· 论著·

鼻胆管引流对内镜下逆行胰胆管造影术后胰腺损害预防的临床观察

李庭赞　陈志坦　朱传会　周艳　孙希芹　刘冬冬　张婷婷

【摘要】 **目的**　了解治疗性内镜下逆行胰胆管造影(ERCP)术后胰腺的损害情况,并研究单纯药物如奥美拉唑和生长抑素、鼻胆管引流(ENBD)以及药物联合 ENBD 等措施对 ERCP 术后胰腺炎的发生及高淀粉酶血症的影响。**方法**　对于患有胆总管结石、十二指肠乳头良性狭窄等良性病变的患者,按 ERCP 术后防治胰腺炎的措施不同,分为四组:对照组(C 组),仅给予一般生命支持及抗菌治疗等;药物组(SA 组),使用奥美拉唑和生长抑素;ENBD 组,仅 ENBD,未联合使用奥美拉唑和生长抑素;药物-鼻胆管组(SAE 组),ENBD 联合使用奥美拉唑和生长抑素。在 ERCP 术后 6、12、24、48、72 h 检测血清淀粉酶,同时密切观测腹痛情况,必要时行上腹部超声或 CT 检查,而后计算各组急性轻症胰腺炎及急性重症胰腺炎的发生情况并做比较。同时还对于各组无 ERCP 术后胰腺炎的患者的血清淀粉酶进行分析。**结果**　ENBD 组及 SAE 组急性轻症胰腺炎患者的发生率显著低于 C 组及 SA 组,同时 ENBD 组与 SAE 组之间,C 组及 SA 组之间无统计学差异。C 组及 SA 组均见个案急性重症胰腺炎,ENBD 组与 SAE 组则未见急性重症胰腺炎。对于各组无 ERCP 术后胰腺炎的患者的血清淀粉酶的水平进行比较,在 ERCP 术后 6、12 h,ENBD 组及 SAE 组非胰腺炎患者的水平显著低于 C 组及 SA 组,同时 EBD 组与 SAE 组之间、C 组及 SA 组之间无统计学差异。**结论**　单纯药物如奥美拉唑和生长抑素等的应用,对减少 ERCP 术后胰腺炎的发生及高淀粉酶血症的作用不显著,ENBD 等措施能显著减少 ERCP 术后胰腺炎的发生及高淀粉酶血症。

【关键词】 胰胆管造影术,内窥镜逆行;　胰腺炎;　奥美拉唑;　生长抑素;　鼻胆管引流

Observations on the precaution of endoscopic nasobiliary drainage against pancreatic damages after endoscopic netrograde cholangiopancreatography

LI Ting-zan, CHEN Zhi-tan, ZHU Chuan-hui, ZHOU Yan, SUN Xi-qin, LIU Dong-dong, ZHANG Ting-ting. Department of Gastroenterology, BENQ Hospital Affiliated to Nanjing Medical University, Nanjing 210019, China

Corresponding author: LI Ting-zan, Email: litingzan88@sina.com

【**Abstract**】 **Objective**　To investigate the incidence of post-endoscopic netrograde cholangiopancreatography (ERCP) pancreatitis and hyperamylasemia in the patients with benign diseases such as choledocholithiasis and duodenal papillitis, and to study the therapeutic effect of medicine such as omeprazole and somatostatin, and the role of endoscopic nasobiliary drainage (ENBD) in the prevention of post-ERCP pancreatitis and hyperamylasemia. **Methods**　According to the differences of therapies, the patients with benign diseases such as choledocholithiasis and duodenal papillitis were divided into four groups as following: group C (group control), group SA (with omeprazole and somatostatin), group ENBD and group SAE (with ENBD and medicine above). At 6th, 12th, 24th, 48th and 72th hours after ERCP, serum concentration of amylase was detected, and clinical symptoms and signs of abdomen and iconographic expressions of pancreas were considered together, and then the stastical differences of the incidences of mild acute pancreatitis, severe acute pancreatitis and the serum amylase concentration were made among different groups. **Results**　The research showed the incidence of mild acute pancreatitis in group ENBD and group SAE were lower than that in group C and group SA with stastical differences, meanwhile there were no significant differences between group C and group SA, group ENBD and group SAE. For the number of the cases of severe acute pancreatitis was too small, valuable contrast among different groups could not be made. The amylase concentrations in group ENBD and group SAE were much lower than those in group C and group SA at 6th, 12th hour after ERCP, but there were no differences between group C and group SA, group ENBD and group SAE. **Conclusions**　The medicine of omeprazole and somatostatin has no significant impact on the incidence of post-ERCP pancreatitis and the serum amylase concentrations in the patients with no pancrestitis after ERCP. but the therpeautic effect of ENBD on the

DOI:10.3877/cma.j.issn.1674-0785.2012.21.019

作者单位:210019　南京明基医院 南京医科大学附属医院消化内科

通讯作者:李庭赞,Email:litingzan88@sina.com

prevention of post-ERCP pancreatitis and hyperamylasemia is noted. the study also shows the detention of bile may be the main reason of the occurrence of post-ERCP pancreatitis and hyperamylasemia which are likely caused by the edema and other mechanical damages during the operation.

【Key words】 Cholangiopancreatography, endoscopic retrograde; Pancreatitis; Omeprazole; Somatostatin; endoscopic nasobiliary drainage

自国内开展内镜下逆行胰胆管造影(ERCP)技术以来,其常见的并发症常常困扰着临床医师,尤其对于 ERCP 术后胰腺炎的预防还没有一个权威的临床指南,ERCP 术后胰腺炎的预防是内镜专家长期需要面对的问题。

本文对于 ERCP 术后胰腺炎预防研究,对几种可能有效的方法进行比较,特别对于鼻胆管引流(ENBD)等措施进行研究,以期筛选出 ERCP 术后胰腺炎明确有效的预防措施,降低 ERCP 术的风险,增加手术的安全性。同时还从临床费用的角度,可以避免无效预防措施带来的资源浪费。

对象和方法

一、研究对象

本次研究对象为消化科住院患者,手术适应证为胆总管结石、十二指肠乳头炎性狭窄等引起的胆总管扩张,需行 ERCP + EST 术治疗且取得成功者。患者年龄 25 ~ 88 岁,其中男 215 例,女 255 例。

研究对象的排除标准:有胰腺炎既往史、术前有胰腺炎、因为各种原因手术失败的患者以及术后出现其他并发症(如穿孔、出血及胆道感染等)、恶性病变引起的胆总管扩张,有内镜检查禁忌等的患者不列入本研究。

二、分组方法

通过对治疗性 ERCP 术后,除了常规治疗如禁食、抗生素的应用、输液等支持治疗外,按如下标准对患者进行随机分组:对照组(C 组):50 例,男 24 例,女 26 例,年龄(52.5 ± 19.1)岁,治疗性 ERCP 术后,仅常规治疗如禁食、抗生素的应用、输液营养支持治疗等;共 3 d;药物组(SA 组):130 例,,男 58 例,女 72 例,年龄(55.5 ±25.5)岁,除了常规治疗同对照组,术后还予以生长抑素 250 μg/h 持续泵入 24 h,奥美拉唑 40 mg 静脉注射,2 次/d,共 3 d;ENBD 组:110 例,男 50 例,女 60 例,年龄(54.5 ±25.5)岁,除了常规治疗同对照组,术后还予以鼻胆管充分引流胆汁 48 h,共 3 d。药物-鼻胆管组(SAE 组):180 例,男 88 例,女 92 例,年龄(50.2 ± 38.5)岁,除了常规治疗同对照组,术后予以生长抑素 250 μg/h,持续维持 24 h,奥美拉唑 40 mg 静脉注射,2 次/d,共 3 d,术后还予以鼻胆管充分引流胆汁 48 h。

三、技术标准

ERCP 术后胰腺炎的诊断标准:ERCP 术后出现逐渐加重的上腹部疼痛并且伴有腰背部牵涉痛超过24 h,血清淀粉酶较之正常有 3 倍以上的异常升高,并根据住院时间及并发症的情况,将 ERCP 术后胰腺炎根据标准分为急性轻症胰腺炎(MAP)和急性重症胰腺炎(SAP)。MAP 病情较轻,经过顺利,住院日小于 10 d,无并发症;而 SAP 重则住院大于 10 d,有局部及全身并发症,胰 CT 扫描对诊断胰腺炎的重要依据之一,如胰实质,坏死及胰周病变等,同时超声及 CT 等影像学提示胰实质水肿、坏死及胰周病变等变化也是确诊的依据[1]。

所用十二指肠镜为 OLYMPUS 系列,ERCP + EST 的操作均由技术娴熟的消化内科主任亲自完成,鼻胆管等附件为 COOK 公司产品。血清淀粉酶检测试剂盒为北京万泰德瑞诊断技术有限公司公司产品。生长抑素及奥美拉唑均为常州第四制药有限公司产品。

四、观察指标

所有患者手术前均予以超声,淀粉酶等检测,对于每例患者 ERCP + EST 术后 6 h、12 h、24 h、48 h、72 h 进行血清淀粉酶的检测,对于淀粉酶升高或非典型腹痛的胰腺炎疑似患者及时予以超声或 CT 检查,了解胰腺肿胀及周围渗出等变化。

五、统计学分析

各组非胰腺炎患者血清淀粉酶水平的比较采用 Newman-Keuls 法;各组胰腺炎的发生率的比较采用 χ^2 检验。$P < 0.05$ 为差异有统计学意义。

结 果

一、各组胰腺炎的发生情况(表 1)

1. 各组 MAP 的发生情况:C 组与 SA 组比较无统计学差异($P = 0.146$),与 ENBD 组($P = 0.021$)、与 SAE 组($P = 0.0158$)比较有统计学差异。SA 组与 ENBD 组($P = 0.0398$)、SAE 组($P = 0.0267$)比较有统计学差异,ENBD 组、SAE 组组间比较无统计学差异($P = 0.2207$)。

表 1 各组胰腺炎的发生情况(例)

组别	例数	MAP	SAP
C 组	50	7	1
SA 组	130	13	1
ENBD 组	110	6	0
SAE 组	180	8	0

表 2　各组非胰腺炎患者血清淀粉酶的检查结果与分析(U/L,$\bar{x} \pm s$)

组别	例数	6 h	12 h	24 h	48 h	72 h
C 组	42	303.5 ± 150.3	360.4 ± 170.3	180.8 ± 100.2	142.5 ± 88.0	93.4 ± 45.5
SA 组	116	298.7 ± 142.5	349.6 ± 165.7	178.7 ± 88.8	146.3 ± 76.2	88.5 ± 70.4
ENBD 组	104	154.6 ± 70.0[ab]	208.4 ± 69.8[ab]	176.5 ± 65.5	105.3 ± 50.9	84.7 ± 56.3
SAE 组	172	143.3 ± 67.6[ab]	177.5 ± 70.2[ab]	165.8 ± 80.1	111.3 ± 60.5	70.4 ± 71.0

注:与 C 组比较,[a]$P<0.05$;与 SA 组比较,[b]$P<0.05$

2. 各组 SAP 的发生情况:C 组与 SA 组各有 1 例 SAP 患者,统计学上未见明显差异,ENBD 组与 SAE 组未出现 SAP 患者。

二、各组非胰腺炎患者血清淀粉酶的检查结果与分析(表 2)

ERCP 术后 6、12、24、48、72 h,对于各组非胰腺炎患者的血清淀粉酶水平进行比较,发现 C 组与 SA 组间比较无统计学差异,ENBD 组与 SAE 组间比较无统计学差异。但是在 ERCP 术后 6、12 h,C 组、SA 组与 ENBD 组、SAE 组之间的差异明显,有统计学意义。

讨　论

ERCP 术后胰腺炎为 ERCP 术常见的并发症,给临床工作带来很大的困扰,然而国内外目前尚缺乏公认的防治手段,药物预防方面,有学者在行 ERCP 前后使用肾上腺糖皮质激素、奥曲肽、生长激素、加贝酯、IL-10 等有一定效果[2-8],然而相反的结论时见报道[9-11]。也有学者在 ERCP 术后置入鼻胰管引流,结果显示该措施可显著减少胰腺炎的发生,然而也有无效的报道[12-17]。ERCP 术后胰腺炎发生的相关因素颇多,机制复杂,胰液引流不畅,胰酶激活导致胰腺的自身消化仍为 ERCP 术后胰腺炎发生的主要机制。

随着对 ERCP 术后胰腺炎研究的深入,一些高危因子已引起人们的重视,近些年来,一些大规模,中心研究认为,既往有 ERCP 术后胰腺炎病史、Oddi 括约肌功能紊乱、年纪轻、胆总管不宽(< 10 mm)、胰胆管插管损伤、括约肌气囊扩张术、十二指肠乳头预切开术、胰管括约肌切开术、造影剂多次重复注射等均易导致 ERCP 术后胰腺炎。机械因素是 ERCP 术后胰腺炎重要的发病原因之一,有报道显示插管损伤是括约肌痉挛或十二指肠乳头水肿常见原因,并阻碍了胰液的引流,导致急性胰腺炎。胰胆管括约肌切开术后发生率更高,但其严重程度低,重症胰腺炎的发生率较之未行十二指肠乳头切开低,有统计学差异,并推测括约肌切开后,引流通畅,胰管内压力下降。有研究显示注射压力过高和注射造影剂量大,术后胰腺炎的发生率明显升高,相反置入导管引流,可明显减少胰腺炎的发生。一些研究提示造影也影响术后胰腺炎的发生率,且与离子性质及使用剂量有关,低剂量似乎更安全[18-24]。

针对 ERCP 术后胰腺炎的发生机制及高危因素,国外一些学者对术后胰腺炎的防治进行了深入的研究,但是观点不尽一致。在器械方面,鼻胰管引流被推荐使用,该观点已被广泛接受,ERCP 术后置入导管,胰液引流通畅,可大大减少 ERCP 的发生;在药物方面,常有矛盾的研究报道,可能与药物的使用剂量、持续时间不同,接受 ERCP 术的原发疾病类型不同有关,有些国家还出台了相关指南,但是只能一定程度地减少 ERCP 术后胰腺炎的发生,目前 MAP 的发生率 1% ~ 15%,SAP 的发生率 0.4% ~0.7%[2,8,25-28]。

本次研究发现,在生长抑素药物组,ERCP 术后 MAP 的发生率与对照组无统计学差异;ENBD 组却能明显减少胰腺炎的发生;ENBD 同时使用生长抑素组,MAP 的发生率较之 ENBD 组,并未能降低胰腺炎的发生,说明胆总管的充分引流,对于减轻胆总管内的压力,对于胰液引流,减轻胰管内压力是非常有益的。本次研究提示药物如奥美拉唑及生长抑素等的预防意义不是非常明显。对于 ERCP 术后 SAP 的预防,由于 SAP 的发生例数过少,无法得出令人信服的结论。对高淀粉酶血症的预防,同样可以得出这样的结果,胆总管的充分引流有助于高血清淀粉酶的预防。由此可见,ERCP 术后胰腺炎发生的主要原因之一是由于 ERCP 术过程中的机械损伤,导致十二指肠乳头水肿等,致使胆汁及胰液引流不畅通,所以 ERCP 术后对于每例患者进行 ENBD 有助于预防胰腺损害的发生;而生长抑素等药物由于不能满意地减轻胆管及胰管内的压力,预防中意义不是十分明显。同时,由于鼻胆引流管较之胰液引流管更易于置入,所以为了预防 ERCP 术后胰腺炎,减少不必要的药物应用,使用鼻胆引流管充分引流意义明确。

参　考　文　献

[1] Lai CH,Lau WY. Management of endoscopic retrograde cholangiopancreatography-related perforation. Surgeon,2008,6:45-48.

[2] Matsushita M,Takakuwa H,Shimeno N,et al. Epinephrine sprayed on the papilla for prevention of post-ERCP pancreatitis. J Gastroenterol,2009,44:71-75.

[3] Omata F,Deshpande G,Tokuda Y,et al. Meta-analysis:somatostatin or its long-acting analogue,octreotide,for prophylaxis against post-ERCP pancreatitis. J Gastroenterol,2010,45:885-895.

[4] Barkay O,Niv E,Santo E,et al. Low-dose heparin for the prevention of post-ERCP pancreatitis:a randomized placebo-controlled trial. Surg

Endosc,2008,22:1971-1976.
[5] Gorelick A,Barnett J,Chey W,et al. Botulinum toxin injection after biliary sphincterotomy. Endoscopy,2004,36:170-173.
[6] Beauchant M, Ingrand P,Favriel JM,et al. Intravenous nitroglycerin for prevention of pancreatitis after therapeutic endoscopic retrograde cholangiography:a randomized,double-blind,placebo-controlled multicenter trial. Endoscopy,2008,40:631-636.
[7] Yoo JW, Ryu JK,Lee SH,et al. Preventive effects of ulinastatin on post-endoscopic retrograde cholangiopancreatography pancreatitis in high-risk patients:a prospective,randomized,placebo-controlled trial. Pancreas,2008,37:366-370.
[8] Lee KT,Lee DH,Yoo BM. The prophylactic effect of somatostatin on post-therapeutic endoscopic retrograde cholangiopancreatography pancreatitis:a randomized,multicenter controlled trial. Pancreas,2008,37:445-448.
[9] Dumot JA,Conwell DL,Zuccaro G Jr,et al. A randomized,double blind study of interleukin 10 for the prevention of ERCP-inducedpancreatitis. Am J Gastroenterol,2001,96:2098-2102.
[10] De Palma GD,Catanzano C. Use of corticosteriods in the prevention of post-ERCP pancreatitis:results of a controlled prospective study. Am J Gastroenterol,1999,94:982-985.
[11] Kaffes AJ,Bourke MJ,Ding S,et al. A prospective,randomized,placebo-controlled trial of transdermal glyceryl trinitrate in ERCP:effects on technical success and post-ERCP pancreatitis. Gastrointest Endosc,2006,64:351-357.
[12] Saad AM,Fogel EL,McHenry L,et al. Pancreatic duct stent placement prevents post-ERCP pancreatitis in patients with suspected sphincter of Oddi dysfunction but normal manometry results. Gastrointest Endosc,2008,67:255-261.
[13] Sofuni A,Maguchi H,Itoi T,et al. Prophylaxis of post-endoscopic retrograde cholangiopancreatography pancreatitis by an endoscopic pancreatic spontaneous dislodgement stent. Clin Gastroenterol Hepatol,2007,5:1339-1346.
[14] Freeman ML. Pancreatic stents for prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis. Clin Gastroenterol Hepatol,2007,5:1354-1365.
[15] Cheon YK,Cho KB,Watkins JL,et al. Frequency and severity of post-ERCP pancreatitis correlated with extent of pancreatic ductal opacification. Gastrointest Endosc,2007,65:385-393.
[16] Fogel EL,Eversman D,Jamidar P,et al. Sphincter of Oddi dysfunction:pancreaticobiliary sphincterotomy with pancreatic stent placement has a lower rate of pancreatitis than biliary sphincterotomy alone. Endoscopy,2002,34:280-285.
[17] Tsuchiya T,Itoi T,Sofuni A,et al. Temporary pancreatic stent to prevent post endoscopic retrograde cholangiopancreatography pancreatitis:a preliminary,single-center,randomized controlled trial. J Hepatobiliary Pancreat Surg,2007,14:302-307.
[18] Wang P,Li ZS,Liu F,et al. Risk factors for ERCP-related complications:a prospective multicenter study. Am J Gastroenterol,2009,104:31-40.
[19] Testoni PA,Mariani A,Giussani A,et al. Risk factors for post-ERCP pancreatitis in high-and low-volume centers and among expert and non-expert operators:a prospective multicenter study. Am J Gastroenterol,2010,105:1753-1761.
[20] Artifon EL,Sakai P,Cunha JE,et al. Guidewire cannulation reduces risk of post-ERCP pancreatitis and facilitates bile duct cannulation. Am J Gastroenterol,2007,102:2147-2153.
[21] Ito K,Fujita N,Noda Y,et al. Pancreatic guidewire placement for achieving selective biliary cannulation during endoscopic retrograde cholangiopancreatography. World J Gastroenterol, 2008, 14:5595-5600.
[22] Lee TH,Park do H,Park JY,et al. Can wire-guided cannulation prevent post-ERCP pancreatitis? A prospective randomized trial. Gastrointest Endosc,2009,69:444-449.
[23] Masci E,Mariani A,Curioni S,et al. Risk factors for pancreatitis following endoscopic retrograde cholangiopancreatography:a meta-analysis. Endoscopy,2003,35:830-834.
[24] Sherman S,Blaut U,Watkins JL,et al. Does prophylactic administration of corticosteroid reduce the risk and severity of post-ERCP pancreatitis:a randomized,prospective,multicenter study. Gastrointest Endosc,2003,58:23-29.
[25] Sherman S,Cheng CL,Costamagna G,et al. Efficacy of recombinant human interleukin-10 in prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis in subjects with increased risk. Pancreas,2009,38:267-274.
[26] Xu LH,Qian JB,Gu LG,et al. Prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis by epinephrinesprayed on the papilla. J Gastroenterol Hepatol,2011,26:1139-1144.
[27] Cheng CL,Sherman S,Watkins JL,et al. Risk factors for post-ERCP pancreatitis: a prospective multicenter study. Am J Gastroenterol,2006,101:139-147.
[28] Freeman ML,Nelson DB,Sherman S,et al. Complications of endoscopic biliary sphincterotomy. N Engl J Med,1996,335:909-918.

(收稿日期:2012-05-07)
(本文编辑:马超)

李庭赞,陈志坦,朱传会,等. 鼻胆管引流对内镜下逆行胰胆管造影术后胰腺损害预防的临床观察[J/CD]. 中华临床医师杂志:电子版,2012,6(21):6678-6681.