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保留灌肠清胰汤联合 ERCP 治疗急性胆源性胰腺炎的疗效及机制探讨 *

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摘要 目的:探讨保留灌肠清胰汤联合内镜逆行胰胆管造影术(endoscopic retrograde pancreatic cholangiography, ERCP)治疗急性胆源性胰腺炎的临床疗效及作用机制。**方法:**选择 2015 年 1 月~2017 年 12 月我院收治的 97 例胆源性胰腺炎患者为研究对象,根据治疗方法不同,将其分为对照组(ERCP 组,46 例)及观察组(保留灌肠清胰汤联合 ERCP 组,53 例)。观察和比较两组的中医临床疗效,治疗前后 7 天的肿瘤坏死因子- α (Tumor necrosis factor- α , TNF- α)、C 反应蛋白(c-reactive protein, CRP)、白细胞介素-6(IL-6)、白细胞介素-8(IL-8)、白细胞介素-10(IL-10)水平及治疗前、治疗后 12 h、24 h、3 d 的血清淀粉酶水平的变化,腹痛缓解时间、平均住院时间、平均住院费用。**结果:**治疗后,观察组的痊愈、显效比例明显高于对照组($P<0.05$)。两组治疗后的血清 TNF- α 、CRP、IL-6、IL-8、IL-10 水平均显著低于治疗前,且观察组的血清 TNF- α 、CRP、IL-6、IL-8 水平均明显低于对照组(P 均 <0.05);两组的平均住院费用对比差异无统计学意义($P>0.05$);观察组的腹痛缓解时间、平均住院时间明显低于对照组($P<0.05$)。与治疗前相比,两组治疗后 12 h、24 h、3 d 时的血清淀粉酶水平均显著降低,且观察组治疗后 12 h、24 h 时的血清淀粉酶水平均明显低于对照组(P 均 <0.05)。**结论:**保留灌肠清胰汤联合 ERCP 治疗可显著提高急性胆源性胰腺炎的治疗痊愈率及有效率,其作用机制可能与降低患者血清 TNF- α 、CRP、IL-6、IL-8 及淀粉酶水平有关。

关键词:保留灌肠;清胰汤;ERCP;急性胆源性胰腺炎;临床疗效;作用机制

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Clinical Efficacy and Mechanism of Action of Retention Enema Clear Pancreas Soup Combined with ERCP in the Treatment of Acute Cholinergic Pancreatitis*

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ABSTRACT Objective: To investigate the clinical efficacy and mechanism of action of retention enema Qing Yi Decoction combined with ERCP in the treatment of acute cholinergic pancreatitis. **Methods:** 97 cases of patients with acute cholinergic pancreatitis from Jan. 2015 to Dec. 2017 in our hospital were selected and divided into the control group (ERCP, 46 cases) and the observation group (retention enema Qing Yi Decoction combined with ERCP, 53 cases) according to different treatment methods. The clinical efficacy of TCM between the two groups were observed and compared. The levels of serum TNF- α , CRP, IL-6, IL-8, IL-10, amylase, abdominal pain relief time, average hospitalization time and average hospitalization cost were observed and compared before and at 12 h, 24 h, 7 days after treatment. **Results:** After treatment, the cure rate and markedly effective ratio of observation group were significantly higher than those of the control group ($P<0.05$). The levels of serum TNF- α , CRP, IL-6, IL-8 and IL-10 in the two groups were significantly lower than those before treatment, and the levels of serum TNF- α , CRP, IL-6 and IL-8 in the observation group were significantly lower than those in the control group ($P<0.05$); there was no significant difference in the average hospitalization expense between the two groups ($P>0.05$); the abdominal pain relief time and the average hospitalization time in the observation group were significantly lower than those in the control group ($P<0.05$). Compared with those before treatment, the serum amylase levels of both groups at 12 h, 24 h and 3 d after treatment were significantly decreased, and the serum amylase levels of observation group at 12 h and 24 h after treatment were significantly lower than those of the control group ($P<0.05$). **Conclusion:** Retention enema Qing Yi Decoction combined with ERCP treatment could significantly improve the heal and efficacy rate of acute cholinergic pancreatitis, and its mechanism may be related to the reduction of serum TNF- α , CRP, IL-6, IL-8 and amylase levels.

Key words: Retention enema; Qing Yi Decoction; ERCP; Acute cholinergic pancreatitis; Clinical efficacy; Mechanism

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前言

急性胆源性胰腺炎是急性胰腺炎中的一种常见类型,发病人数占急性胰腺炎总数的 40%~60%。在胆源性胰腺炎中,炎症因子、细胞因子会引起胰腺损伤,同时引起急性炎症介质的级联反应,造成全身炎症反应,甚至造成多器官衰竭或全身多器官功能综合征^[4]。外科手术是治疗急性胆源性胰腺炎的一种手段,其中内镜逆行胰胆管造影术(endoscopic retrograde pancreatic cholangiography, ERCP) 是治疗急性胆源性胰腺炎的一种手术方式,具有创伤小、效果好、恢复快等优势,治疗适应性较广,对患者主要脏器功能影响小^[1-3]。虽然内镜介入治疗是治疗胆源性胰腺炎的有效手段,但其仅能解决胆道的致病因素,但是不能立即缓解已经诱发的胆道感染和胰腺炎症^[5,6]。在 ERCP 术后如何行临床治疗,是胆源性胰腺炎治疗的一个重要环节,甚至会影响疾病的转归、预后^[7]。

急性胆源性胰腺炎的主要炎症状为腹痛腹胀,且伴有皮肤巩膜黄染、寒战发热、恶心呕吐、舌黄腻、关、尺脉弦紧,中医辨病为“腹痛”、“胃痛”、“胁痛”、“结胸”、“黄疸”等,其发病机制为湿热内蕴、气滞血瘀、肝胆失疏、不通则痛,因此其治疗应通腑泻热、行气化瘀^[8]。清胰汤主治肝郁气滞为主的肝胆胰腺病,具有疏肝解郁、活血行气、通腑攻下之效,可用于急性胰腺炎的治疗^[9]。我院以保留灌肠清胰汤联合 ERCP 治疗急性胆源性胰腺炎,疗效显著,并探讨了其作用机制,现报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 1 月~2017 年 12 月我院收治的 97 例胆源性胰腺炎患者。纳入标准:符合《中国急性胰腺炎诊治指南》诊断标准,且 CT、MRI 及 MRCP 等检查发现胆道结石及胆总管扩张;同时符合中华中医药学会《急性胰腺炎中医诊疗专家共识意见》中关于肝胆湿热证型的诊断标准;年龄范围为 24~73 岁;于发病 72 h 后入院;患者神志清楚、生命体征相对平稳、配合治疗。排除标准:发病超过 72 h 者;患者神志不清、生命体征不平稳、且不能沟通配合者;对造影剂过敏、上消化道狭窄内镜等存在 ERCP 治疗禁忌症者;合并心脑血管、造血系统、肝、肾等严重原发性疾病者;3 个月内有中药或中成药治疗者;有药物过敏史者;妊娠或哺乳期妇女;其他胰腺疾病者或慢性胰腺

炎急性发作者等。97 例胆源性胰腺炎患者中,男 54 例,女 43 例,平均年龄 52.1 ± 14.3 岁。根据治疗方法不同,将 97 例胆源性胰腺炎患者分为对照组(ERCP 组,46 例)及观察组(清胰汤联合 ERCP 组,53 例),两组一般资料对比差异不显著($P>0.05$),具有可比性。

1.2 治疗方法

对照组行 ERCP 术,选择 OLYPUS JF240 型十二指肠镜,选择 76%泛影葡胺造影剂,使用生理盐水稀释至 30%,由本院操作熟练人员进行检查、操作。术前 6 h、术后 24 h 禁食禁水,术前 15 min 肌注 50 mg 杜冷丁、0.5 mg 阿托品、10 mg 安定,术后常规行鼻胆管引流,同时行抗生素,维持水电解质平衡等处理。

观察组行 ERCP 治疗,同时术后第一天开始给予清胰汤胃管注入治疗及保留灌肠。清胰汤组方:柴胡 15 g、胡连 10 g、黄芩 10 g、木香 10 g、白芍 15 g、延胡索 10 g、芒硝(冲服)10 g、大黄(后下)20 g、赤芍 15 g、丹参 15 g。术后每日以清水煎 200 mL 药液,每天 2 次保留灌肠,100 mL/次,每天至少保留 2 h,直至出院。

1.3 观察指标

(1)两组的中医临床疗效^[10]:中医临床症状治疗 3 天内缓解,治疗 7 天内消失,且血淀粉酶恢复正常为痊愈;治疗 7 天内中医临床症状好转,血淀粉酶恢复正常为显效;治疗 7 天内中医临床症状减轻,血淀粉酶恢复且下降有效;治疗 7 天内中医临床症状、体征无减轻甚至加重,血淀粉酶未降低为无效;(2)两组治疗前后 7 天 TNF- α 、CRP、白细胞介素 IL-6、IL-8、IL-10 水平:采用酶联免疫吸附法检测;(3)两组腹痛缓解时间、平均住院时间及住院费用;(4)两组治疗前、治疗后 12 h、24 h、3 d 的血清淀粉酶水平:采用碘-淀粉比色法进行检测。

1.4 统计学方法

采用 SPSS19.0 软件进行统计学分析,计数资料用 $\bar{x} \pm s$ 表示,组间比较行 t 检验;计量资料用 n 表示,组间比较行卡方检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组中医临床疗效对比

治疗后,观察组痊愈、显效比例均明显高于对照组($P<0.05$),但两组总有效率比较差异无统计学意义($P>0.05$)。

表 1 两组中医临床疗效对比

Table 1 Comparison of the clinical efficacy of traditional Chinese Medicine between two groups

Group	n	Recovery	Obvious effect	Effective	Ineffective	Total Effective Rate
control group	43	37	7	2	0	100
observation group	53	52	1	0	0	100
χ^2	-	8.476	5.726	2.405	0.000	0.000
P	-	0.004	0.017	0.121	1.000	1.000

2.2 两组治疗前后血清 TNF- α 、CRP、IL-6、IL-8、IL-10 水平对比

治疗前,两组血清 TNF- α 、CRP、IL-6、IL-8、IL-10 水平比较

无显著差异;两组治疗后 7 天上述指标均显著低于治疗前,且观察组明显低于对照组(P 均 <0.05)。

表 2 两组治疗前和治疗后 7 天血清 TNF- α 、CRP、IL-6、IL-8、IL-10 水平对比Table 2 Comparison of the serum TNF- α , CRP, IL-6, IL-8 and IL-10 levels before and at 7 days after treatment between two groups

Group	Time	n	TNF- α (ng/L)	CRP(mg/L)	IL-6(ng/L)	IL-8(ng/L)	IL-10(ng/L)
Control group	Before treatment	46	153.6 $\pm$ 24.1	73.9 $\pm$ 19.2	107.8 $\pm$ 21.5	241.3 $\pm$ 63.6	147.9 $\pm$ 22.7
	After treatment	53	55.7 $\pm$ 25.2*	48.6 $\pm$ 15.9*	65.9 $\pm$ 21.3*	114.8 $\pm$ 29.6*	72.9 $\pm$ 15.8*
Observation group	Before treatment	46	154.9 $\pm$ 26.2	72.8 $\pm$ 21.4	108.7 $\pm$ 19.6	243.9 $\pm$ 67.8	142.8 $\pm$ 17.2
	After treatment	53	45.2 $\pm$ 13.0* [#]	22.9 $\pm$ 5.4* [#]	38.6 $\pm$ 12.9* [#]	84.1 $\pm$ 21.9* [#]	73.2 $\pm$ 14.9*

Note: compared with before treatment, *P<0.05; compared with the control group, [#]P<0.05.

2.3 两组的腹痛缓解时间、平均住院时间、平均住院费用对比

痛缓解、平均住院时间明显短于对照组(P<0.05)。

两组的平均住院费用比较无显著差异(P>0.05);观察组腹

表 3 两组的腹痛缓解时间、平均住院时间、平均住院费用对比

Table 3 Comparison of the abdominal pain relief time, average hospitalization time and average hospitalization cost between the two groups

Group	n	Abdominal pain relief time (h)	Average hospitalization time (d)	Average hospitalization cost (yuan)
Observation group	46	13.9 $\pm$ 4.8	9.0 $\pm$ 2.5	34158.9 $\pm$ 7109.6
Control group	53	16.1 $\pm$ 4.9	12.6 $\pm$ 3.2	33295.8 $\pm$ 6451.3
t	-	-2.253	-6.277	0.629
P	-	0.026	<0.001	0.531

2.4 两组治疗前、治疗后 12 h、24 h、3 d 的血清淀粉酶水平比较

低于对照组(P 均 <0.05)。两组治疗前及治疗后 3 d 的血清淀粉

酶水平比较无显著差异(P>0.05)。

酶水平比较无显著差异(P>0.05)。治疗后 12 h、24 h、3 d,两组的血清淀粉酶水平平均较治疗前

酶水平比较无显著差异(P>0.05)。

显著降低,且观察组治疗后 12、24 h 时血清淀粉酶水平平均明显

表 4 两组治疗前、治疗后 12 h、24 h、3 d 的血清淀粉酶水平的变化比较

Table 4 Comparison of the changes of serum amylase between two groups before and at 12 h, 24 h, 3 d after treatment

Group	n	Before treatment	At 12h after treatment	At 24h after treatment	At 3d after treatment
Observation group	46	818.6 $\pm$ 213.6	626.8 $\pm$ 161.9* [#]	532.4 $\pm$ 139.8* [#]	89.9 $\pm$ 18.6*
Control group	53	821.4 $\pm$ 221.8	696.7 $\pm$ 178.9*	621.5 $\pm$ 151.9*	92.7 $\pm$ 25.8*
t	-	-0.064	-2.040	-3.038	-0.625
P	-	0.949	0.044	0.003	0.533

Note: compared with before treatment, *P<0.05; compared with the control group, [#]P<0.05.

3 讨论

急性胆源性胰腺炎是内外科常见的危急症状之一,在发病早期尽快解除胆道梗阻,使胆汁、胰液排泄通畅是治疗急性胆源性胰腺炎的重要方法,同时控制内毒素、炎症因子,减少血小板聚集,改善胰腺微循环,促进胃肠功能快速恢复,防止细菌移位^[11-13]。ERCP 是治疗急性胆源性胰腺炎的重要方法,其可以迅速引流胆汁、解除梗阻,降低胆道的压力,减少高压下胆汁反流,迅速改善患者症状,创伤小,对急性胆源性胰腺炎导致的疼痛、感染有显著优势,但对于由此引起的肠道微生态紊乱、肠麻痹、细菌移位、禁食导致的胃肠粘膜受损有一定局限性。此外,虽然 ERCP 能快速解除梗阻因素,但不易减少已经释放的炎症因子^[14-18]。《中国急性胰腺炎诊治指南》(上海,2013)指出对于急性胆源性胰腺炎,单味、复方制剂等中药制剂在临床实践有效,具有活血化瘀、清热解毒的中药可减少急性胆源性胰腺炎的吸收,防止细菌移位,抑制胰酶活性,改善微循环^[9]。因此,本院选择清胰汤对急性胆源性胰腺炎患者进行治疗,并探究其疗效及

作用机制。

本研究结果显示保留灌肠清胰汤的患者痊愈、显效比例明显高于仅接受 ERCP 的患者,患者血清 TNF- α 、CRP、IL-6、IL-8、IL-10 水平显著降低,分析原因可能主要是由于清胰汤中的黄芩在体外对溶血性链球菌等多种细菌具有抑制作用;大黄可松弛括约肌,抑制胰酶分泌,减轻病变部位的水肿,促进炎症消退;白芍提取物可抑制急性炎症,同时可使细胞免疫功能恢复正常^[20-25]。本研究中,两组治疗后血清 IL-10 水平无显著差异,清胰汤抗炎可能不是通过降低 IL-10 水平来实现。芒硝可促进胃肠蠕动,促进胃肠功能恢复;延胡索、白芍具有平肝止痛、补血养阴的效果;柴胡、木香可以疏肝理气;黄芩具有清热解毒、理气活血、利湿退黄的作用。同时,清胰汤可以促进胰腺组织的再生,联合胰酶抑制剂,可有效提高表皮生长因子、转化生长因子的基因表达,对胰腺的修复、再生有促进作用,从而缩短患者的住院时间^[26-28]。治疗后 12 h、24 h、3 d,两组的血清淀粉酶水平均显著降低,且治疗后 12 h、24 h 时,观察组血清淀粉酶均明显低于对照组,表明清胰汤可显著降低患者术后的血清淀

粉酶水平。使用清胰汤保留灌肠可避免经过上消化道时胃酸及酶对药物的影响,可避免药物刺激胰酶分泌及肝脏的首过效应,而且提高了药物的生物利用度;也可以清洁肠道,减少肠源性细菌移位^[29,30]。此外,清胰汤并未显著增加患者的经济负担。

综上所述,保留灌肠清胰汤联合 ERCP 治疗可显著提高急性胆源性胰腺炎的治疗痊愈率及有效率,其作用机制可能与降低患者血清 TNF- α 、CRP、IL-6、IL-8 及淀粉酶水平有关。

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