留血清，采用酶联免疫吸附法(Enzyme-linked immunosorbent assay，ELISA)对两组患者治疗前及治疗 72 h 的 CRP、IL-6、TNF-α 水平进行检测，并实施组间对比以及组内前后水平对比，炎症因子水平检测严格按照说明书实施，每个指标检测 3 次取平均值。

1.3.4 **治疗前后 APACHE II 评分对比** 采用 APACHE II 量表评估两组患者治疗前及治疗 72 h 的评分，该量表能够对患者的体温、心率、呼吸、氧合等指标实施监测，共分为急性生理学评分、年龄评分及慢性健康评分 3 部分，最高分为 71 分，15 分以上即被归为重症，得分越高代表病情越严重[11]。

1.4 统计学方法

使用 SPSS 19.0 对采集的数据实施分析，计数资料以率(%)的形式表示，采用卡方检验，计量资料以($\bar{x}\pm s$)的形式表示，采用 t 检验，以 $P<0.05$ 为差异有统计学意义[12]。

2 结果

2.1 两组一般临床资料对比

两组患者一般临床资料如性别比例、平均年龄、婚姻状况、吸烟史、饮酒史等对比差异不具有统计学意义($P>0.05$)，具有可比性，具体数据如表 1 所示。

表 1 两组患者一般临床资料对比

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

Indicators		Experimental group (n=49)	Control group(n=33)
Men and women		27/22	18/15
Age (years)		49.98±3.09	50.28±2.77
Marital status	Married	40	30
	Unmarried	9	3
Smoking history	Yes	32	23
	No	17	10
Drinking History Yes	Yes	40	29
	No	9	4

2.2 两组患者一般临床指标对比

研究组患者住院时间、感染发生率、腹痛缓解时间均明显低于对照组患者，组间对比差异具有统计学意义(P<0.05)，具体数据如表 2 所示。

表 2 两组患者一般临床指标对比

Table 2 Comparison of the general clinical indicators between the two groups of patients

Groups	n	Hospitalization time (d)	Incidence of infection	Abdominal pain relief time (h)
Experimental group	49	19.78±4.09*	7(14.29)*	34.99±3.09*
Control group	33	22.88±5.22	12(36.36)	41.87±3.22

Note: Compared with the control group, *P<0.05.

2.3 两组患者治疗前后肾功能指标对比

入院时，两组患者 BUN、SCr 水平对比差异不具有统计学意义(P>0.05)；治疗 72 h 后，两组患者上述指标水平均明显下降，对比入院时差异具有统计学意义 (P<0.05)，研究组患者 BUN、SCr 水平低于对照组患者(P<0.05)，具体如表 3 所示。

表 3 两组患者治疗前后肾功能指标对比($\bar{x}\pm s$)

Table 3 Comparison of the renal function indexes between two groups of patients before and after treatment($\bar{x}\pm s$)

Groups	n	BUN(mmol/L)		SCr(μmol/L)	
		On admission	After 72 h of treatment	On admission	After 72 h of treatment
Experimental group	49	46.77±3.87	18.98±2.21*#	833.87±20.77	351.98±21.90*#
Control group	33	46.98±3.08	30.87±2.77*	829.98±22.98	502.78±20.77

Note: Compared with the same group on admission, *P<0.05; compared with the control group at the same time, #P<0.05.

2.4 两组患者治疗前后炎症因子水平对比

入院时，两组患者血清 CRP、IL-6、TNF-α 水平对比差异不具有统计学意义(P>0.05)；治疗 72 h 后，两组患者上述指标水平均较入院时有明显降低，前后对比差异具有统计学意义(P<0.05)，研究组患者上述因子水平低于对照组患者(P<0.05)，具体如表 4 所示。

表 4 两组患者治疗前后炎症因子水平对比($\bar{x}\pm s$)

Table 4 Comparison of the inflammatory factor levels before and after treatment between two groups of patients($\bar{x}\pm s$)

Groups	n	CRP(mg/L)		IL-6(pg/mL)		TNF-α(pg/mL)	
		On admission	After 72 h of treatment	On admission	After 72h of treatment	On admission	After 72h of treatment
Experimental group	49	177.98±20.88	40.71±3.90	140.87±14.98	70.89±18.77	122.89±10.87	60.87±5.33
Control group	33	181.09±17.87	87.98±4.11	138.87±15.01	98.97±6.33	121.77±11.98	87.90±2.09

Note: Compared with the same group on admission, *P<0.05; compared with the control group at the same time, #P<0.05.

2.5 两组患者治疗前后 APACHE II 评分对比

治疗前，两组患者 APACHE II 评分对比差异不具有统计学意义(P>0.05)；治疗 72 h 后研究组患者 APACHE II 评分明显低于对照组患者(P<0.05)，具体如表 5 所示。

表 5 两组患者治疗前后 APACHE II 评分对比

Table 5 Comparison of the APACHE II scores before and after treatment between two groups of patients

Groups	Case	Before treatment	After 72h of treatment
Experimental group	49	18.77±2.09	10.88±2.89
Control group	33	18.69±2.51	15.86±2.76

Note: Compared with the same group before treatment, *P<0.05; compared with the control group at the same time, #P<0.05.

3 讨论

重症胰腺炎是临床上常见的急腹症之一，具有起病凶险、病情发展快等特点，患者多合并出现脏器功能障碍，或出现坏死、脓肿或假性囊肿等局部并发症，病死率较高[13,14]。随着近些年居民饮食结构以及疾病谱的变化，重症胰腺炎的发病率有逐年递增的趋势，已成为急腹症严重热点之一。目前，重症胰腺炎尚缺乏特异性治疗手段，在该病的病情进展中存在 2 个死亡危险期，一是在胰酶被大范围激活的疾病早期，此时患者机体会释放大量的炎症因子，诱发强烈的炎性反应，该时期约维持 1 周左右，二是炎症因子、细胞内毒素等导致患者肠粘膜屏障破坏进而导致胰周和全身感染，此时多器官功能障碍综合征出现几率较高，会对患者造成二次威胁，数据显示多器官功能障碍综合征是导致重症胰腺炎患者死亡主要原因，约占死亡例数的

20 %~40 %左右[15-18]。

目前研究表明炎性病变在重症胰腺炎的发生发展中发挥着重要作用,重症胰腺炎患者多数会经历全身炎症反应 - 代偿性抗炎反应和混合性拮抗反应,而过量的炎症因子释放入血是诱发多器官功能障碍综合征的重要原因之一[19,20]。还有研究指出炎症因子可使机体产生大量的氧自由基,炎性细胞的过度活跃会产生连锁反应,加重患者病情,这也是引发全身炎性反应和器官功能障碍的物质基础,因而目前临床上已开始重视从缓解炎性反应这一路径对重症胰腺炎患者实施干预[22,23]。连续性血液净化技术又被称为连续性肾脏替代技术,该技术最早始于上世纪末,应用之初是为了提高重症肾衰患者的治疗效果,随着对该技术的研究深入逐渐将其应用于其他多种临床治疗中[24,25]。本研究结果显示对重症胰腺炎患者实施连续性血液净化可以降低其机体内 BUN、SCr、CRP、IL-6、TNF-α 水平,同时还能够降低患者的 APACHE Ⅱ 评分,与国内学者龚芳[26]和国外学者 Putzu A[27]等的研究结果一致,提示连续性血液净化可有效减轻患者的炎症反应,有利于重症胰腺炎患者的预后得到改善。分析主要原因可能是提示连续性血液净化可有效降低患者的炎症反应,经合成膜纤维的渗透、对流、吸附等方式减少炎症介质浓度,进而调节炎症介质水平,有利于重症胰腺炎患者的炎症反应及预后得到改善。

近些年,营养支持对重症胰腺炎患者病情影响的越来越受重视,有多项研究指出[28]过度消耗营养不良、持续炎症状态以及免疫抑制是重症胰腺炎患者的典型临床特征,约有 30 %-50 %的胰腺炎患者住院期间存在营养不良,重症胰腺炎患者该数据可高达 88 %[29,30]。肠内营养治疗是当前临床上常用的营养支持方式,本研究显示在连续性血液净化的基础上加用肠内营养治疗可以显著降低重症胰腺炎住院时间、腹痛缓解时间以及感染发生率,同时经实验室检测可显示联合治疗对降低患者 BUN、SCr、CRP、IL-6、TNF-α 水平也有较好的效果。重症胰腺炎患者治疗原则多以 " 胰腺休息理论 " 为基础,施行禁食水、全肠外营养理念,长期禁食水虽然能够减少食物对胰腺的刺激,但长期禁食水会使患者的肠道黏膜缺乏刺激,导致肠道黏膜更新能力下降、消化液杀菌能力降低,这样会增加肠道菌群失调、肠道黏膜过度凋亡和肠黏膜屏障损伤的几率,最终导致肠道衰竭[31,32]。本研究中,研究组患者通过加用肠内营养支持,切实降低了感染发生率以及患者炎症状态,分析其原因为适量的肠内营养刺激使患者的胃肠保持蠕动,避免了肠道功能因长期停滞而出现细菌移位和肠黏膜坏死的可能性,此外肠内营养还能够促进肠黏膜细胞增生,对维护肠黏膜屏障功能具有积极作用[28]。目前,国内外对于肠内营养支持联合连续性血液净化对重症胰腺炎患者的治疗在临床上尚存在一定争议,本研究进行创新性的应用,取得了一定的效果,为后期治疗重症胰腺炎提供了思路。

总之,连续血液净化联合肠内营养支持对重症胰腺炎患者具有较好的治疗效果,能够显著加快重症胰腺炎患者转归,改善患者肾损伤及机体炎症状态。但本研究也存在一定的不足,如样本量少,结果可能存在一定的偏倚,没有对患者治疗期间的不良反应和远期效果进行观察,在后续研究中需要进一步的深入探讨。

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