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腹腔穿刺引流对胰腺炎患者胰蛋白酶原激活肽、白介素-6 表达的影响 *

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摘要 目的:探讨腹腔穿刺引流对胰腺炎患者胰蛋白酶原激活肽(Trypsinogen activating peptide, TAP)、白介素-6(Interleukin-6, IL-6)表达的影响。**方法:**2017年8月至2019年12月选择在本院诊治的胰腺炎患者64例作为研究对象,根据随机数字表法把患者分为引流组与对照组各32例。对照组给予开腹引流手术治疗,引流组给予超声引导下腹腔穿刺引流治疗,记录不同时间点血清TAP、IL-6表达变化情况。**结果:**治疗后引流组的总有效率为100.0%,显著高于对照组的87.5%($P<0.05$)。引流组的术后住院时间与术中出血量显著少于对照组($P<0.05$),两组手术时间对比无统计学意义($P>0.05$)。引流组术后14d的消化道瘘、腹腔出血、感染、胆漏等并发症发生率为6.3%,显著低于对照组的25.0%($P<0.05$)。两组术后14d的血清TAP、IL-6值低于术前1d,引流组低于对照组,对比差异都有统计学意义($P<0.05$)。**结论:**腹腔穿刺引流治疗胰腺炎患者有利于抑制TAP、IL-6的释放,并不会增加手术难度,且能减少对患者的创伤,降低并发症的发生,从而提高总体治疗效果。

关键词:腹腔穿刺;胰腺炎;胰蛋白酶原激活肽;白介素-6;并发症

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Effect of Abdominal Puncture and Drainage on Expression of Trypsinogen-activating Peptide and Interleukin-6 in Patients with Pancreatitis*

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ABSTRACT Objective: To investigate the effect of peritoneal drainage on the expression of trypsinogen activating peptide (TAP) and interleukin-6 (IL-6) in patients with pancreatitis. **Methods:** From August 2017 to December 2019, 64 cases of patients with pancreatitis diagnosed and treated in our hospital were selected as the research object, and the patients were divided into drainage group and control group of 32 patients in each groups accorded to the random number table method. The control group were given open-drainage surgery, and the drainage group were given ultrasound-guided abdominal puncture and drainage treatment, and the changes of serum TAP and IL-6 expression at different time points were recorded. **Results:** The total effective rates of the drainage group after treatment were 100.0%, which were significantly higher than 87.5% of the control group ($P<0.05$). The postoperative hospital stay and the amount of bleeding in the drainage group were significantly less than those in the control group ($P<0.05$), and there were no statistically significant difference in the operation time compared between the two groups ($P>0.05$). The incidence of complications such as gastrointestinal fistula, abdominal hemorrhage, infection, and bile leakage in the drainage group at 14 days after operation were 6.3 %, significantly lower than that in the control group (25.0 %)($P<0.05$). The serum TAP and IL-6 values at 14 days after operation in the two groups were lower than 1 day before operation, and the drainage group were lower than the control group, and compared the difference were statistically significant ($P<0.05$). **Conclusion:** Peritoneal drainage treatment of pancreatitis patients is beneficial to inhibit the release of TAP and IL-6, it does not increase the difficulty of surgery, and can reduce the trauma to patients and reduce the occurrence of complications, thereby improve the overall treatment effect.

Key words: Abdominal puncture; Pancreatitis; Trypsinogen activating peptide; Interleukin-6; Complications

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前言

胰腺炎是临床中常见的急腹症之一,具有死亡率高、病情重、并发症发生率高、进展快等特点,严重威胁患者的生命^[1,2]。该病是胰腺消化酶被激活后导致胰腺自身消化所引起的化学性炎症,其中 15% 左右的患者可转为重症胰腺炎^[3]。该病的发生机制还不明确,不过涉及的病因包括暴饮暴食、先天性解剖异常、酗酒、高脂血症、胆道系统疾病、先天性解剖异常等^[4-6]。当前对胰腺炎的严重程度及预后的判断尚无理想的标志物,也为临床救治与预后判定带来一定的困难^[7]。胰蛋白酶原激活肽(Trypsinogen activating peptide, TAP)是胰蛋白酶原氨基端的一段短肽,在胰蛋白酶原激活后可进入血液循环,然后随尿被排出体外,可直接反映胰腺炎的病情^[8]。而白介素-6(Interleukin-6, IL-6)浓度的高低与胰腺炎的严重程度及并发症相关,因此,在胰腺炎的早期诊断价值有待提高^[9,10]。手术为胰腺炎的主要治疗方法,治疗原则是胰腺坏死组织清除、开放引流、大流量灌洗,但是对于患者的创伤过大^[11,12]。在影像学实时引导下进行腹

腔穿刺引流符合早期损伤控制的外科理念,具有安全、微创、操作简单等优势^[13,14]。本文具体探讨了腹腔穿刺引流对胰腺炎患者 TAP、IL-6 表达的影响,以明确该方法的应用效果与机制,现总结报道如下。

1 资料与方法

1.1 研究对象

2017 年 8 月至 2019 年 12 月选择在本院诊治的胰腺炎患者 64 例作为研究对象,纳入标准:符合胰腺炎的诊断标准;年龄 25~70 岁;腹腔或盆腔液体积聚 ≥ 100 mL;本院伦理委员会批准了此次研究;发病 24 h 内入院的患者;患者签署了知情同意书。排除标准:继发于胆管感染或药物引起的胰腺炎患者;有免疫缺陷病史或腹部手术史的患者;临床资料缺乏者;自动放弃医学治疗即自动出院或转院的患者;妊娠与哺乳期妇女。

根据随机数字表法把患者分为引流组与对照组各 32 例,两组患者的 RANSON 评分、APACHE II 评分、发病时间等对比差异无统计学意义($P>0.05$),见表 1。

表 1 两组一般资料对比

Table 1 Comparison of two sets of general information

Groups	n	RANSON score (scores)	APACHE II score (scores)	Time of onset (h)	Gender (Male/Female)	Age (years)	BMI (kg/m ²)
Drainage group	32	4.83 $\pm$ 0.32	8.92 $\pm$ 0.19	7.22 $\pm$ 0.52	18/14	55.30 $\pm$ 1.32	23.94 $\pm$ 2.19
Control group	32	4.78 $\pm$ 0.18	8.99 $\pm$ 0.27	7.82 $\pm$ 0.13	16/16	55.10 $\pm$ 3.22	23.11 $\pm$ 1.67

1.2 治疗方法

对照组:给予开腹引流手术治疗,开腹后清除部分坏死组织并进行胃肠减压、抑酸抑酶等综合治疗。

引流组:给予超声引导下腹腔穿刺引流治疗,术前采用超声确定积液区范围,记录穿刺点和穿刺路径。逐层麻醉腹壁,垂直进针入病灶部位,抽取积液,接引流袋并固定。患者积液区域无液体积聚且生命体征稳定后拔除引流管。

1.3 观察指标

(1)疗效标准:一是腹胀、高热、腹部疼痛、恶心呕吐等基本消失;二是上腹部压痛、腹肌紧张等基本消失;三是肝肾功能、生化指标等恢复正常。显效:7 d 之内达到上述标准;有效:7~10 d 之内达到上述标准;无效:超过 10 d 未达到上述标准甚或恶化。总有效率=(显效例数+有效例数)/总例数 $\times 100\%$ 。(2)记录两组术后 14 d 出现的消化道瘘、腹腔出血、感染、胆漏

等并发症情况。(3)记录两组的手术时间、术中出血量、术后住院时间等指标。(4)在术前 1 d 与术后 14 d 抽取静脉血,低温 2000 rpm(离心半径 15 cm)取上层血清,采用酶联免疫法检测血清 TAP、IL-6 含量。

1.4 统计方法

选择 SPSS 19.00 软件对本文数据进行统计分析,计量资料用均数 $\pm$ 标准差表示(对比为 t 检验),计数数据采用百分比表示(对比为卡方 χ^2 检验),统计学有意义的标准为 $P<0.05$ 。

2 结果

2.1 总有效率对比

治疗后引流组的总有效率为 100.0%,对照组的总有效率为 87.5%,经过对比引流组总有效率显著高于对照组($\chi^2=4.267$, $P=0.039$, $P<0.05$),见表 2。

表 2 两组总有效率对比(例,%)

Table 2 Comparison of the total effective rates of the two groups (n,%)

Groups	n	Excellence	Effective	Invalid	Total effective rate
Drainage group	32	30	2	0	32 (100.0)*
Control group	32	24	4	4	28 (87.5)

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

2.2 围手术指标对比

引流组的术后住院时间显著短于对照组($t=87.166$, $P=0.000$),术中出血量显著少于对照组($t=26.144$, $P=0.000$),对比均

有统计学意义($P<0.05$)。两组手术时间对比无统计学意义($P>0.05$),见表 3。

表 3 两组围手术指标对比($\bar{x} \pm s$)

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

Groups	n	Intraoperative blood loss (mL)	Operation time (min)	Postoperative hospital stay (d)
Drainage group	32	45.11 $\pm$ 2.48*	122.93 $\pm$ 11.73	7.20 $\pm$ 0.13*
Control group	32	231.21 $\pm$ 11.82	120.74 $\pm$ 10.32	13.33 $\pm$ 1.32

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

2.3 并发症情况对比

引流组术后 14 d 的消化道瘘 1 例,腹腔出血 0 例,感染 0 例,胆漏 1 例,并发症发生率为 6.3 %,对照组术后 14 d 的消化

道瘘 2 例,腹腔出血 3 例,感染 2 例,胆漏 1 例,并发症发生率为 25.0 %,对比引流组显著低于对照组($\chi^2=4.254, P=0.035, P < 0.05$),见表 4。

表 4 两组术后 14 d 并发症发生情况对比(例,%)

Table 4 Comparison of complications between the two groups after 14 days (n,%)

Groups	n	Gastrointestinal fistula	Abdominal bleeding	Infection	Bile leakage	Total
Drainage group	32	1	0	0	1	2 (6.3)*
Control group	32	2	3	2	1	8 (25.0)

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

2.4 血清 TAP、IL-6 表达变化对比

两组术前 1 d 的血清 TAP、IL-6 值对比均无统计学意义($P > 0.05$); 两组术后 14 d 的血清 TAP、IL-6 值低于术前 1 d,且

引流组低于对照组,对比差异都有统计学意义($P < 0.05$),见表 5。

表 5 两组手术前后血清 TAP、IL-6 表达变化对比($\bar{x} \pm s$)

Table 5 Comparison of expression changes of serum TAP and IL-6 between two groups before and after operation ($\bar{x} \pm s$)

Groups	n	TAP (mmol/L)		IL-6 (pg/L)	
		1 d before operation	14 d postoperatively	1 d before operation	14 d postoperatively
Drainage group	32	12.42 $\pm$ 1.33	2.78 $\pm$ 0.14**	104.22 $\pm$ 12.33	12.89 $\pm$ 1.00**
Control group	32	12.87 $\pm$ 1.03	7.88 $\pm$ 0.13*	105.92 $\pm$ 8.11	25.86 $\pm$ 2.11*

Note: Compared with 1 d before operation, * $P < 0.05$; compared with the control group, ** $P < 0.05$.

3 讨论

胰腺炎是一种起病急、病情重、进展快的常见急腹症,常表现为胰腺坏死、全身炎症反应,严重者甚或出现多器官功能障碍^[15]。特别是当前很多患者伴随有各种基础疾病,使得炎症递质大量释放,可引发瀑布效应加重全身应激反应,导致严重预后的发生^[16]。传统治疗胰腺炎的方法是在开腹条件下清除胰腺坏死组织,然后进行引流,具有手术成功率高、操作简单方便等特点,但是对于患者的创伤比较大,术后并发症也比较多^[17]。当前微创技术发展迅速,并在诸多领域广泛应用,这也为微创治疗胰腺炎创造了条件^[18]。超声引导下腹腔穿刺引流并增加窦道冲洗的方法,可使脱落的坏死组织逐步清除,能提高引流效果^[19]。并且该方法在术中不强求清创,本着“损伤控制”的原则,在减少清除的坏死组织的同时,减少血管暴露时间,可降低术后感染的风险。本研究显示治疗后引流组的总有效率为 100.0 %,显著高于对照组的 87.5 %;引流组的术后住院时间与术中出血量显著少于对照组,两组手术时间对比无统计学意义,与罗文婷等^[20]学者的研究类似,重症急性胰腺炎患者先经

过腹腔穿刺引流治疗,而后超声引导经皮腹膜后穿刺置管引流,治疗效果显著高于超声引导经皮腹膜后穿刺置管引流术,表明超声引导下腹腔穿刺引流并不会增加手术难度,且能减少对患者的创伤,减少器官系统的衰竭,提高临床疗效。从机制上分析,超声引导下腹腔穿刺引流可有效并充分处理坏死组织,缓解局部炎性积液形成的压力对积液周围组织的损伤侵袭,有利于新生肉芽组织生长和修复周围组织^[21,22]。同时苏江林^[23]等学者的研究发现腹腔引流穿刺时机对重症急性胰腺炎患者预后也有重要的影响,发现 48 h 内穿刺引流是腹腔穿刺引流治疗伴有大量腹腔积液的重症急性胰腺炎患者的最佳时间窗。

胰腺炎患者多伴随有血管内液及炎症介质的大量释放,部分毛细血管壁渗漏至腹腔,形成腹水,导致患者出现持续发热、腹内压升高等临床表现^[24]。手术为胰腺炎早期治疗的金标准,可以清除游离腹腔积液中的有毒物质,但是不利于患者术后康复。超声引导下腹腔穿刺引流为进一步满足临床诊治需要而发展起来的微创新技术,是在超声监视下完成各种手术操作,能达到与外科手术相同的效果^[25,26]。本研究显示引流组术后 14 d 的消化道瘘、腹腔出血、感染、胆漏等并发症发生率为 6.3 %,显

著低于对照组的 25.0%,与张德梁^[27]的研究类似,该学者分析了经皮腹腔穿刺引流术治疗重症急性胰腺炎的临床疗效,发现经皮腹腔穿刺引流术治疗重症急性胰腺炎患者的并发症总发生率为 6.67%,显著低于常规开腹引流术治疗,表明该方法的应用能减少术后并发症的发生。分析其原因主要在于该方法可以改善患者的器官功能状况,有利于阻止其他系统器官功能的进一步损害,从而促进患者术后康复,减少并发症的发生率。

胰腺炎为胰腺消化酶被激活后导致胰腺自身消化所引起的炎症,其中胰腺组织受胰蛋白酶的自身消化作用是该病发生的重要因素^[28,29]。TAP 是胰蛋白酶原氨基末端的激活肽,其生物学特性及其在胰腺炎发病、诊断及预后中的作用受到了广泛关注^[30]。正常情况下胰液内的胰蛋白酶原无活性,当胰腺在各种致病因素作用下,致使酶原在细胞内活化,然后被坏死溶解,为此测定 TAP 可直接反映胰腺的受损程度^[31,32]。胰腺炎的发病可导致腺泡细胞受损,使得一些炎症细胞释放大量促炎细胞因子(如 IL-6 等),后者可损伤胰腺星形细胞,从而导致胰腺炎的发生^[33,34]。本研究显示两组术后 14 d 的血清 TAP、IL-6 值低于术前 1 d,引流组低于对照组,与王东和^[35]等学者的研究类似,发现经过腹腔穿刺引流术治疗重症胰腺炎患者,炎症因子指标 IL-6 水平均显著降低。血清 TAP 水平超声引导下腹腔穿刺引流中的研究国内还没有相关研究,但是国外 Yasuda H 等^[36]学者研究发现 TAP 是急性胰腺炎中胰腺外炎症的有用标志物,在胰腺炎患者中,TAP 的水平显着升高,治疗后会降低。表明超声引导下腹腔穿刺引流的应用有利于抑制 TAP、IL-6 的表达与释放。本研究也存在一定不足,样本数量较少,且没有进行动态观察与分析,将在后续研究中深入探讨。

总之,腹腔穿刺引流治疗胰腺炎患者有利于抑制 TAP、IL-6 的释放,并不会增加手术难度,且能减少对患者的创伤,降低并发症的发生,从而提高总体治疗效果。

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