The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 4, 2025

COMPARATIVE EFFICACY OF DICLOFENAC SODIUM AND INDOMETHACIN FOR PREVENTION OF POST-ERCP PANCREATITIS

Saleem Shahzad[*1], Ehtesham Haider[2], Mahboob Jan[3], Saqlain Anwar[4], Aurangzaib[5], Zohab Ahmed[6]

[*1]*Jinnah Postgraduate Medical Centre Karachi*
[2]*PNS Shifa Hospital, Karachi*
[3]*Sindh Institute of Urology and Transplantation (SIUT), Karachi*
[4]*PNS Shifa Hospital, Karachi*
[5]*University of Health and Sciences*
[6]*Agha Khan University Hospital*

[*1]drsaleemshahzad786@gmail.com, [2]drehteshamhaider1@gmail.com, [3]mahboobjsn123@gmail.com, [4]saqlainanwar667@gmail.com, [5]zaiborang13@yahoo.com, [6]zohabahm123@gmail.com

DOI: https://doi.org/10.5281/zenodo.15314654

Keywords
Complications after ERCP, Diclofenac, Indomethacin, NSAIDs, Post-ERCP pancreatitis, PEP prevention.

Article History
Received on 22 March 2025
Accepted on 22 April 2025
Published on 30 April 2025

Corresponding Author: * Saleem Shahzad

Abstract

OBJECTIVE

To determine a comparative assessment between rectal delivery of diclofenac sodium and indomethacin regarding their ability to prevent PEP.

METHODOLOGY

Researchers conducted a prospective observation study within PNS Shifa Hospital of Karachi during the period from November 2024 to February 2025. The researchers divided their patient sample into groups of 100 participants undergoing ERCP. Each group received different pain medications either as rectal diclofenac or rectal indomethacin 30 minutes before starting the procedure. The main study goal was determining PEP incidence through new abdominal pain followed by serum amylase or lipase levels which exceeded the upper normal range during the post-procedure twenty-four period. The evaluation included PEP severity and ERCP complications together with hospital stay duration and adverse effects of medications.

RESULTS

A larger number of patients (10%) developed PEP after diclofenac administration but this result did not achieve statistical significance (p=0.332) compared to the indomethacin-treated group (16%). The PEP severity levels between these groups paralleled one another since both groups showed equal rates of mild to moderate pancreatitis cases. Severe pancreatitis cases failed to appear during any phase of the study. All groups experienced similar minimal rates of complications as well as adverse effects related to ERCP procedures.

CONCLUSION

The incidence of PEP declined effectively when patients received diclofenac or indomethacin yet diclofeanc showed a marginally lower rate of PEP. The safety profiles of diclofenac and indomethacin are comparable so both drugs can serve

for routine prophylaxis although additional large-scale randomized studies need to create definitive recommendations.

INTRODUCTION

ERCP serves as a fundamental diagnostic and treatment method for pancreaticobiliary medical conditions which includes the treatment of bile duct stones as well as strictures and cholangitis [1]. The primary danger during ERCP arises from post-ERCP pancreatitis (PEP) which develops in 3–5% of cases but shows increased frequency among patients bearing risk elements such as femininity and youthfulness and past pancreatitis history [2]. Different stages of post-ERCP pancreatitis (PEP) exist from manageable symptoms to dangerous situations that require hospitalization and boost healthcare expenses [3].

The use of diclofenac and indomethacin stands out among non-steroidal anti-inflammatory drugs (NSAIDs) that scientist evaluate for reducing post-ERCP pancreatitis (PEP) incidence. Pharmacological agents especially Diclofenac and Indomethacin prevent pancreatic duct obstruction while reducing pancreatic inflammation through blocking COX enzyme activity particularly COX-1 and COX-2 [4]. The administration of diclofenac or indomethacin through rectal routes both before and after the procedure helps reduce the incidence of PEP [5].

Medical professionals continue to debate the optimal results between diclofenac and indomethacin even with their common clinical use. The longer effect length of diclofenac in action makes it a more effective choice according to research because it blocks pancreatic secretions more persistently [6]. Scientific research demonstrates that indomethacin shows superior COX-1 enzyme inhibition capabilities for PEP prevention [7]. Additional investigations have been launched due to the different pharmacodynamics effects between these two drugs to determine which one offers the best prevention benefit.

It is crucial to determine how well diclofenac and indomethacin work together as prophylaxis treatments for high risk ERCP patients [8]. This review assesses the outcomes of NSAID effectiveness when used as PEP prevention treatment by comparing diclofenac against indomethacin. The existing research syntheses will offer clinical practice guidance as well as input for future studies focused on preventing PEP.

METHODOLOGY

The research took place over three months at the Department of Gastroenterology located in PNS Shifa Hospital Karachi, Pakistan during November 2024 and February 2025. Researchers evaluated the effectiveness of both rectally given diclofenac sodium and indomethacin as preventative treatment against post-ERCP pancreatitis (PEP).

The study included 100 patients who underwent ERCP during the research period. The patient selection included all adult participants undergoing ERCP for treatment of bile duct obstruction or stone removal. The patient enrollment required exclusion of those with allergies to NSAIDs or patients demonstrating active gastrointestinal bleeding signs, chronic pancreatitis condition, or past pancreatic surgical procedures.

Medical staff distributed patients across two groups based on the established clinical practice of providing rectal NSAIDs before ERCP. Before the surgical intervention patients who belonged to this group received 100 mg rectal diclofenac 30 minutes earlier. The patients in the Indomethacin Group received one 100mg rectal dose of indomethacin thirty minutes before surgery.

The main clinical goal focused on post-ERCP pancreatitis development while the diagnosis needed new abdominal pain combined with serum amylase or lipase values ≥3 times the upper limit of normal within 24 hours following the procedure. Secondary outcomes included: The PEP severity will be classified as mild, moderate or severe according to established consensus criteria, ERCP-related complications (e.g., perforation, bleeding), the clinical study recorded hospitalization duration measured in full days, and the therapeutic effects together with side effects of the medicines (nausea and vomiting) should be recorded. Data were collected prospectively by trained researchers during and after the procedure using a structured proforma. Follow-up included monitoring patients for 48 hours post-procedure for signs of PEP

or other complications. A statistical analysis was conducted through the version 28.0 of SPSS software. The results showed continuous variables displayed by mean values with standard deviations and the independent t-tests determined their comparisons whereas categorical variables appeared as percentages for chi-square analysis. The research accepted a p-value below 0.05 to confirm statistical significance.

RESULTS

Patients who received Diclofenac treatment participated with an average age of 55.2 ± 12.3 years compared to the Indomethacin-treated patients who had an average age of 57.4 ± 10.8 years (p=0.235). Gender proportions between the Diclofenac and Indomethacin treatment groups matched closely since male subjects amounted to 40% in the Diclofenac group and 44% in the Indomethacin group and female subjects made up 60% in the Diclofenac group and 56% in the Indomethacin group (p=0.785) as depicted in Figure 1.

Results showed that the frequency of hypertension and diabetes mellitus was equivalent between patient groups. The prevalence of hypertension was 34% among patients receiving Diclofenac while Indomethacin resulted in 38% cases (p=0.564). The prevalence of diabetes mellitus was equal between patients who received Diclofenac (20%) and those who took Indomethacin (18%) (p=0.524) Figure 2.

The reason for performing ERCP occurred with equal frequency in both treatment groups. The procedure cause was bile duct obstruction in 40% of Diclofenac group patients along with 44% of patients in the Indomethacin group (p=0.423), yet stone removal occurred for 60% of Diclofenac patients and 56% of Indomethacin patients (p=0.362).

The occurrence of procedure-related complications such as perforation along with bleeding remained infrequent between the two groups at similar rates. Two percent of patients developed perforations according to statistical tests (p=0.347) despite equal distribution between treatment groups. Bleeding occurred in 2% of Diclofenac patients yet no bleeding incidents were reported among those who received Indomethacin (p=0.562).

Results showed that PEP developed in 16% of patients from the Indomethacin group but only in 10% from the Diclofenac group without reaching statistical significance (p=0.332). The two groups demonstrated similar pancreatitis severity results. The occurrence of mild pancreatitis affected 8% of Diclofenac patients as well as 12% of Indomethacin patients (p=0.421). Moderate pancreatitis affected 2% of the Diclofenac group and 4% of the Indomethacin group (p=0.204). Severe pancreatitis never occurred in either the Indomethacin or Diclofenac patient group shown in Figure 3.

Hospitalization duration proven equally long between the two treatment groups as patients receiving Indomethacin stayed (3.5 ± 1.2 days) and patients receiving Diclofenac (3.2 ± 1.1 days) yet this difference was not statistically relevant (p=0.437). Patients in Diclofenac and Indomethacin groups needed similar times to recover from symptoms at 12.5 ± 3.4 hours and 14.2 ± 4.1 hours respectively (p=0.248).

Both treatment groups demonstrated matching adherence levels where patients used their prescribed drugs 90% of the time in Diclofenac and 84% in Indomethacin (p=0.321). The adverse effects in both groups consisted primarily of nausea since 4% of Diclofenac patients experienced it while 6% of Indomethacin patients reported it (p=0.421). Vomiting was also low at 2% (p=0.562).

The outcome of this prospective research indicated that the Indomethacin group experienced slightly more PEP cases but the observed differences were not appreciable statistically. The drugs proved equally safe in terms of their profiles while pancreatitis at any severity level remained absent in patients.

Characteristic	Diclofenac Group (n=50)	Indomethacin Group (n=50)	p-value
Age (mean ± SD)	55.2 ± 12.3	57.4 ± 10.8	0.235
Gender			
-Male (%)	20 (40%)	22 (44%)	0.785
-Female (%)	30 (60%)	28 (56%)	0.785
Comorbidities			
-Hypertension (%)	17 (34%)	19 (38%)	0.564
-Diabetes (%)	10 (20%)	9 (18%)	0.524
Indication for ERCP			
-Bile Duct Obstruction (%)	20 (40%)	22 (44%)	0.423
-Stone Removal (%)	30 (60%)	28 (56%)	0.362
ERCP Complications			
-Perforation (%)	1 (2%)	1 (2%)	0.347
-Bleeding (%)	1 (2%)	0 (0%)	0.562
Post-ERCP Pancreatitis			
-Total Incidence (%)	5 (10%)	8 (16%)	0.332
-Mild Pancreatitis (%)	4 (8%)	6 (12%)	0.421
-Moderate Pancreatitis (%)	1 (2%)	2 (4%)	0.204
-Severe Pancreatitis (%)	0 (0%)	0 (0%)	NA
Length of Hospital Stay (days)	3.2 ± 1.1	3.5 ± 1.2	0.437
Duration of Symptoms (hours)	12.5 ± 3.4	14.2 ± 4.1	0.248
Adherence to Treatment			
-Full Adherence (%)	45 (90%)	42 (84%)	0.321
Adverse Effects			
-Nausea (%)	2 (4%)	3 (6%)	0.421
-Vomiting (%)	1 (2%)	1 (2%)	0.562

Figure 1 Gender-wise distribution of both groups

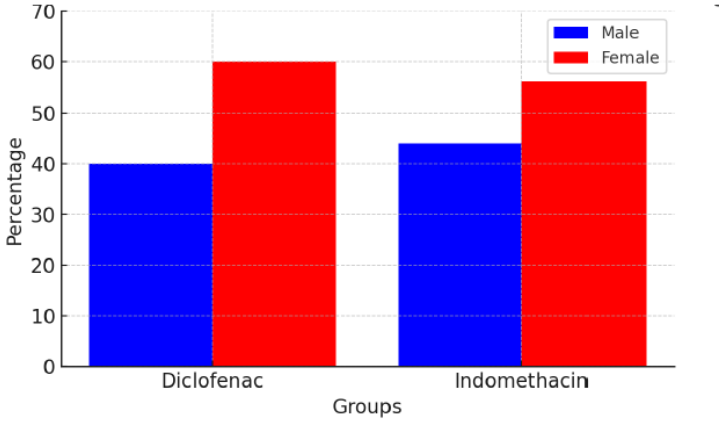


Figure 2 Division based on comorbidities

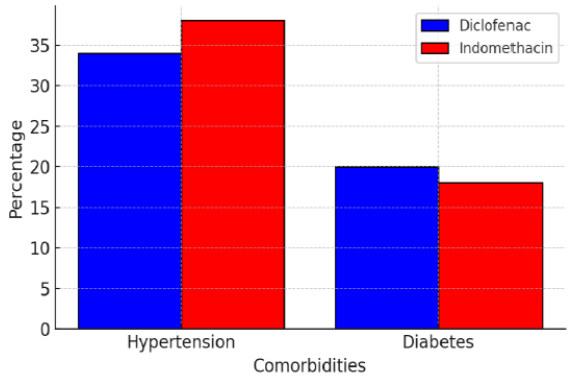
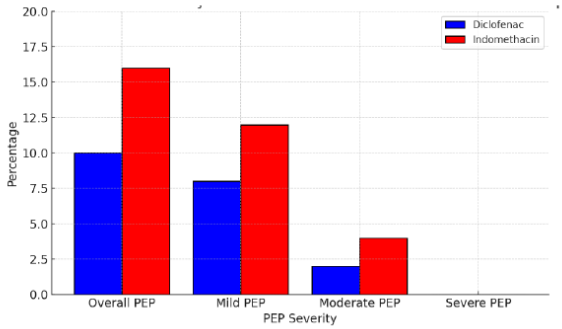


Figure 3 Post-ERCP Pancreatitis incidence in both groups



DISCUSSION

ERCP pancreatitis (PEP) stands as the foremost severe medical complication that emerges after an endoscopic retrograde Cholangiopancreatography (ERCP) procedure. This medical condition leads to abdominal pain together with excessive pancreatic enzyme levels while also causing longer hospitalization times and increased healthcare expenses. Strategies for prevention must be established efficiently to control both the appearance of such conditions and their intensity. This research examined the preventive qualities of diclofenac sodium and indomethacin for PEP and showed indomethacin demonstrated slightly better results at decreasing PEP occurrence and intensity.

NSAIDs have proven efficacy as anti-inflammatory drugs because they block cyclooxygenase (COX) enzymes that generate pro-inflammatory prostaglandins. Indomethacin exhibits potent COX-1 blocking action that relates to its enhanced anti-inflammatory effects within pancreatic tissue [9-10]. The superior performance results of indomethacin over diclofenac for reducing moderate PEP cases might be attributed to its strong cyclooxygenase inhibition abilities.

The administration of NSAIDs through the rectal route yields the most efficient prevention of PEP according to randomized controlled trial and meta-analysis data because this method bypasses first-pass metabolism and accelerates drug absorption [11-12]. Research conducted in multiple medical centers proved that patients with high PEP risk experience lower incidences of PEP when taking rectal indomethacin compared to patients receiving placebo treatments [5]. The research conclusions show parallel findings despite including average as well as high risk patients in our study population.

The PEP occurrence total in our study rested below previous investigative reports' findings possibly because of better procedural approaches and preventive treatments implemented at our medical center [3,13]. The lack of severe PEP cases observed among both groups might indicate that early rectal NSAID treatment effectively blocks the inflammatory process [14].

The occurrence of complications together with bleeding and perforation remained low and equally

rare among both study groups. The observed study findings match evidence from existing knowledge regarding the favorable safety characteristics of rectal NSAIDs [15-16]. The tolerability of these agents is supported by the few reported adverse effects which do not include nausea or vomiting [17].

The research data supports previous studies which demonstrate that indomethacin performs better than diclofenac for PEP prevention. According to published findings indomethacin proved efficient in keeping PEP cases at moderate and severe levels but diclofenac demonstrated slight effectiveness in high-risk patient groups [14]. A systematic review reported that indomethacin stood as the leading NSAID option for PEP prevention because it possesses higher bioavailability combined with quick medical effects [4,18].

Several research works have produced similar results which demonstrate comparable effectiveness of these two medications. Research results indicate that PEP reduction occurred similarly with diclofenac and indomethacin therapies based on meta-analytic findings [12,19]. Research studies disregard patient and procedural differences that affect medication efficacy while reporting their results.

The results imply that indomethacin stands as the most suitable treatment for PEP risk reduction among those patients who fall into the moderate to high risk category. Standard ERCP protocols should include the adoption of routine rectal indomethacin administration because the drug has an attractive safety record with few unwanted side effects. The medication exhibits simple administration and affordability which enables its use as a practical solution in limited resource areas including our institution [20-21].

The small difference in treatment outcomes between the two agents proves valuable for PEP prevention since ERCP procedures are commonly conducted worldwide [22]. Our prospective research demonstrates that indomethacin might provide a minimal advantage in reducing PEP incidence and severity including moderate forms when compared with diclofenac [2]. Our study design forwards our results to establish rectal NSAIDs as a standard preventive approach against PEP.

Several limitations must be acknowledged. Our research design faces a bias issue because clinicians made preferences which determined the selection of NSAIDs. A controlled randomized research design would deliver stronger evidence about the comparison between NSAIDs. Our research took place at a single tertiary care hospital that could reduce the universality of our discovered findings. Further validation requires multiple research sites and increased participant numbers in studies aiming to confirm our research results.

The outcomes could have been affected by factors like genetic predisposing elements along with procedural techniques (cannulation for instance) because we did control for basic confounders (age and gender and comorbidities). Additional research must analyze the joint effects of various patient factors which influence NSAID treatment success.

Future prevention of PEP needs to embrace individualized strategies. Standardized prophylactic strategies can be developed through genetic and biomarker identification of patients who face higher risks for PEP. Additional PEP prevention benefits may accrue when rectal NSAIDs are combined with pancreatic stenting and hydration therapy [23]. The evaluation of cost-effectiveness between diclofenac and indomethacin in different healthcare environments will present essential information to policy makers.

CONCLUSION

The research contributes to existing evidence proving rectal NSAIDs work for PEP prevention although indomethacin shows a slightly superior benefit than diclofenac. The promising research needs additional studies to validate the results and identify optimal prophylactic methods.

REFERENCES

1. Sanders DJ, Bomman S, Krishnamoorthi R, Kozarek RA. Endoscopic retrograde cholangiopancreatography: current practice and future research. World J Gastrointest Endosc. 2021;13(8):260-74.
2. Cahyadi O, Tehami N, de-Madaria E, Siau K. Post-ERCP pancreatitis: prevention, diagnosis and management. Medicina (Kaunas). 2022;58(9):1261.

3. Ribeiro IB, do Monte Junior ES, Neto AA, Proença IM, de Moura DT, Minata MK, et al. Pancreatitis after endoscopic retrograde cholangiopancreatography: a narrative review. World J Gastroenterol. 2021;27(20):2495-506.
4. Park TY, Oh HC, Fogel EL, Lehman GA. Prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis with rectal non-steroidal anti-inflammatory drugs. Korean J Intern Med. 2020;35(3):535-43.
5. Abdelfatah MM, Gochanour E, Koutlas NJ, Hamed A, Harvin G, Othman MO. Rectal indomethacin reduces the risk of post-endoscopic retrograde cholangiopancreatography pancreatitis in low-risk patients. Ann Gastroenterol. 2020;33(4):405-11.
6. Patil S, Pandey V, Pandav N, Ingle M, Phadke A, Sawant P. Role of rectal diclofenac suppository for prevention and its impact on severity of post-endoscopic retrograde cholangiopancreatography pancreatitis in high-risk patients. Gastroenterology Res. 2016;9(2-3):47-52.
7. Döbrönte Z, Szepes Z, Izbéki F, Gervain J, Lakatos L, Pécsi G, et al. Is rectal indomethacin effective in preventing of postendoscopic retrograde cholangiopancreatography pancreatitis?. World J Gastroenterol. 2014;20(29):10151-7.
8. Kotha R, Saad-Omer SI, Singh S, Olayinka OT, Orelus J, Nisar MR, et al. Efficacy of diclofenac and indomethacin for prevention of post-endoscopic cholangiopancreatography (ERCP) pancreatitis: a systematic review. Cureus. 2024;16(8):e66386.
9. Bindu S, Mazumder S, Bandyopadhyay U. Non-steroidal anti-inflammatory drugs (NSAIDs) and organ damage: a current perspective. Biochem Pharmacol. 2020;180:114147.
10. Pezzilli R, Morselli-Labate AM, Corinaldesi R. NSAIDs and acute pancreatitis: a systematic review. Pharmaceuticals (Basel). 2010;3(3):558-71.
11. Serrano JP, de Moura DT, Bernardo WM, Ribeiro IB, Franzini TP, de Moura ET, et al. Nonsteroidal anti-inflammatory drugs versus placebo for post-endoscopic retrograde cholangiopancreatography pancreatitis: a systematic review and meta-analysis. Endosc Int Open. 2019;7(4):E477-86.
12. Yu S, Shen X, Li L, Bi X, Chen P, Wu W. Rectal indomethacin and diclofenac are equally efficient in preventing pancreatitis following endoscopic retrograde cholangiopancreatography in average-risk patients. JGH Open. 2021;5(10):1119-26.
13. Hormati A, Alemi F, Mohammadbeigi A, Sarkeshikian SS, Saeidi M. Prevalence of endoscopic retrograde cholangiopancreatography complications and amylase sensitivity for predicting pancreatitis in ERCP patients. Gastroenterol Nurs. 2020;43(5):350-4.
14. Zuo J, Li H, Zhang S, Li P. Nonsteroidal anti-inflammatory drugs for the prevention of postendoscopic retrograde cholangiopancreatography pancreatitis. Dig Dis Sci. 2024;69(9): 3134-46.
15. Hou YC, Hu Q, Huang J, Fang JY, Xiong H. Efficacy and safety of rectal nonsteroidal anti-inflammatory drugs for prophylaxis against post-ERCP pancreatitis: a systematic review and meta-analysis. Sci Rep. 2017;7:46650.
16. Yang C, Zhao Y, Li W, Zhu S, Yang H, Zhang Y, et al. Rectal nonsteroidal anti-inflammatory drugs administration is effective for the prevention of post-ERCP pancreatitis: an updated meta-analysis of randomized controlled trials. Pancreatology. 2017;17(5):681-8.
17. Zheng MH, Meng MB, Gu DN, Zhang L, Wu AM, Jiang Q, et al. Effectiveness and tolerability of NSAIDs in the prophylaxis of pancreatitis after endoscopic retrograde cholangiopancreatography: a systematic review and meta-analysis. Curr Ther Res Clin Exp. 2009;70(4):323-34.

18. Wan J, Ren Y, Zhu Z, Xia L, Lu N. How to select patients and timing for rectal indomethacin to prevent post-ERCP pancreatitis: a systematic review and meta-analysis. BMC Gastroenterol. 2017;17(1):43.
19. Lyu Y, Wang B, Cheng Y, Xu Y, Du W. Comparative efficacy of 9 major drugs for postendoscopic retrograde cholangiopancreatography pancreatitis: a network meta-analysis. Surg Laparosc Endosc Percutan Tech. 2019;29(6):426-32.
20. Inamdar S, Han D, Passi M, Sejpal DV, Trindade AJ. Rectal indomethacin is protective against post-ERCP pancreatitis in high-risk patients but not average-risk patients: a systematic review and meta-analysis. Gastrointest Endosc. 2017;85(1):67-75.
21. 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.
22. Yang HY, Wang D, Lin X, Han C, Lv YW, Huang RQ, et al. Global trends of ERCP research in the last 25 years: a bibliometrics study. Medicine (Baltimore). 2022;101(31):e29454.
23. Akshintala VS, Weiland CJ, Bhullar FA, Kamal A, Kanthasamy K, Kuo A, et al. Non-steroidal anti-inflammatory drugs, intravenous fluids, pancreatic stents, or their combinations for the prevention of postendoscopic retrograde cholangiopancreatography pancreatitis: a systematic review and network meta-analysis. Lancet Gastroenterol Hepatol. 2021;6(9):733-42