Journal of the Association of General Surgeons of Thailand under the Royal Patronage of HM the King

วารสารสมาคมศัลยแพทย์ทั่วไปแห่งประเทศไทยในพระบรมราชูปถัมภ์

Journal homepage : http://agst.in

ORIGINAL ARTICLE

A Comparative study between 60 mg Etoricoxib per-oral and 100 mg indomethacin rectally in post-endoscopic retrograde cholangiopancreatography pancreatitis prevention.

Suphakarn Techapongsatorn, M.D.,[1,*] Natikorn Phuwtong, M.D.,[1]
Wisit Kasetsermwiriya, M.D.,[1] Amarit Tansawet, M.D.,[1] Issaree Laopiamthong, M.D.,[1]

ABSTRACT

Background: Endoscopic Retrograde cholangiopancreatography (ERCP) is a diagnostic and therapeutic procedure for the biliary and pancreatic ductal disease. One of the post-ERCP complications is post-ERCP pancreatitis; the incidence is 10% and causes prolonged hospital stay, financial burden, and developing severe pancreatitis, which may increase the burden to patients. A recent study shows the effectiveness of NSAIDs uses for post-ERCP pancreatitis prevention, especially 100 mg Indomethacin rectally. This outcome use as the research to routine practice in the Surgical Department of Vajira hospital. With interest in COX-2 inhibitor that same mechanism pathway with NSAIDs and reduce the patient's gastric complication.

Objective: To compare post-ERCP pancreatitis prevention effectiveness using 60 mg Etoricoxib per-oral and 100 mg indomethacin rectally.

Material and Methods: Retrospective study designs evaluated the patients who underwent ERCP at Vajira hospital from January 2012- December 2013. The demographic data indicate ERCP, endoscopic time, ERCP procedure, post-ERCP complication, and post-ERCP pancreatitis recorded.

Result: One hundred and fifty patients who underwent ERCP included 70 cases that received 60 mg Etoricoxib per-oral and 80 cases that received 100 mg indomethacin rectally before ERCP. Post-ERCP pancreatitis incidence was 6.67% (10/150), 4 and 6 cases in Etoricoxib and Indomethacin groups, respectively. All cases were mild pancreatitis and full recovery without mortality.

Conclusion: Etoricoxib is safe and can provide PEP prevention as effective as standard indomethacin rectally, but still required future large-scale randomized controlled trials.

Keywords: post-ERCP pancreatitis, prevention, indomethacin, etoricoxib

[1]Department of Surgery, Faculty of Medicine Vajira Hospital, Navamindrahiraj University

*Corresponding authors: Suphakarn Techapongsatorn
e-mail: suphakarn@nmu.ac.th

Journal of the Association of General Surgeons of Thailand under the Royal Patronage of HM the King

วารสารสมาคมศัลยแพทย์ทั่วไปแห่งประเทศไทยในพระบรมราชูปถัมภ์

Journal homepage : http://agst.in

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a pragmatic diagnostic and therapeutic method for managing biliary and pancreatic disease.[1] The advanced and new development of this procedure, making ERCP a safe and highly effective approach. However, post-ERCP complications can still be found, including bleeding, perforation, infection, and pancreatitis.[2, 3]

Post-ERCP pancreatitis (PEP) is the most common and serious complication, with about 2-10% incidence.[4] Therefore, the prevention of PEP strategies is essential and makes the best effective outcome with good quality of life. The prevention strategies involve multifactorial aspects, such as the pre-operative patient's risk assessment, administration of pharmacological agents, and procedural techniques.[2, 5]

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a drug that proven efficacy to prevent PEP by using 100 mg of diclofenac or indomethacin administered rectally pre-procedural period. The four main mechanisms by which NSAIDs act are: inhibition of cyclooxygenase (COX), inhibition of phospholipase A2, prevention of leukocyte adhesion and migration, and inhibition of integrins.[6-8] The best-described mechanism is the inhibition of the COX-2 enzyme, which may or may not be selective. The COX-2 inhibitors drug is a subclass of nonsteroidal anti-inflammatory drugs with more benefit than NSAIDs given upper gastrointestinal safety.

This study aims to evaluate the effectiveness of oral COX-2 inhibitor versus rectally NSAIDs in PEP prevention.

Material and Methods

Study designs

The Vajira Institutional Review Board approved the study protocol. The retrospective analyzed the patient who indicated for ERCP in the Surgical department with pre-procedural administration of 100 mg indomethacin rectally or 60 mg Etoricoxib per-oral from January 2012 to December 2013. The exclusion criteria were patients with severe pancreatitis before ERCP and history of NSAIDs or Sulfonamide or COX-2 antagonist allergy.

Procedure protocol

All patients were in-patient department. The pre-endoscopic management was pre-endoscopic laboratory (CBC, BUN, creatinine, liver function test, amylase), non-peroral for 6 hours, conscious sedation with 50 mg Pethidine and 10 mg Midazolam intravenous, and 100% oxygen via oxygen cannula. All patients were performed ERCP in a supine position with single surgeons—the deep cannulation using guidewire confirmation to common bile duct before contrast injection. The postoperative laboratory (liver function test and amylase) was evaluated.

The criteria for PEP diagnosis in patients who develop symptoms and signs of acute pancreatitis (i.e., abdominal pain) with an elevation of pancreatic enzymes (serum amylase or urine amylase)

Journal of the Association of General Surgeons of Thailand under the Royal Patronage of HM the King

วารสารสมาคมศัลยแพทย์ทั่วไปแห่งประเทศไทยในพระบรมราชูปถัมภ์

Journal homepage : http://agst.in

Data Collection

The demographic data, endoscopic time, ERCP finding & management, pre-operative & post-endoscopic laboratory, post endoscopic clinical signs, and adverse events were all recorded.

Statistical analysis

Statistical analyses were performed using the STATA program version 14. The categorical data described as number and frequency, while continuous data described as mean±standard deviation or mean (range and interquartile range) depend on normally and non-normally distributed data.

For the primary endpoint outcome, the development of PEP was described by frequencies and was compared between two groups using a chi-square test with a significant statistical level of 95%.

Results

In this study, one hundred fifty patients were recruited; seventy cases received 60 mg etoricoxib per-oral, and eighty cases received 100 mg indomethacin rectally—the demographic data described in Table 1.

Table 1: Demographic data

Variables	Etoricoxib group (n=70)	Indomethacin group (n=80)
Age	52.23 ± 3.45	50.57 ± 4.21
Male Sex (%)	48 (68.57)	50 (62.5)
BMI	24.28 ± 1.25	25.36 ± 3.24
Diagnosis (Number)		
- CBD stone	62	66
- Benign stricture	8	10
- Malignant stricture	0	4
Endoscopic times (min)	68.75 ± 4.58	70.45 ± 4.69
ERCP procedure		
- Sphincterotomy	70	80
- Pre-cut sphinterotomy	1	0
- Pancreatic duct injection	0	0
- Stone extraction	62	66
- Biliary stent	4	4
- Pancreatic duct stent	0	0
- Balloon dilatation	4	10
- Cannulation time (min)	7.5 ± 1.23	7.24 + 1.07

There were 4 and 6 cases in Etoricoxib and Indomethacin group diagnosed with PEP; there were no statistically significant. All of this was mild formed pancreatitis. There were no gastrointestinal complications, other adverse events, and mortality.

Discussion

Post-ERCP pancreatitis is the acute pancreatitis form that occurs following endoscopic retrograde cholangiopancreatography.[9, 10] PEP's pathophysiology is due to the secretion of

Journal of the Association of General Surgeons of Thailand under the Royal Patronage of HM the King

วารสารสมาคมศัลยแพทย์ทั่วไปแห่งประเทศไทยในพระบรมราชูปถัมภ์

Journal homepage : http://agst.in

inflammatory mediators and cytokine such as prostaglandins, phospholipase-A2, cyclooxygenase in the peri- and post-procedural period.[5] Ninety percent of cases are mild form pancreatitis, and supportive treatment can be successful management in mild pancreatitis; only 0.3-0.6% will be severe pancreatitis that needs more intervention for investigation and treatment with increasing post-procedural mortality rate.[1, 10]

PEP's diagnostic criteria included clinical abdominal pain within 24 hours post-ERCP and a rising serum amylase level.[5] PEP's risk factor such as 1) patient-related risk factor such as female, young age group, previous history of pancreatitis and sphincter of Oddi dysfunction, 2) procedural-related risk factors such as difficult/failed cannulation, precut sphincterotomy, the extent of pancreatic duct injection, sphincter balloon dilatation, pancreatic sphincterotomy, and minor papilla sphincterotomy, 3) operator-related risk factors or experience of the endoscopist.[9, 10]

This condition's prevention strategies consisted of patient risk stratification, the precaution of pancreatic duct cannulation, injection or sphincterotomy, aggressive hydration during an endoscopic time, and pharmacological intervention.[10]

Diclofenac and indomethacin rectally in pre-operative is the proven medication that uses for prevention strategies. NSAIDs' mechanism is to inhibit the phospholipase A2.[6, 8, 11] The other drug that can inhibit phospholipase A2 is a COX-2 antagonist, such as etoricoxib.

This study aims to demonstrate the effect of COX-2 antagonist for PEP prevention compared with standard NSAIDs rectally. There were showed post-ERCP pancreatitis about 6.67%, 5.71% in the etoricoxib group, and 7.5% in the indomethacin group without a statistical difference, which the results demonstrated overall PEP rate did not decrease compared with patients that not received pre-procedural NSAIDs administration compared with the previous study (2-10%).[12, 13]

The benefit of COX-2 antagonist over the conventional NSAIDs is the easier drug administration, only one time daily, the effectiveness on postoperative pain control, and lower side effects on the gastrointestinal tract.

The previous studies using a Cox-2 antagonist to PEP prevention were reported by Kato K et al., comparing 400 mg of celecoxib versus saline infusion and that Cox-2 antagonist had no benefit for PEP prevention.[14] Bhatia V et al. conducted a comparative study of 20 mg of valdecoxib versus glyceryl trinitrate intravenous. The results showed that valdecoxib and glyceryl trinitrate were not useful for the prevention of PEP.[15]

This study may be the first investigation to suggest using COX-2 antagonists compared with standard NSAIDs rectally in PEP's prevention. We selected 60 mg of etoricoxib because it was a low dose and more comfortable of drug administration by per-oral. The limitation of this study is the small sample size. Large scale randomized controlled trials may be required in the future to prove this research hypothesis.

Conclusion

Etoricoxib is a safe alternative option for PEP prevention strategies as standard indomethacin rectally but still required future large scale randomized controlled trials.

Journal of the Association of General Surgeons of Thailand under the Royal Patronage of HM the King

วารสารสมาคมศัลยแพทย์ทั่วไปแห่งประเทศไทยในพระบรมราชูปถัมภ์

Journal homepage : http://agst.in

Reference

1.Mine T, Morizane T, Kawaguchi Y, Akashi R, Hanada K, Ito T, et al. Clinical practice guideline for post-ERCP pancreatitis. J Gastroenterol. 2017;52(9):1013-22.
2.Freeman ML, Nelson DB, Sherman S, Haber GB, Herman ME, Dorsher PJ, et al. Complications of endoscopic biliary sphincterotomy. N Engl J Med. 1996;335(13):909-18.
3.Loperfido S, Angelini G, Benedetti G, Chilovi F, Costan F, De Berardinis F, et al. Major early complications from diagnostic and therapeutic ERCP: a prospective multicenter study. Gastrointest Endosc. 1998;48(1):1-10.
4.Thaker AM, Mosko JD, Berzin TM. Post-endoscopic retrograde cholangiopancreatography pancreatitis. Gastroenterol Rep (Oxf). 2015;3(1):32-40.
5.Tryliskyy Y, Bryce GJ. Post-ERCP pancreatitis: Pathophysiology, early identification and risk stratification. Adv Clin Exp Med. 2018;27(1):149-54.
6.Sheikh I, Fontenot E, Waghray N, Ismail MK, Tombazzi C, Smith JL. The role of nonsteroidal anti-inflammatory drugs in the prevention of post endoscopic retrograde cholangiopancreatography pancreatitis. Jop. 2014;15(3):219-24.
7.Lyu Y, Cheng Y, Wang B, Xu Y, Du W. What is impact of nonsteroidal anti-inflammatory drugs in the prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis: a meta-analysis of randomized controlled trials. BMC Gastroenterol. 2018;18(1):106.
8.Elmunzer BJ, Scheiman JM, Lehman GA, Chak A, Mosler P, Higgins PD, et al. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. N Engl J Med. 2012;366(15):1414-22.
9.Pungpapong S, Kongkam P, Rerknimitr R, Kullavanijaya P. Experience on endoscopic retrograde cholangiopancreatography at tertiary referral center in Thailand: risks and complications. J Med Assoc Thai. 2005;88(2):238-46.
10.Arata S, Takada T, Hirata K, Yoshida M, Mayumi T, Hirota M, et al. Post-ERCP pancreatitis. J Hepatobiliary Pancreat Sci. 2010;17(1):70-8.
11.Dai HF, Wang XW, Zhao K. Role of nonsteroidal anti-inflammatory drugs in the prevention of post-ERCP pancreatitis: a meta-analysis. Hepatobiliary Pancreat Dis Int. 2009;8(1):11-6.
12.Freeman ML, Guda NM. Prevention of post-ERCP pancreatitis: a comprehensive review. Gastrointest Endosc. 2004;59(7):845-64.
13.Mallery JS, Baron TH, Dominitz JA, Goldstein JL, Hirota WK, Jacobson BC, et al. Complications of ERCP. Gastrointest Endosc. 2003;57(6):633-8.
14Kato K, Shiba M, Kakiya Y, Maruyama H, Ominami M, Fukunaga S, et al. Celecoxib Oral Administration for Prevention of Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis: A Randomized Prospective Trial. Pancreas. 2017;46(7):880-6.
15.Bhatia V, Ahuja V, Acharya SK, Garg PK. A randomized controlled trial of valdecoxib and glyceryl trinitrate for the prevention of post-ERCP pancreatitis. J Clin Gastroenterol. 2011;45(2):170-6.