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非甾体类抗炎药预防经内镜逆行胰胆管造影术后胰腺炎的研究进展

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Application of non-steroidal anti-inflammatory drugs in prevention of pancreatitis after endoscopic retrograde cholangiopancreatography

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Abstract

Endoscopic retrograde cholangiopancreatography (ERCP) is one of the most important methods for the clinical diagnosis and treatment of biliary and pancreatic diseases. Post-ERCP pancreatitis (PEP) is the most common complication. Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used in clinical prevention of PEP, but the application standards are not unified. This article reviews the progress in the research of the preventive effect of different types of NSAIDs on PEP, their administration routes, timing, and dosage, and combination with other drugs, as well as the preventive effect of NSAIDs in different risk stratification populations, and points out that indomethacin and diclofenac are the most commonly used types of NSAIDs, which should be given at 100 mg *via* rectal administration before ERCP in all non-selected patients with no contraindications.

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Key Words: Cholangiopancreatography; Endoscopic retrograde; Pancreatitis; Non-steroidal anti-inflammatory drugs

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摘要

经内镜逆行胰胆管造影术(endoscopic retrograde cholangiopancreatography, ERCP)是目前临床上诊治

胆胰疾病的重要方法之一。胰胆管造影术后胰腺炎(post-Endoscopic retrograde cholangiopancreatography pancreatitis, PEP)是其最常见的并发症。非甾体类抗炎药(non-steroidal anti-inflammatory drugs, NSAIDs)作为临床预防PEP的常用药物,其应用标准尚不统一。本文综述了NSAIDs不同的药物类型、给药途径、给药时机、给药剂量、联合其它药物以及对不同风险分层人群的PEP预防效果的研究进展,并指出NSAIDs中的吲哚美辛与双氯芬酸是目前最常使用的药物类型,应常规在术前对所有无禁忌症、未选择患者直肠给药100 mg预防PEP的发生。

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关键词: 胰胆管造影术; 内镜逆行; 胰腺炎; 非甾体类抗炎药

核心提要: 非甾体类抗炎药(non-steroidal anti-inflammatory drugs, NSAIDs)在预防经内镜逆行胰胆管造影术后胰腺炎(post-endoscopic retrograde cholangiopancreatography pancreatitis, PEP)中的应用标准尚不统一。本文综述了NSAIDs不同的药物类型、给药途径、给药时机、给药剂量、联合其它药物以及对不同风险分层人群的PEP预防效果的最新研究进展,以期待给临床及研究工作提供一定的参考价值。

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0 引言

经内镜逆行胰胆管造影术(endoscopic retrograde cholangiopancreatography, ERCP)与传统的手术相比,具有创伤小、恢复快、适合高龄患者等优点,目前已广泛用于胆道和胰腺疾病的诊断与治疗,但也引发了许多相关并发症。ERCP术后胰腺炎(post-ERCP pancreatitis, PEP)是其中最常见术后并发症。据报道,PEP总的发生率为9.7%,其中高危患者达14.7%,不同地区存在差异^[1],且近些年来住院率和死亡率有上升的趋势^[2]。如何有效预防PEP的发生是临床研究的热点,目前临床上降低PEP发生的主要方法分为导丝引导插管、放置胰管支架等的机械预防和药物预防。关于药物预防,自1977年报道的临床药物试验以来,已有超过35种药物用于预防PEP,然而大部分药物对PEP预防没有明显的疗效。近些年来,非甾体类抗炎药(non-steroidal anti-inflammatory drugs, NSAIDs)在PEP的预防中体现出良好的应用前景^[3]。最近的一项

动物研究表明,选择性和非选择性NSAIDs均可通过抑制环氧合酶2(cyclooxygenase 2, COX2)的表达,减少炎症介质的产生和腺泡细胞凋亡,从而预防PEP发生^[4]。目前NSAIDs对PEP的预防效果尚缺乏系统概述,故本文将对NSAIDs不同的药物类型、给药途径、给药时机、给药剂量、联合其它药物以及对不同风险分层人群的PEP预防效果的研究现状进行总结。

1 不同NSAIDs的预防效果

NSAIDs是一类不含有甾体结构而具有解热镇痛抗炎作用的药物,根据其不同作用机制分为非选择性COX抑制药和选择性COX2抑制药。近年来,有研究评估了非选择性NSAIDs中的吲哚美辛、双氯芬酸、萘普生、酮洛芬和选择性NSAIDs中的塞来昔布对PEP的预防效果。2003年Murray等^[5]进行的一项前瞻性随机双盲对照研究首次探讨了预防性使用双氯芬酸对PEP的预防效果,结果显示双氯芬酸组与安慰剂组PEP的发生率分别为6.4%与15.5%($P = 0.049$),双氯芬酸可降低PEP发生率。随后Elmunzer等^[6]的一项多中心研究表明直肠消炎痛栓,即吲哚美辛也可有效的预防PEP。Mansour等^[7]发现单剂量萘普生对PEP的发生也有保护作用。Mohammad等^[8]进一步比较双氯芬酸、吲哚美辛与萘普生之间的预防效果,发现双氯芬酸和吲哚美辛因更能诱导脂氧素A4和E1分解素的生成,这两种物质可下调促炎基因的表达^[9],从而较萘普生更降低PEP的发生率(分别为4%、5.8%、15.9%)。有关酮洛芬和塞来昔布的临床随机对照研究没有显示出疗效^[10-12]。其它的NSAIDs则仍需要更进一步的研究探讨其有效性。

2 NSAIDs不同给药途径的预防效果

常用药物中的吲哚美辛有口服和直肠给药两种方式,考虑到口服对胃黏膜的损伤,以往关于吲哚美辛的研究均采用直肠给药的方式,Elmunzer等^[6]和Luo等^[13]的两项多中心研究均表明直肠给予吲哚美辛可有效预防PEP发生。双氯芬酸具有口服、肌注、直肠给药等多种方式,因双氯芬酸的活性物质是在离开胃部之后才释放,对胃的损伤作用小,故有研究采用除直肠外的其它给药方式。Ishiwatari等^[14]研究发现ERCP前后口服双氯芬酸对预防PEP没有益处。Geraci等^[15]比较了直肠给药与口服双氯芬酸的预防效果,PEP的发生率分别为0%与15%($P < 0.001$),与口服给药相比,直肠给药可降低PEP的发生。至于肌注的预防效果, Park等^[16]研究表明肌注双氯芬酸不能降低PEP的发生,但Kalantzi等^[17]的研究却显示双氯芬酸直肠给药和肌注的预防效果无统计学差异(5.2% vs 3.9%, $P = 0.633$)。综上,由于口服NSAIDs受首过代谢的影响^[18],其浓度在到达体循环之前会大大降低,从而未能发挥有效

的预防作用, 相关实验表明静脉给予NSAIDs也未能起到较好的保护作用^[10]. 临床一般倾向于直肠给药, 在不能直肠给药的患者中是否可考虑肌注双氯芬酸, 仍然需要多中心、大样本的临床研究进一步证实.

3 NSAIDs不同给药时机的预防效果

NSAIDs的最佳给药时机目前尚无明确的标准. 栓剂形式的吲哚美辛在给药后的30 min-90 min达到峰值浓度, 消除半衰期为4.5 h^[19]. 关于给药时机可分为术前、术中与术后给药, 研究显示术前^[7]和术后^[5,6]给药均可起到有效的预防作用, 而术中^[20]给药尚不能降低PEP的发生. Luo等^[13]研究表明术前30 min予以直肠吲哚美辛较术后立即用药更能有效的预防高危患者PEP的发生. 国内李敏利等^[21]2020年发布的一项研究显示与术后2 h用药相比, 术前30 min给药的预防效果更佳. 最近两项分时段给药的随机对照研究报道, 实验组在ERCP前4 h-5 h首次给予直肠吲哚美辛, 术后立即再次给药^[22], 以及实验组在ERCP后立即接受直肠吲哚美辛, 术后4 h再次给药^[23], 对照组均为术后立即给药, 结果显示分时段给药与对照组比较均未能起到更好的保护作用. 根据当前研究及药物代谢动力学, 倾向于术前30 min-90 min给药, 因为该时机给药可有效保证药物浓度在ERCP术中达到峰值, 从而有效阻断早期炎症瀑布级联反应, 若术前未能给药, 术后立即给药也能起到一定的保护作用, 不建议术中或术后4 h额外给药. 但具体的最佳给药时机仍需进一步的大样本前瞻性对照研究探讨证实.

4 NSAIDs不同给药剂量的预防效果

据研究报道^[24], 包括吲哚美辛和双氯芬酸在内的NSAIDs疗效具有剂量依赖性, 表明在保证用药安全的情况下需要足够剂量的NSAIDs来抑制炎症级联反应以预防PEP的发生. 学者们探讨了不同用药剂量(25 mg、50 mg、100 mg、200 mg)预防PEP的有效性与安全性. 迄今为止, 多数研究显示100 mg的直肠NSAIDs可有效预防PEP的发生^[5,6,13]. 然而在有些国家100 mg剂量高于常用量且不被批准使用. 2012年Otsuka等^[25]人探讨了50 mg低剂量双氯芬酸的疗效, 并对体重<50 Kg的患者用量减少至25 mg, 结果发现50 mg的双氯芬酸可有效预防PEP, 25 mg组和50 mg组PEP的发生率亦无统计学差异; Okuno等^[26]研究显示对符合入组条件患者均给予25 mg低剂量双氯芬酸也可有效的预防PEP的发生; 然而, 2020年Tomoda等^[27]的研究却表明对于体重<50 kg的患者, 25 mg剂量的双氯芬酸与对照组相比不足以降低PEP的发生(12.1% vs 10.6%, $P = 0.78$), 建议加大剂量用药; Katoh等^[28]的前瞻性研究显示对体重>50 kg的患者给予50 mg和对体重<50

kg的患者给予25 mg均不能降低PEP的发生率, 目前低剂量用药(25 mg和50 mg)能否有效地预防PEP仍存在争议. 在Lai等^[22]和Fogel等^[23]剂量增加至200 mg的研究中, 200 mg的直肠NSAIDs与100 mg相比PEP的发生率无额外减少. 关于药物的安全性, 从以上的研究中发现25 mg至200 mg的剂量用药均是安全的, 即使200 mg用量也没有额外增加不良事件的发生. 而对于有效性, 尚缺乏全面的前瞻性的研究直接比较25 mg、50 mg、100 mg与200 mg之间的预防差异^[22,23,25-28]. 目前推荐常规使用100 mg剂量预防, 而不同体重患者的最佳给药剂量尚需进一步的前瞻性研究.

5 NSAIDs对不同风险分层患者的预防效果

2019年发布的ESGE指南^[29]认为至少明确存在一种或可能存在两种患者相关性(可疑oddi括约肌功能障碍、女性、胰腺炎病史等)或手术相关性(困难插管、胰管内造影剂注射等)的危险因素时, 应考虑将患者列为PEP高危患者. Elmunzer等^[6]进行了一项多中心研究显示直肠予以吲哚美辛与安慰剂相比可有效降低高危患者PEP的发生率(9.2% vs 16.9%, $P < 0.005$). 随后Levenick等^[20]研究表明, 对于70%处于平均风险患者(即非高危患者)的人群, 使用直肠吲哚美辛与安慰剂相比并不能降低PEP的发生(7.2% vs 4.9%, $P = 0.33$). 而Luo等^[13]的一项大型多中心研究显示, 与安慰剂相比, 吲哚美辛可降低平均风险患者PEP的发生率(6% vs 3%, $P = 0.0003$), 且在未选择患者(包括高危患者和平均风险患者)中常规使用比仅在高危患者中使用更能有效预防PEP的发生(4% vs 8%, $P < 0.0001$). 综上, 倾向于在所有无禁忌症的高危患者中均使用直肠NSAIDs, 且在未选择的患者中常规使用比仅在高危患者中使用更能降低PEP的发生, 而对于平均风险患者而言, 其预防效果仍存在争议, 需更进一步的研究继续探讨.

6 NSAIDs联合其他药物联合的预防效果

近些年来, 许多研究评估了直肠NSAIDs联合其他药物预防PEP的效果, 包括联合静脉注射乳酸林格氏溶液^[30,31]、舌下含服硝酸异山梨酯^[32,33]、肾上腺素局部喷洒十二指肠乳头^[34-36]和注射生长抑素^[37]等. 液体复苏能够防止微循环低灌注, 是治疗胰腺炎的基础措施之一, 有研究表明术中及术后静脉滴注乳酸钠林格液对PEP有一定预防作用^[30], 但最近Sperna等^[31]研究显示直肠给予双氯芬酸或吲哚美辛联合乳酸钠林格液与单独使用NSAIDs相比, 联合方案并未能起到更好的保护作用(8% vs 9%, $P = 0.53$). Sotoudehmanesh等^[32]和Tomoda等^[33]两项临床研究评估了直肠NSAIDs联合舌下含服硝酸异山梨酯的预防效果, 两

项试验均显示, 与单独使用直肠NSAIDs相比, 联合治疗能起到更有益的作用(6.7% vs 15.3%, $P = 0.016$ 和5.6% vs 9.5%, $P = 0.03$). 至于直肠NSAIDs联合肾上腺素局部喷洒十二指肠乳头的疗效, Hatami等^[34]研究发现直肠吲哚美辛联合肾上腺素较直肠吲哚美辛更进一步降低PEP的发生; 而随后Kamal等^[35]研究表明联合用药并未能起到更有益的作用; Luo等^[36]进行的一项大样本研究显示, 与单独使用直肠吲哚美辛相比, 联合肾上腺素反而增加PEP发生的风险(5.3% vs 8.5%, $P = 0.33$). 最近Norouzi等^[37]比较了直肠吲哚美辛联合生长抑素和仅予以吲哚美辛的预防效果, PEP的发生率分别为11.4%与15.2%($P = 0.666$), 联合用药未能起到更有效的预防作用. 综上所述, 使用直肠NSAIDs预防PEP时, 联合使用硝酸甘油可能起到更好的保护作用, 然而联合其他药物的疗效仍存在争议, 尚需要研究进一步验证.

7 总结

PEP是ERCP术后最常见并发症, 药物预防是减少PEP发生最重要的预防措施之一, 其中NSAIDs因其成本低、疗效确切在PEP的预防中显示出独特的优势, 吲哚美辛与双氯芬酸是目前疗效最佳和最常使用的药物, 推荐在所有无禁忌症未选择患者中术前常规的直肠使用100 mg剂量预防, 在不能经直肠给药的患者中可考虑采用肌注双氯芬酸的方式, 联合硝酸甘油效果可能更佳. 但关于其它NSAIDs药物的有效性、具体的最佳给药时机、不同体重患者的最佳给药剂量、对平均风险患者的有效性以及联合其他药物预防的效果均需进一步探讨.

8 参考文献

- Kochar B, Akshintala VS, Afghani E, Elmunzer BJ, Kim KJ, Lennon AM, Khashab MA, Kalloo AN, Singh VK. Incidence, severity, and mortality of post-ERCP pancreatitis: a systematic review by using randomized, controlled trials. *Gastrointest Endosc* 2015; 81: 143-149. e9 [PMID: 25088919 DOI: 10.1016/j.gie.2014.06.045]
- Mutneja HR, Vohra I, Go A, Bhurwal A, Katiyar V, Palomera Tejeda E, Thapa Chhetri K, Baig MA, Arora S, Attar B. Temporal trends and mortality of post-ERCP pancreatitis in the United States: a nationwide analysis. *Endoscopy* 2021; 53: 357-366 [PMID: 32668463 DOI: 10.1055/a-1220-2242]
- 王安, 蔡旺, 秦鸣放, 李宁. 新型NSAIDs药物对ERCP术后胰腺炎发生的影响. *世界华人消化杂志* 2013; 21: 3881-3886 [DOI: 10.11569/wjcd.v21.i34.3881]
- Geng C, Li X, Li Y, Song S, Wang C. Nonsteroidal anti-inflammatory drugs alleviate severity of post-endoscopic retrograde cholangiopancreatography pancreatitis by inhibiting inflammation and reducing apoptosis. *J Gastroenterol Hepatol* 2020; 35: 896-904 [PMID: 32064683 DOI: 10.1111/jgh.15012]
- Murray B, Carter R, Imrie C, Evans S, O'Suilleabhain C. Diclofenac reduces the incidence of acute pancreatitis after endoscopic retrograde cholangiopancreatography. *Gastroenterology* 2003; 124: 1786-1791 [PMID: 12806612 DOI: 10.1016/s0016-5085(03)00384-6]
- Elmunzer BJ, Scheiman JM, Lehman GA, Chak A, Mosler P, Higgins PD, Hayward RA, Romagnuolo J, Elta GH, Sherman S, Waljee AK, Repaka A, Atkinson MR, Cote GA, Kwon RS, McHenry L, Piraka CR, Wamsteker EJ, Watkins JL, Korsnes SJ, Schmidt SE, Turner SM, Nicholson S, Fogel EL; U.S. Cooperative for Outcomes Research in Endoscopy (USCORE). A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. *N Engl J Med* 2012; 366: 1414-1422 [PMID: 22494121 DOI: 10.1056/NEJMoa1111103]
- Mansour-Ghanaei F, Joukar F, Taherzadeh Z, Sokhanvar H, Hasandokht T. Suppository naproxen reduces incidence and severity of post-endoscopic retrograde cholangiopancreatography pancreatitis: Randomized controlled trial. *World J Gastroenterol* 2016; 22: 5114-5121 [PMID: 27275104 DOI: 10.3748/wjg.v22.i21.5114]
- Mohammad Alizadeh AH, Abbasnazar M, Hatami B, Abdi S, Ahmadpour F, Dabir S, Nematollahi A, Fatehi S, Pourhoseingholi MA. Comparison of rectal indomethacin, diclofenac, and naproxen for the prevention of post endoscopic retrograde cholangiopancreatography pancreatitis. *Eur J Gastroenterol Hepatol* 2017; 29: 349-354 [PMID: 27849643 DOI: 10.1097/MEG.0000000000000787]
- Russell CD, Schwarze J. The role of pro-resolution lipid mediators in infectious disease. *Immunology* 2014; 141: 166-173 [PMID: 24400794 DOI: 10.1111/imm]
- de Quadros Onofrio F, Lima JCP, Watto G, Lehmen RL, Oba D, Camargo G, Dos Santos CEO. Prophylaxis of pancreatitis with intravenous ketoprofen in a consecutive population of ERCP patients: a randomized double-blind placebo-controlled trial. *Surg Endosc* 2017; 31: 2317-2324 [PMID: 27651353 DOI: 10.1007/s00464-016-5234-x]
- Makhoul E, El Mir J, Harb M. Does rectal ketoprofen prevent post ERCP pancreatitis? *Arab J Gastroenterol* 2019; 20: 141-144 [PMID: 31582291 DOI: 10.1016/j.ajg.2019.09.004]
- Kato K, Shiba M, Kakiya Y, Maruyama H, Ominami M, Fukunaga S, Sugimori S, Nagami Y, Watanabe T, Tominaga K, Fujiwara Y. Celecoxib Oral Administration for Prevention of Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis: A Randomized Prospective Trial. *Pancreas* 2017; 46: 880-886 [PMID: 28697127 DOI: 10.1097/MPA.0000000000000852]
- Luo H, Zhao L, Leung J, Zhang R, Liu Z, Wang X, Wang B, Nie Z, Lei T, Li X, Zhou W, Zhang L, Wang Q, Li M, Zhou Y, Liu Q, Sun H, Wang Z, Liang S, Guo X, Tao Q, Wu K, Pan Y, Guo X, Fan D. Routine pre-procedural rectal indometacin versus selective post-procedural rectal indometacin to prevent pancreatitis in patients undergoing endoscopic retrograde cholangiopancreatography: a multicentre, single-blinded, randomised controlled trial. *Lancet* 2016; 387: 2293-2301 [PMID: 27133971 DOI: 10.1016/S0140-6736(16)30310-5]
- Ishiwatari H, Urata T, Yasuda I, Matsusaki S, Hisai H, Kawakami H, Ono M, Iwashita T, Doi S, Kawakubo K, Hayashi T, Sonoda T, Sakamoto N, Kato J. No Benefit of Oral Diclofenac on Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis. *Dig Dis Sci* 2016; 61: 3292-3301 [PMID: 27447477 DOI: 10.1007/s10620-016-4251-x]
- Geraci G, Palumbo VD, D'Orazio B, Maffongelli A, Fazzotta S, Lo Monte AI. Rectal Diclofenac administration for prevention of post-Endoscopic Retrograde Cholangio-Pancreatography (ERCP) acute pancreatitis. Randomized prospective study. *Clin Ter* 2019; 170: e332-e336 [PMID: 31612188 DOI: 10.7417/CT.2019.2156]
- Park SW, Chung MJ, Oh TG, Park JY, Bang S, Park SW, Song SY. Intramuscular diclofenac for the prevention of post-ERCP pancreatitis: a randomized trial. *Endoscopy* 2015; 47: 33-39 [PMID: 25409167 DOI: 10.1055/s-0034-1390743]
- Kalantzis I, Poulou A, Papatheodorou A, Gkoumas K. Rectal versus intramuscular diclofenac in prevention of post-endoscopic

- retrograde cholangiopancreatography pancreatitis: experience of a Greek tertiary referral center. *Ann Gastroenterol* 2020; 33: 412-417 [PMID: 32624663 DOI: 10.20524/aog.2020.0487]
- 18 Willis JV, Kendall MJ, Flinn RM, Thornhill DP, Welling PG. The pharmacokinetics of diclofenac sodium following intravenous and oral administration. *Eur J Clin Pharmacol* 1979; 16: 405-410 [PMID: 527637 DOI: 10.1007/BF00568201]
 - 19 Jensen KM, Grenabo L. Bioavailability of indomethacin after intramuscular injection and rectal administration of solution and suppositories. *Acta Pharmacol Toxicol (Copenh)* 1985; 57: 322-327 [PMID: 4090993 DOI: 10.1111/j.1600-0773.1985.tb00052.x]
 - 20 Levenick JM, Gordon SR, Fadden LL, Levy LC, Rockacy MJ, Hyder SM, Lacy BE, Bensen SP, Parr DD, Gardner TB. Rectal Indomethacin Does Not Prevent Post-ERCP Pancreatitis in Consecutive Patients. *Gastroenterology* 2016; 150: 911-917 [PMID: 26775631 DOI: 10.1053/j.gastro.2015.12.040]
 - 21 李敏利, 汪志明, 刘炯, 郭美霞, 王彬, 吴晓尉, 周俊明, 张晓华. 不同剂量咪唑美辛预防内镜逆行胰胆管造影术后胰腺炎的应用效果. *医学研究生学报* 2020; 33: 1273-1277 [DOI: 10.16571/j.cnki.1008-8199.2020.12.008]
 - 22 Lai JH, Hung CY, Chu CH, Chen CJ, Lin HH, Lin HJ, Lin CC. A randomized trial comparing the efficacy of single-dose and double-dose administration of rectal indomethacin in preventing post-endoscopic retrograde cholangiopancreatography pancreatitis. *Medicine (Baltimore)* 2019; 98: e15742 [PMID: 31096538 DOI: 10.1097/MD.00000000000015742]
 - 23 Fogel EL, Lehman GA, Tamasky P, Cote GA, Schmidt SE, Waljee AK, Higgins PDR, Watkins JL, Sherman S, Kwon RSY, Elta GH, Easler JJ, Pleskow DK, Scheiman JM, El Hajj II, Guda NM, Gromski MA, McHenry L Jr, Arol S, Korsnes S, Suarez AL, Spitzer R, Miller M, Hofbauer M, Elmunzer BJ; US Cooperative for Outcomes Research in Endoscopy (USCORE). Rectal indomethacin dose escalation for prevention of pancreatitis after endoscopic retrograde cholangiopancreatography in high-risk patients: a double-blind, randomised controlled trial. *Lancet Gastroenterol Hepatol* 2020; 5: 132-141 [PMID: 31780277 DOI: 10.1016/S2468-1253(19)30337-1]
 - 24 Giagoudakis G, Markantonis SL. Relationships between the concentrations of prostaglandins and the nonsteroidal antiinflammatory drugs indomethacin, diclofenac, and ibuprofen. *Pharmacotherapy* 2005; 25: 18-25 [PMID: 15767216 DOI: 10.1592/phco.25.1.18.55618]
 - 25 Otsuka T, Kawazoe S, Nakashita S, Kamachi S, Oeda S, Sumida C, Akiyama T, Ario K, Fujimoto M, Tabuchi M, Noda T. Low-dose rectal diclofenac for prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis: a randomized controlled trial. *J Gastroenterol* 2012; 47: 912-917 [PMID: 22350703 DOI: 10.1007/s00535-012-0554-7]
 - 26 Okuno M, Shiroko J, Taguchi D, Yamaguchi K, Takada J, Imai S, Sato H, Thanabashi S. The Effectiveness of the Rectal Administration of Low-dose Diclofenac for the Prevention of Post-endoscopic Retrograde Cholangiopancreatography Pancreatitis. *Intern Med* 2018; 57: 2289-2294 [PMID: 29607957 DOI: 10.2169/internalmedicine.0554-17]
 - 27 Tomoda T, Kato H, Miyamoto K, Matsumi A, Ueta E, Fujii Y, Saragai Y, Yamazaki T, Uchida D, Matsumoto K, Horiguchi S, Tsutsumi K, Okada H. Efficacy of low dose rectal diclofenac for preventing post-endoscopic retrograde cholangiopancreatography pancreatitis: Propensity score-matched analysis. *Dig Endosc* 2021; 33: 656-662 [PMID: 32881078 DOI: 10.1111/den.13828]
 - 28 Katoh T, Kawashima K, Fukuba N, Masuda S, Kobatake H, Masaki K, Araki Y, Kawano K, Nishi K, Takenaka M, Ishihara S, Kinoshita Y. Low-dose rectal diclofenac does not prevent post-ERCP pancreatitis in low- or high-risk patients. *J Gastroenterol Hepatol* 2020; 35: 1247-1253 [PMID: 31788849 DOI: 10.1111/jgh.14948]
 - 29 Dumonceau JM, Kapral C, Aabakken L, Papanikolaou IS, Tringali A, Vanbiervliet G, Beyna T, Dinis-Ribeiro M, Hritz I, Mariani A, Paspatis G, Radaelli F, Lakhtakia S, Veitch AM, van Hooft JE. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2020; 52: 127-149 [PMID: 31863440 DOI: 10.1055/a-1075-4080]
 - 30 Park CH, Paik WH, Park ET, Shim CS, Lee TY, Kang C, Noh MH, Yi SY, Lee JK, Hyun JJ, Lee JK. Aggressive intravenous hydration with lactated Ringer's solution for prevention of post-ERCP pancreatitis: a prospective randomized multicenter clinical trial. *Endoscopy* 2018; 50: 378-385 [PMID: 29237204 DOI: 10.1055/s-0043-122386]
 - 31 Sperna Weiland CJ, Smeets XJNM, Kievit W, Verdonk RC, Poen AC, Bhalla A, Venneman NG, Witteman BJM, da Costa DW, van Eijck BC, Schwartz MP, Römkens TEH, Vrolijk JM, Hadithi M, Voorburg AMCJ, Baak LC, Thijs WJ, van Wanrooij RL, Tan ACITL, Seerden TCJ, Keulemans YCA, de Wijkerslooth TR, van de Vrie W, van der Schaar P, van Dijk SM, Hallensleben NDL, Sperna Weiland RL, Timmerhuis HC, Umans DS, van Hooft JE, van Goor H, van Santvoort HC, Besselink MG, Bruno MJ, Fockens P, Drenth JPH, van Geenen EJM; Dutch Pancreatitis Study Group. Aggressive fluid hydration plus non-steroidal anti-inflammatory drugs versus non-steroidal anti-inflammatory drugs alone for post-endoscopic retrograde cholangiopancreatography pancreatitis (FLUYT): a multicentre, open-label, randomised, controlled trial. *Lancet Gastroenterol Hepatol* 2021; 6: 350-358 [PMID: 33740415 DOI: 10.1016/S2468-1253(21)00057-1]
 - 32 Sotoudehmanesh R, Eloubeidi MA, Asgari AA, Farsinejad M, Khatibian M. A randomized trial of rectal indomethacin and sublingual nitrates to prevent post-ERCP pancreatitis. *Am J Gastroenterol* 2014; 109: 903-909 [PMID: 24513806 DOI: 10.1038/ajg.2014.9]
 - 33 Tomoda T, Kato H, Ueki T, Akimoto Y, Hata H, Fujii M, Harada R, Ogawa T, Wato M, Takatani M, Matsubara M, Kawai Y, Okada H. Combination of Diclofenac and Sublingual Nitrates Is Superior to Diclofenac Alone in Preventing Pancreatitis After Endoscopic Retrograde Cholangiopancreatography. *Gastroenterology* 2019; 156: 1753-1760.e1 [PMID: 30772342 DOI: 10.1053/j.gastro.2019.01.267]
 - 34 Hatami B, Kashfi SMH, Abbasnazar M, Nazemalhosseini Mojarad E, Pourhoseingholi MA, Zali MR, Mohammad Alizadeh AH. Epinephrine in the Prevention of Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis: A Preliminary Study. *Case Rep Gastroenterol* 2018; 12: 125-136 [PMID: 29805355 DOI: 10.1159/000479494]
 - 35 Kamal A, Akshintala VS, Talukdar R, Goenka MK, Kochhar R, Lakhtakia S, Ramchandani MK, Sinha S, Goud R, Rai VK, Tandan M, Gupta R, Elmunzer BJ, Ngamruengphong S, Kumbhari V, Khashab MA, Kalloo AN, Reddy DN, Singh VK. A Randomized Trial of Topical Epinephrine and Rectal Indomethacin for Preventing Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis in High-Risk Patients. *Am J Gastroenterol* 2019; 114: 339-347 [PMID: 30730860 DOI: 10.14309/ajg.0000000000000049]
 - 36 Luo H, Wang X, Zhang R, Liang S, Kang X, Zhang X, Lou Q, Xiong K, Yang J, Si L, Liu W, Liu Y, Zhou Y, Wang S, Yang M, Chen W, Han Y, Shang G, Yang X, He Y, Zou Q, Guo W, Dai Y, Zeng W, Zhu X, Gong R, Li X, Nie Z, Wang Q, Wang L, Pan Y, Guo X, Fan D. Rectal Indomethacin and Spraying of Duodenal Papilla With Epinephrine Increases Risk of Pancreatitis Following Endoscopic Retrograde Cholangiopancreatography. *Clin Gastroenterol Hepatol* 2019; 17: 1597-1606.e5 [PMID: 30391434 DOI: 10.1016/j.cgh.2018.10.043]
 - 37 Norouzi A, Ghasem Poori E, Kaabe S, Norouzi Z, Sohrabi A, Amlashi FI, Tavasoli S, Besharat S, Ezabadi Z, Amirani T. Effect of Adding Intravenous Somatostatin to Rectal Indomethacin on Post-Endoscopic Retrograde Cholangiopancreatography (ERCP) Pancreatitis in High-risk Patients: A Double-blind Randomized



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