

doi: 10.13241/j.cnki.pmb.2017.26.024

连续性血液净化治疗对急性胰腺炎的临床效果和预后状况分析

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摘要 目的:探讨连续性血液净化(CBP)对急性胰腺炎(AP)的治疗效果及预后的影响。**方法:**选取2010年1月至2016年12月间我院1200例AP患者作为研究对象,按照随机数字表法分为常规治疗组及CBP治疗组,每组600例。常规治疗组接受常规药物治疗,CBP治疗组在常用药物治疗的基础上联合应用CBP治疗。对比治疗后两组患者临床症状消失时间以及治疗前、治疗后72h炎症因子水平变化情况和肠道功能变化情况,并对比两组治疗后7d的死亡率。**结果:**CBP治疗组治疗后的腹痛消失时间、腹胀消失时间及腹部压痛消失时间均低于常规治疗组($P<0.05$)。两组治疗前内毒素、C反应蛋白(CRP)、淀粉酶(AMS)、二胺氧化酶及丙二醛比较无统计学差异($P>0.05$);治疗后72h,内毒素、CRP、AMS、二胺氧化酶及丙二醛水平平均较治疗前降低,且CBP治疗组低于常规治疗组($P<0.05$)。治疗后7d CBP治疗组死亡率低于常规治疗组,差异具有统计学意义($P<0.05$)。**结论:**CBP可有效的提高AP的临床治疗效果,并改善患者的临床预后。

关键词:连续性血液净化;急性胰腺炎;治疗效果;预后

中图分类号:R576; R459.5 文献标识码:A 文章编号:1673-6273(2017)26-5111-04

Clinical Effect and Prognosis of Continuous Blood Purification in Patients with Acute Pancreatitis

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ABSTRACT Objective: To investigate the therapeutic effect of continuous blood purification (CBP) on acute pancreatitis (AP) and its influence on prognosis. **Methods:** 200 patients with AP in our hospital from January 2010 to December 2016 were selected as the subjects, and they were divided into conventional treatment group and CBP treatment group according to the random number table method, 600 cases in each group. The conventional treatment group was received conventional drug therapy, and the CBP treatment group was treated with CBP on the basis of commonly used drugs. The disappeared time of clinical symptoms after treatment and the changes of inflammatory factors and the changes of intestinal function before and 72 h after treatment were compared between the two groups, the mortality rate was compared between the two groups at 7 d after treatment. **Results:** Abdominal pain disappeared time, abdominal distension disappeared time and abdominal tenderness disappeared time in CBP treatment group after treatment were lower than the conventional treatment group ($P<0.05$). There was no significant difference in the levels of endotoxin, C reactive protein (CRP), amylase (AMS), two amine oxidase and malondialdehyde before treatment in the two groups ($P>0.05$). At 72 h after treatment, endotoxin, CRP, AMS, two amine oxidase and malondialdehyde levels were lower than those before treatment, and the CBP treatment group was lower than the conventional treatment group ($P<0.05$). The mortality rate of CBP treatment group was lower than that of conventional treatment group at 7 d after treatment, the difference was statistically significant ($P<0.05$). **Conclusion:** CBP can effectively improve the clinical therapeutic effect of AP, and improve the clinical prognosis of patients.

Key words: Continuous blood purification; Acute pancreatitis; Therapeutic effect; Prognosis

Chinese Library Classification(CLC): R576; R459.5 **Document code:** A

Article ID: 1673-6273(2017)26-5111-04

前言

急性胰腺炎(Acute pancreatitis, AP)是临床上较为常见的消化系统疾病,相关研究显示AP的发病率可达134-178/10万人以上,且近年来呈现出了明显的上升趋势^[1]。AP的发生发展,可以导致患者多器官功能衰竭的发生,病死率明显上升^[2]。通过抑制胰酶分泌、降低胃肠内压力及营养支持等治疗,可以显著

改善AP患者的消化系统增殖,降低胰酶持续性释放导致的腹腔内器官的损伤。但相关研究显示既有的临床综合性治疗措施的总体有效率不足35%,治疗后患者的心肺功能衰竭、肾水肿出血及肝功能失代偿等的发生率仍然维持在较高的水平^[3-4]。连续性血液净化(Continuous blood purification, CBP)可以通过清除体内多余的蛋白酶、脂肪酶或者炎症介质等,进而减轻病情的持续性进展,改善临床预后^[5-7]。为了进一步指导临床上AP的综合治疗,本研究将1200例AP患者分为常规治疗组及CBP治疗组,探讨CBP联合常规药物治疗AP的临床效果。

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(收稿日期:2017-04-16 接受日期:2017-05-12)

1 资料与方法

1.1 一般资料

选取 2010 年 1 月至 2016 年 12 月间我院 1200 例 AP 患者作为研究对象,纳入标准:①符合中华医学会外科学会制定的诊断标准^[6];②本人或直系亲属签署本研究知情同意书;③本研究治疗方案经我院伦理委员会批准。排除标准:①存在 CBP 治疗禁忌症者;②对本研究治疗药物过敏者;③合并其他急慢性感染者;④已接受药物或手术治疗者;⑤存在严重心肺疾病者;⑥存在意识障碍者。应用随机数字表法将患者分为常规治疗组及 CBP 治疗组,每组 600 例。常规治疗组接受常规药物治疗, CBP 治疗组在常用药物治疗的基础上联合应用 CBP 治疗。常规治疗组,男 368 例,女 232 例;年龄 43-60 岁,平均(52.18±6.11)岁;病程 6-16h,平均(11.21±3.37)h;胆源性急性胰腺炎 305 例,高脂血症急性胰腺炎 215 例,酒精性急性胰腺炎 50 例,特发性胰腺炎 30 例。CBP 治疗组,男 371 例,女 229 例;年龄 44-59 岁,平均(51.85±5.83)岁;病程 6-15h,平均(11.15±3.12)h;胆源性急性胰腺炎 310 例,高脂血症急性胰腺炎 222 例,酒精性急性胰腺炎 58 例,特发性胰腺炎 10 例。两组间性别、年龄、病程及疾病类型资料比较,未见统计学差异($P>0.05$),具可比性。

1.2 治疗方法

常规治疗组:持续胃肠减压,防止呕吐和误吸,给予全胃肠动力药减轻腹胀;经静脉补充液体、电解质和热量,以维持循环稳定和水电解质平衡;发病早期可对症给予止痛药,但宜同时给解痉药,禁用吗啡;给予胃管减压、H₂受体阻滞剂、抗胆碱能药、生长抑素等抑制胰酶的分泌。

CBP 治疗组在常规治疗组的基础上联合进行 CBP 治疗:采用 selding 中心静脉技术植入静脉导管,可以采取股静脉或者颈内静脉,采用德国西门子公司生产的 BAXTER 25 型机器进行血液净化,置换液体为南京凯基生物科技有限公司生产,采用前稀释的方式进行置换,速度控制在 200-250 mL/min,连续置换 48 h,滤过膜为 AN29(购自罗氏公司),面积为 1.0 m²,每 24 h 更换一次,连续治疗 7 d。

1.3 观察指标

于患者接受治疗后,统计并对比患者腹痛症状消失、腹胀症状消失及腹部压痛消失的时间。同时于患者治疗前及接受治疗后 72 h,抽取患者空腹肘静脉血,进行血清炎症因子及肠粘膜屏障功能因子进行检测。所观察的血清炎症因子包括内毒素、C 反应蛋白(C reactive protein, CRP)、淀粉酶(Amylase, AMS),其中内毒素检测方法为动态浊度法,CRP 检测方法为免疫比浊法,AMS 检测方法为酶速率法;肠粘膜屏障功能因子包括二胺氧化酶及丙二醛,二胺氧化酶检测方法为双抗体夹心法,丙二醛检测方法为硫代巴比妥酸法。此外,对所有患者治疗后 7 d 的死亡率进行统计和对比。

1.4 统计学方法

应用 SPSS 19.0 软件进行数据分析,计量资料应用($\bar{x} \pm s$)表示,以 t 检验分析,计数资料应用(%)表示,以 χ^2 检验分析。所得统计学结果中 $P<0.05$ 为具统计学差异。

2 结果

2.1 两组症状消失时间比较

CBP 治疗组接受治疗后的腹痛消失时间、腹胀消失时间及腹部压痛消失时间均低于常规治疗组($P<0.05$)。

表 1 两组症状缓解时间比较($\bar{x} \pm s, d$)

Table 1 Comparison of symptom relief time between the two groups ($\bar{x} \pm s, d$)

Groups	Abdominal pain disappeared time	Abdominal distention disappeared time	Abdominal tenderness disappeared time
Conventional treatment group (n=600)	5.36±1.26	5.26±1.07	6.25±1.16
CBP treatment group(n=600)	4.03±1.02 ^a	3.52±1.02 ^a	5.12±1.09 ^a
t	20.096	28.831	17.389
P	0.000	0.000	0.000

2.2 两组炎症因子变化情况

两组间治疗前内毒素、CRP 及 AMS 比较,无统计学差异

($P>0.05$);治疗后 72 h,两组内毒素、CRP 及 AMS 均较治疗前降低,且 CBP 治疗组低于常规治疗组($P<0.05$)。

表 2 两组炎症因子变化情况($\bar{x} \pm s$)

Table 2 The change of inflammatory factors in the two groups ($\bar{x} \pm s$)

Groups	Endotoxin (ng/L)		CRP (mg/L)		AMS (IU/L)	
	Before treatment	72h after treatment	Before treatment	72h after treatment	Before treatment	72h after treatment
Conventional treatment group(n=600)	1.21±0.33	0.53±0.22 ^a	155.39±10.63	53.37±6.21 ^a	555.28±100.23	133.92±28.31 ^a
CBP treatment group(n=600)	1.19±0.31	0.26±0.23 ^a	156.28±10.07	23.63±5.81 ^a	553.09±109.87	53.26±17.21 ^a
t	1.082	20.779	-1.488	85.730	0.360	59.635
P	0.279	0.000	0.136	0.000	0.718	0.000

Note: compared with before treatment, ^a $P<0.05$.

2.3 两组肠粘膜屏障功能比较

治疗前两组间二胺氧化酶及丙二醛比较,无统计学差异

($P>0.05$); 治疗后 72 h, 两组二胺氧化酶及丙二醛均较治疗前降低, 且 CBP 治疗组低于常规治疗组 ($P<0.05$)。

表 3 两组肠粘膜屏障功能比较($\bar{x}\pm s$)Table 3 Comparison of intestinal mucosal barrier function between the two groups($\bar{x}\pm s$)

Groups	Two amine oxidase(umol/mL)		Malondialdehyde(nmol/mL)	
	Before treatment	72h after treatment	Before treatment	72h after treatment
Conventional treatment group(n=600)	1.66± 0.65	1.35± 0.53 ^a	3.65± 1.02	2.88± 0.71 ^a
CBP treatment group (n=600)	1.71± 0.41	1.21± 0.39 ^a	3.63± 0.96	2.39± 0.63 ^a
t	-1.593	5.211	0.349	12.644
P	0.111	0.025	0.726	0.019

Note: compared with before treatment, ^a $P<0.05$.

2.4 两组治疗死亡情况比较

治疗后 7 d 常规治疗组死亡率为 11.00%, CBP 治疗组死

亡率为 3.50%, CBP 治疗组死亡率低于常规治疗组 ($P<0.05$)。

表 4 两组治疗死亡情况比较[n(%)]

Table 4 Comparison of the mortality rate between the two groups [n (%)]

Groups	Acute renal failure	Septic shock	Sepsis	Total mortality rate
Conventional treatment group(n=600)	20(3.33)	36(6.00)	10(1.67)	66(11.00)
CBP treatment group (n=600)	6(1.00)	10(1.67)	5(0.83)	21(3.50)
χ^2				25.095
P				0.000

3 讨论

过度饮酒、胆道系统疾病或者短时间内高蛋白饮食等,均可以促进 AP 的发生发展,特别是在具有胆道系统结石的患者中,AP 的发病率更高,可较普通人群上升 3-4 倍^[9,10]。常规药物治疗虽然可以通过抑制消化酶的分泌减轻持续性胰酶释放导致的肠道黏膜损伤,以及抑制自身炎症因子激活导致的肝脏实质细胞膜完整性的破坏^[11],但一项汇集了 110 例样本量的临床回顾性分析研究显示,包括生长抑素联合灌肠、胃肠减压等综合性治疗后,AP 患者的病死率仍然可达 5%以上^[11-13]。炎症因子的激活,如 IL-6 或者 IL-10 的上调,影响到了氧自由基的氧化应激反应,肾小管、肝小叶结构等明显受到破坏^[14,15];酸碱代谢平衡的紊乱,可以通过影响细胞能量代谢环境的改变,促进代谢性酸中毒发生,高碳酸血症导致的呼吸中枢暂停等严重代谢性脑病的发生^[16,17];AP 可合并严重的毒血症,内源性代谢导致的代谢毒素的上升,激活 rock 炎症因子通路,心肌细胞及冠状动脉血管内皮细胞的凋亡率上升^[18,19]。CBP 是连续性的血液净化技术,在营养支持治疗的同时,具有纠正酸碱代谢平衡紊乱的功能,纠正低钾血症、促进高磷的代谢或者排出,并可以促进细胞炎症因子或者内毒素等代谢废物的清除,从而改善病情^[20-22]。已有的研究探讨了 CBP 治疗 AP 的临床效果,认为 CBP 可以提高其治疗总体有效率,降低患者多器官功能衰竭的发生

率,但缺乏对于治疗后肠粘膜屏障功能指标的分析。

本研究发现,CBP 联合常规药物等治疗 AP 后,观察组患者的腹部症状的消失较为明显,在短时间内即可明显改善,且其症状消失时间明显短于对照组,差异具有统计学意义。从机制上考虑,CBP 治疗 AP 后对于患者腹胀、腹痛等的改善可能与下列因素有关:(1)CBP 清除了内毒素,避免内毒素对于腹膜的持续性刺激导致的腹痛的发生;(2)CBP 对于胰淀粉酶的清除,可以降低自身性免疫反应激活导致的自身胰腺组织消化引起的疼痛感。张远超等^[23]研究者通过前瞻性分析了 63 例样本量的重度 AP 的临床资料,发现 CBP 联合生长抑素治疗 AP 后,患者腹胀在 3d 内即可明显改善,这与本研究的结论较为相似。内毒素、CRP 及 AMS 可激活单核细胞、巨噬细胞及肥大细胞,促进其对于肠道黏膜的浸润,加剧病情进展^[24]。本研究中治疗后的观察组患者的血清相关炎症因子明显下降,低于对照组,一方面考虑与 CBP 的机械性清除作用有关,另一方面考虑可能与 CBP 治疗后腹膜反应减轻、自身氧化应激损伤程度抑制等有关^[25,26]。二胺氧化酶及丙二醛是反应肠道黏膜屏障的指标,二胺氧化酶及丙二醛的上升促进肠道柱状上皮细胞极基底细胞膜的线粒体代谢障碍,促进 ATP 依赖性的细胞膜能量运输、蛋白转运等障碍,影响到肠道功能,治疗后 CBP 治疗组患者的相关肠道功能指标下降程度较高,肠道功能达到了明显的保护^[27,28]。同时也可以观察到治疗后 7 d CBP 治疗组患者的死

亡率较低,主要死因为肾功能衰竭或者感染性疾病的发生,值得注意的是临床上在实际 CBP 治疗的过程中,需动态观察患者的尿常规中性粒细胞或者急性炎症反应蛋白等指标,评估感染或者肾功能失代偿风险^[29,30]。

综上所述,CBP 可有效的提高 AP 的临床治疗效果,改善腹部症状、降低病死率,其机制可能与抑制炎症因子的表达、促进体内代谢毒素的排出等有关。

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