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吗啉美辛联合生长抑素对 ERCP 术后胰腺炎的预防作用*

黎 涛¹ 赵 平¹ 汤国彬¹ 王彩桦¹ 周丽梅²

(1 四川省广元市中心医院 消化内科 四川 广元 628000; 2 成都大学附属医院 消化科 四川 成都 610041)

摘要 目的:研究吗啉美辛联合生长抑素对内镜逆行胰胆管造影(ERCP)术后胰腺炎的预防作用及对血清淀粉酶的影响。**方法:**选取2015年7月至2016年6月在我院行ERCP术的患者共72例,根据随机数字法分为观察和对照组,每组36例。对照组在术前使用生长抑素完成治疗,观察组在此基础上联合吗啉美辛栓剂完成治疗。分析和比较两组患者ERCP术后5、10、24、48h的血清淀粉酶水平,ERCP术后48h胰腺炎的发生率、肝功能变化情况和临床症状改善情况。**结果:**术前,两组患者血清淀粉酶水平比较无显著差异($P>0.05$),术后5h,两组患者的血清淀粉酶水平较高,和术后5h相比,两组术后10、24、48h的血清淀粉酶水平明显降低($P<0.05$),但观察组各时点血清淀粉酶水平均低于对照组($P<0.05$)。术前,两组患者GGT、ALP、AST水平比较无显著差异($P>0.05$),术后48h,两组患者GGT、ALP、AST水平较术前无明显变化($P>0.05$)。术后48h,观察组的胰腺炎发生率显著低于对照组[8.33% (3/36) vs. 36.11% (13/36)]($P<0.05$)。观察组的皮肤瘙痒、腹泻、恶心、厌食、感染的减轻率均高于对照组($P<0.05$)。**结论:**吗啉美辛联合生长抑素能有效降低ERCP术后胰腺炎的发生率,降低血清淀粉酶水平。

关键词:吗啉美辛;生长抑素;内镜逆行胰胆管造影术;血清淀粉酶

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Preventive Effect of Indomethacin and Somatostatin on the Pancreatitis after ERCP*

LI Tao¹, ZHAO Ping¹, TANG Guo-bin¹, WANG Cai-hua¹, ZHOU Li-me²

(1 Department of Gastroenterology, Guangyuan Central Hospital, Guangyuan, Sichuan, 628000, China;

2 Department of Gastroenterology, Affiliated Hospital of Chengdu University, Chengdu, Sichuan, 610041, China)

ABSTRACT Objective: To study the effect of indomethacin and somatostatin on the prevention of pancreatitis after endoscopic retrograde cholangiopancreatography (ERCP) and its effect on serum amylase. **Methods:** A total of 72 patients with ERCP were selected from July 2015 to June 2016 in our hospital. According to the random number method, those patients were divided into observation group and control group, 36 cases in each group. The control group was treated with somatostatin before surgery, and the observation group was treated with indomethacin suppository on the basis of control group. The levels of serum amylase were analyzed at 5h, 10h, 24h after operation and 48 hours after operation. The incidence of pancreatitis after ERCP was compared between the two groups. Observe the change of liver function and the improvement of clinical symptoms in both groups. **Results:** Before operation, serum amylase level between the two groups had no difference ($P>0.05$), serum amylase level was higher in the two groups after 5 hours postoperation, and the levels of serum amylase were decreased in the two groups ($P<0.05$), but the observation group was always lower than the control group ($P<0.05$). Before surgery, there was no significant difference in GGT, ALP and AST levels between the two groups ($P>0.05$). At 48 hours after operation, GGT, ALP, and AST levels did not change significantly ($P>0.05$). There was no significant difference in GGT, ALP and AST levels in the control group ($P>0.05$). The incidence of pancreatitis in the observation group was significantly lower than that in the control group [8.33% (3/36) vs 36.11% (13/36)] ($\chi^2=8.036$, $P<0.05$). The skin pruritus, diarrhea, nausea, anorexia, and infection reduction rate in the observation group were higher than those in the control group ($P<0.05$). **Conclusion:** Indomethacin combined with somatostatin can effectively reduce the incidence of pancreatitis after ERCP, and then decrease the level of serum amylase.

Key words: Indomethacin; Somatostatin; Endoscopic retrograde cholangiopancreatography; Serum amylase

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前言

内镜逆行胰胆管造影 (endoscopic retrograde cholangiopancreatography, ERCP)术属于肝胆疾病中一种较为常见的诊治手

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作者简介:黎涛(1970-),男,本科,副主任医师,研究方向:消化内科及消化内镜专业,E-mail: zhanglizhong1003@163.com,电话:13698331800

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段,但 ERCP 术后易引发化学性胰腺炎和一过性血清淀粉酶水平升高,严重者可能会危及患者生命^[1,2]。因此,预防 ERCP 术后并发症显得尤为重要。曾有研究者提出 ERCP 术后胰腺炎的发病可能和十二指肠乳头的痉挛、化学性及机械性损伤、感染等因素而致的胰酶激活及一系列炎症反应有关,因此,可通过抑制炎症反应从而预防 ERCP 术后并发症^[3]。

生长抑素主要包括 14 个氨基酸的肽类激素,胃肠道药理作用较多,能有效阻碍胰腺分泌,多用于治疗急性胰腺炎^[4]。吡啶美辛属于非甾体抗炎药,能缓解患者肿胀和疼痛感,主要是通过抑制环氧合酶从而降低前列腺素的合成,阻碍炎症组织痛觉神经冲动的形成和炎症反应,常常应用于炎症、软组织受损、创伤后痛、术后疼痛等方面。为给临床在预防 ERCP 术后胰腺炎的发生,本文就吡啶美辛联合生长抑素对 ERCP 术后胰腺炎的预防作用及对血清淀粉酶的影响进行分析,报道如下。

1 资料与方法

1.1 临床资料

选取 2015 年 7 月至 2016 年 6 月在我院行 ERCP 术的患者共 72 例,纳入标准:① 近半个月未出现急性胰腺炎或急性高淀粉酶血症情况;② 意识清晰,无精神障碍者;③ 心、肺、肾功能健全者;④ 能接受十二指肠镜检查。排除标准:① 慢性胰腺炎基础病者;② 无 ERCP 禁忌症;③ 胰腺功能异常者;④ 胆道感染严重者。本次研究已获得我院伦理委员会批准实施,同时得到患者及其家属知情同意。

根据随机数字法将本次研究对象分为观察和对照组,每组 36 例。观察组中,男 21 例,女 15 例;年龄 51~72 岁,平均(63.46±2.33)岁;病因:胆总管结石 26 例,化脓性胆管炎 1 例,胆管恶性肿瘤 4 例,胆管狭窄 1 例,壶腹部恶性肿瘤 1 例,胰头癌 3 例。对照组中,男 24 例,女 12 例;年龄为 48~73 岁,平均(64.02±2.28)岁;病因:胆总管接受 27 例,化脓性胆管炎 2 例,

胆管恶性肿瘤 3 例,胆管狭窄 2 例,壶腹部恶性肿瘤 1 例,胰头癌 1 例。两组患者一般资料比较无统计学差异($P>0.05$),具有可比性。

1.2 治疗方法

ERCP 术前,患者需禁食 6h 以上,术前 30 min 肌肉注射 10 mg 山莨菪碱,10 mg 安定。对照组在 ERCP 术前 30 min 将 1000 mL 的生理盐水和 6 mg 的生长抑素(生产厂家:武汉华龙生物制药有限公司,生产批号:20150214,规格:3mg)混合后,采取静脉滴注的方式,匀速滴注 24h。观察组在对照组基础上将 100 mg 的吡啶美辛栓剂(生产厂家:马应龙药业集团股份有限公司,生产批号:20150215,规格:50 mg×10 s)插入肛门处。

1.3 观察指标

检测两组患者 ERCP 术前、术后 5、10、24、48h 血清淀粉酶水平,检测方法为速率法。分析两组患者术前、术后 48h 血清谷氨酰转氨酶、碱性磷酸酶、谷草转氨酶水平的变化。观察和比较两组患者皮肤瘙痒、腹泻、恶心、厌食、感染的改善情况及 ERCP 术后胰腺炎的发生率。

1.4 统计学处理

用 spss11.5 软件包处理本实验数据,用($\bar{x} \pm s$)表示计量资料多组间比较行单因素方差分析,两组间比较行 t 检验,用[n(%)]表示计数资料,组间比较行 χ^2 检验,以 $P<0.05$ 表明差异有统计学意义。

2 结果

2.1 两组术后不同时点血清淀粉酶水平比较

术前,两组患者的血清淀粉酶水平比较无显著差异($P>0.05$)。术后 5h,两组患者的血清淀粉酶水平均较高,和术后 5h 相比,两组患者术后 10、24、48h 的血清淀粉酶水平均显著降低($P<0.05$),且观察组不同时点血清淀粉酶水平均低于对照组($P<0.05$),见表 1。

表 1 两组患者术后不同时点血清淀粉酶水平比较($\bar{x} \pm s$)

Table 1 Comparison of the serum amylase levels at different time points postoperation between two groups($\bar{x} \pm s$)

Groups	Case	Time	Serum amylase
Observation group	36	Before postoperation	151.23±11.35
		At 5h postoperation	358.54±26.02
		At 10h postoperation	245.32±26.15**
		At 24h postoperation	201.43±21.15**
		At 48h postoperation	168.43±15.21**
Control group	36	Before postoperation	152.18±11.14
		At 5h postoperation	436.43±45.43
		At 10h postoperation	347.59±35.11*
		At 24h postoperation	302.54±28.66*
		At 48h postoperation	215.54±22.48*

Note: Compared with Postoperative 5h, * $P<0.05$; Compared with control group at the same time, # $P<0.05$.

2.2 两组患者术前和术后肝功能指标比较

术前,两组患者血清 GGT、ALP、AST 水平比较差异无统计学意义($P>0.05$)。术后 48h,两组患者血清 GGT、ALP、AST 水

平较术前均无明显变化($P>0.05$),见表 2。

2.3 两组患者 ERCP 术后胰腺炎发生情况比较

观察组 ERCP 术后胰腺炎发生率为 8.33%(3/36),对照组

的胰腺炎发生率为 36.11%(13/36), 观察组 ERCP 术后胰腺炎发生率显著低于对照组($P<0.05$)。

2.4 两组患者 ERCP 术后临床症状变化情况比较

表 2 两组患者术前和术后肝功能指标比较($\bar{x}\pm s$)

Table 2 Comparison of the liver function index between two groups before and after operation($\bar{x}\pm s$)

Groups	Case	Time	GGT(U/L)	ALP(U/L)	AST(U/L)
Observation group	36	Before operation	282.44± 26.45	173.21± 15.43	118.54± 15.43
		At 48h postoperation	279.98± 27.01	171.49± 14.87	116.54± 14.25
Control group	36	Before operation	281.09± 25.98	172.51± 16.04	119.49± 14.98
		At 48h postoperation	280.94± 26.32	169.93± 15.32	114.87± 13.76

Note: GGT: gamma-glutamyl transpeptidase, ALP: alkaline phosphatase, AST: aspartate aminotransferase.

表 3 两组患者 ERCP 术后临床症状变化情况比较

Table 3 Comparison of the changes of clinical symptoms after ERCP between two groups

Groups	Case	Reduce skin itching	Diarrhoea reduction	Nausea relief	Anorexia reduction	Reduced infection
Observation group	36	32(88.89)*	26(72.22)*	26(72.22)*	31(86.11)*	29(80.56)*
Control group	36	21(58.33)	12(33.33)	18(50.00)	22(61.11)	18(50.00)

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

3 讨论

胰腺炎及高淀粉酶血症是 ERCP 术中最为常见的并发症,其胰腺炎的发病率占到 8%左右,若是高危患者,其发病率超过 25%,术后无症状的高淀粉酶血症超过 70%^[5,6]。相关研究者提出 ERCP 术后胰腺炎的发病可能和十二指肠乳头的痉挛、化学性及机械性损伤、感染等因素而致的胰酶激活及一系列炎症反应有关,在 ERCP 操作过程中因各种器械刺激性影响而导致 Oddi 括约肌痉挛,再加之反复插管或切开会造造成机械性损伤,引发十二指肠乳头水肿,发生胰液或胆汁反流,以至于在 ERCP 术后出现胰腺炎及高淀粉酶血症^[7-9]。也有研究者认为 ERCP 术后胰腺炎的发生和胰管造影、留置胰管导丝、预切开、多次插管、插管困难等因素有关^[10,11]。

按照胰腺炎的发病机制,目前将预防胰腺炎的药物分为以下几类:降低 Oddi 括约肌压力、抑制炎症瀑布效应、阻断胰酶激活、降低胰腺炎分泌^[12-14]。胰腺炎常常被视为是胰腺分泌的酶对胰周脂肪的自身消化和胰腺腺泡。生长抑素属于人工合成的环状十四肽,在作用和化学结构方面和天然生长抑素完全相同,能直接降低消化酶的分泌,在阻碍胆囊收缩素和促胰泌素方面能直接影响胰腺的外分泌功能,同时生长抑素能下调细胞因子的级联效应和细胞因子,对胰腺细胞起着保护性作用^[15,16]。此外,生长抑素能阻碍胃蛋白酶、胃酸、胃泌素的分泌,降低内脏器官的血流量^[17]。有关动物实验表明非甾体类抗炎药能降低胰腺炎有关的死亡率,也有研究者提出吡罗美辛能改善胰腺炎患者的临床预后^[18-20]。

本研究结果显示通过 ERCP 手术患者术前予以吡罗美辛联合生长抑素在术后 10h、术后 24h、术后 48h 的血清高淀粉酶水平呈降低趋势,且联合治疗者降低的效果显著优于单纯生长抑素治疗者,同时不会影响患者肝功能。吡罗美辛联合生长抑素治疗者的皮肤瘙痒、腹泻、恶心、厌食、感染减轻率均显著低

于单纯生长抑素治疗者,提示联合治疗能有效缓解患者临床症状。此外,吡罗美辛联合生长抑素治疗者的胰腺炎发生率显著低于单纯生长抑素治疗者。究其原因主要是因为吡罗美辛属于环氧合酶抑制剂,在抑制反应的同时进而预防 ERCP 术后胰腺炎的发生。

总之,吡罗美辛联合生长抑素能有效降低 ERCP 术后胰腺炎的发生率,降低血清淀粉酶水平。

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