

Pharmacologic and Endoscopic Interventions for Prevention of Post Endoscopic Retrograde Cholangiopancreatography Pancreatitis

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Abstract

Background: Post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP) is the predominant and clinically relevant consequence of ERCP, resulting in considerable morbidity and healthcare burden. Both pharmacologic and endoscopic prophylactic strategies have been proposed to decrease its incidence, particularly in high-risk cases.

Aim: To compare the effectiveness and clinical outcomes of rectal indomethacin, prophylactic pancreatic duct stenting, and standard care in the avoidance of PEP.

Methods: This randomized controlled clinical trial included 120 adult cases having ERCP, who were randomly allocated into 3 equal groups. Group A received a single 100-milligram rectal indomethacin suppository 30 minutes prior to ERCP, Group B underwent prophylactic pancreatic duct stenting utilizing a 5 Fr plastic stent, and Group C received standard care without prophylaxis. **Results:** Baseline demographic characteristics and ERCP results were comparable among groups. The frequency of PEP was significantly lowered in the pancreatic stent group (2%) compared to the indomethacin group (10%) and the control group (20%) (p-value equal to 0.01). Post-ERCP serum amylase and lipase concentrations at twenty-four hours were significantly reduced in the stent group (p-value under 0.05). Statistically insignificant variances were found among groups regarding the severity of pancreatitis or other complications like perforation, cholangitis, or bleeding.

Conclusion: Both rectal indomethacin and prophylactic pancreatic duct stenting effectively lessen the frequency of PEP. However, pancreatic stenting demonstrated superior efficacy and was related to the lowest PEP frequency, supporting its role as the most effective preventive approach in high-risk cases.

Keywords: ERCP, PEP, indomethacin, pancreatic duct stenting

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Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is frequently used for the detection and treatment of pancreato-biliary disorders; nevertheless, the technique may lead to several possible complications, with PEP being the most prevalent (1).

The frequency of PEP ranges from three to five percent. However, a current systematic review of over two thousand high-risk cases who had ERCP revealed a frequency of 14.7 percent, with a corresponding fatality rate of 0.2% (2).

Considering the elevated occurrence of post-ERCP pancreatitis, which is related to significant morbidity, death, and annual costs of health care about two hundred million dollars in the United States, it is unsurprising that many preventive measures, both pharmacological and endoscopic, were applied (3).

Multiple investigations assess various pharmacologic prophylaxes for PEP in high-risk cases, including the administration of rectal NSAIDs or intensive hydration utilizing lactated Ringer's solution (4).

Acute pancreatitis following ERCP can be categorized as severe, moderate, or mild according to the American Gastroenterology Association and the American College of Gastroenterology (5): (1) mild-amylase concentration twenty-four hours following the examination, remaining up to 3 folds the reference value with essential hospitalization; (2) moderate-requirement for hospitalization of four to ten days; & (3) severe-requirement for hospital stay over ten days or requirement for invasive therapeutic intervention

The utilization of NSAIDs for prophylaxis against post-endoscopic retrograde cholangiopancreatography has been established in

ERCP protocols. The current ESGE guidelines cited twenty-seven meta-analyses illustrating a drop in PEP with NSAID prophylaxis, indicating a specific Number Needed to Treat (NNT) to avoid PEP (5). Intravenous fluids must be considered when NSAIDs are isn't advised. 2 meta-analyses support the efficacy of fluid treatment for the prophylaxis of PEP (6).

The goal of this research is to compare the effectiveness and clinical outcomes of endoscopic and pharmacologic interventions for the prevention of PEP.

Patients and methods

This was a randomized clinical controlled trial performed to compare the effectiveness of rectal indomethacin, prophylactic pancreatic stenting, and standard care in preventing post-ERCP pancreatitis.

Inclusion Criteria: Adults (≥ 18 years) with at least one episode of post-ERCP pancreatitis.

Exclusion Criteria: Allergy to aspirin or NSAIDs, active or current (within four weeks) gastrointestinal hemorrhage, unwillingness or inability to consent, and history of chronic pancreatitis

Sample Size

Sample size calculation using Stata 16 ($\alpha = 0.05$, power 80%) required 40 patients per group based on expected post-ERCP pancreatitis rates. A total of 120 cases has been enrolled (40 per group).

Randomization

Cases were randomized into three groups utilizing computer-generated numbers: **Group A:** Indomethacin suppository, **Group B:** Prophylactic pancreatic stent, and **Group C:** No prophylactic intervention

Methods

All Patients were subjected to the following:

All patients underwent a thorough history and clinical examination, including personal, medical, and surgical history, assessment of vital signs, and a general physical examination. Abdominal examination was performed systematically, incorporating inspection, auscultation, percussion, and palpation to evaluate tenderness, guarding, and signs such as Murphy's sign.

Investigations

All patients underwent laboratory and radiological investigations. Laboratory tests involved kidney and hepatic function tests, complete blood count, serum amylase and lipase, blood glucose, electrolytes, lipid profile, and C-reactive protein. Radiological assessment comprised abdominal ultrasonography using 3.5 MHz and 7.5 MHz probes, while contrast-enhanced CT scanning was performed in patients with suspected post-ERCP acute pancreatitis.

Interventions

Cases have been assigned to one of three intervention groups. Group A received a single 100 mg rectal indomethacin suppository thirty minutes prior to ERCP. Group B underwent prophylactic pancreatic stenting using a 5 Fr plastic stent under fluoroscopic guidance. Group C received standard care without any prophylactic intervention.

Outcome Measures

The 1st result was the rate of post-ERCP pancreatitis among the three groups.

Statistical Analysis

Continuous information was represented as mean $\pm$ standard deviation or median (range) and analyzed utilizing the Mann-Whitney U test or Student's t-test. Categorical variables were represented as percents and examined with the Fisher's exact test or chi-square test. A p-value under 0.05 has been deemed statistically significant.

Ethical Considerations

Research permitted by the Ethics Committee, Faculty of Medicine, Aswan University. Written informed consent has been gathered from all cases. Confidentiality was maintained; cases could withdraw at any time without affecting their care.

Results

Table 1: Demographic data

Parameters		Group A (Fifty cases)	Group B (Fifty cases)	Group C (Fifty cases)	P value
Age (Mean $\pm$ SD). (Years)		39.92 $\pm$ 4.8	40.96 $\pm$ 3.94	40.46 $\pm$ 3.59	0.104
Sex	Female	23 (46%)	29 (58%)	25 (50%)	0.47
	Male	27 (54%)	21 (42%)	25 (50%)	

There was insignificant variance among groups as regards demographic information (p-value above 0.05). (Table 1)

Table 2: Complication other than acute pancreatitis.

	Group	Group	Group	P
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	A	B	C	value
Bleeding	1 (2%)	3 (60%)	2 (4%)	0.59
Perforation	1 (2%)	0 (0%)	0 (0%)	0.36
Cholangitis	1 (2%)	1 (2%)	2 (4%)	0.77

There was insignificant variance among groups with regard to bleeding, perforation, and cholangitis ($P>0.05$). (Table 2)

Table 3: ERCP Findings.

	Group A	Group B	Group C	P value
Choledocholithiasis	43 (86%)	38 (76%)	40 (80%)	0.44
Benign featuring Stricture	2 (4%)	1 (2%)	1 (2%)	0.77
Malignant featuring stricture	5 (10%)	10 (20%)	8 (16%)	0.37
? Passed CBD stone (dilated CBD without obvious etiology).	0 (0%)	1 (2%)	1 (2%)	0.6

There was a statistically insignificant variance among examined groups with regard to ERCP findings (p-value above 0.05). (Table 3)

Table 4: Serum Amylase and lipase prior to and following 24 hours of ERCP

	Group A	Group B	Group C	P value
Serum Amylase U/L before ERCP	77.9 ± 18.87	83 ± 17.85	80.73 ± 19.43	>0.05
serum Lipase U/L before ERCP	44.8 ± 14.02	52.96 ± 16.25	49.37 ± 15.38	>0.05

Serum Amylase after 24 h U/L	87.51 ± 38.74	83.79 ± 23.01	102.42 ± 44.66	<0.005
serum Lipase after 24 h U/L	80.89 ± 90.3	55.84 ± 45.48	114.06 ± 123.82	<0.005

There was a significant decrease in group B than other groups with regard to serum amylase and lipase after 24 hours (P-value under 0.05). (Table 4)

Table 5: Incidence of pancreatitis

	Group A	Group B	Group C	P value
Pancreatitis	5 (10%)	1 (2%)	10 (20%)	0.01
Mild	2 (4%)	1 (2%)	5 (10%)	0.87
Moderate	1 (2%)	0 (0%)	2 (4%)	
Severe	2 (4%)	0 (0%)	3 (6%)	

There was a significant drop in group B compared to other groups as regards the incidence of pancreatitis (p-value under 0.05), but there was insignificant variance between the studied groups as regards the severity of pancreatitis (p-value above 0.05). (Table 5)

Discussion

Endoscopic retrograde cholangiopancreatography is a significant endoscopic method utilized for the identification and management of pancreatic duct and biliary tract illnesses. This technique involves cannulating the ampulla of the 2nd portion of the duodenum with either dilation or sphincterotomy. The biliary system and/or pancreatic duct can be viewed by fluoroscopy through injecting contrast material following cannulation (8).

Furthermore, in cases involving stones, malignancy, or stenosis, the operation entails the removal of the stone and/or the dilation of the stenosis via balloon catheters or baskets, along with the potential placement of a stent in the stenosis region if needed (9).

Our results showed that the mean age in group A was 39.92 ± 4.8 years; 23 (46%) patients were females, and 27 (54%) were males. The mean age in group B was 40.96 ± 3.94 ; 29 (58%) patients were females, and 21 (42%) were males. The mean age in group C was 40.46 ± 3.59 years, and 25 (50%) patients were females. We found that there was a statistically insignificant variance among the examined groups

with regard to age, sex, hypertension, and diabetes mellitus.

Our results aligned with those of **Icacan et al. (10)**, who evaluated the effectiveness of stents versus indomethacin suppositories in preventing acute pancreatitis following ERCP. With a mean age of 54.00 (varying from 49.00 to 68.75 years), the stent group had a mean age of 54.00, the indomethacin group had a mean age of 56.50 (varying from 37.25 to 68.25 years), and the control group had a mean age of 47.50 (ranging from 38.50 to 59.75 years). In the indomethacin group, 20 cases (62.5%) were women and 12 cases (37.5%) were men; in the stent group, 9 cases (56.3%) were women and 7 patients (43.8%) were men; in the control group, 16 (57.1%) were women and 12 patients (42.9%) were men. Insignificant variance existed between the three groups for age and gender distribution.

Furthermore, our research agreed with the findings of **Sotoudehmanesh et al., (11)**, which indicated a statistically insignificant variance among the examined groups concerning age and sex. They assessed the efficacy of pancreatic duct (PD) stenting combined with pharmacological prophylaxis versus pharmacological prophylaxis alone in preventing PEP in high-risk cases.

Our study illustrated that there were statistically insignificant variances among the studied groups in terms of complications like hemorrhage, perforation, or cholangitis. Bleeding was reported in 1 patient (2%) in Group A, 3 cases (6%) in Group B, and 2 cases (4%) in Group C (p-value equal to 0.59). Perforation occurred in only 1 case (2%) in Group A and wasn't reported in Groups B and C (p-value equal to 0.36). Cholangitis was observed in 2% of cases in Groups A and B and 4% in Group C, with a statistically insignificant variance (P-value equal to 0.77).

These outcomes are relatively in agreement with the research by **Sotoudehmanesh et al., (11)**, which reported low rates of complications, including significant bleeding at the sphincterotomy location in two cases (0.5 percent), retroperitoneal perforation in four cases (1.0 percent), and fever in twenty-two cases (5.3 percent). All complications in that study have been treated conservatively. Notably, no adverse events were attributed to the use of prophylactic measures such as sublingual isosorbide, indomethacin suppository, or Ringer's lactate, or mechanical prophylaxis (pancreatic duct stenting) in any case. No mortalities have occurred as a result of PEP.

Similarly, the study by **Li et al., (12)** reported no major complications (like hemorrhage, stent migration, severe biliary infection, perforation, or kidney failure) in either group. The most common complication was abdominal pain, reported in 20% of

the stent group and 16.6% of the indomethacin group, with a statistically insignificant variance ($P=0.447$).

Our results showed that in groups A, B, and C, the mean serum amylase was 77.9 ± 18.87 , 83 ± 17.85 , and 80.73 ± 19.43 , respectively. The mean serum lipase was 44.8 ± 14.02 , 52.96 ± 16.25 , and 49.37 ± 15.38 , respectively. The mean serum amylase after 24 24h was 87.51 ± 38.74 , 83.79 ± 23.01 , and 102.42 ± 44.66 , respectively. The mean serum lipase after 24 24h was 80.89 ± 90.3 , 55.84 ± 45.48 , and 114.06 ± 123.82 , correspondingly. There was a significant reduction in group B compared to other groups with regard to serum amylase and lipase following twenty-four hours.

Our study was inconsistent with **Icacan et al., (10)** who revealed that in the groups with and without ERCP pancreatitis, as predictable, a significant variance has been observed in laboratory variable values measured prior to ERCP, six hours, and twenty-four hours after ERCP, as lipase and amylase levels measured at six and twenty-four hours after ERCP were significantly higher in those who developed post-ERCP pancreatitis.

Our study shows 5 (10%), 1 (2%), and 10 (20%) patients had pancreatitis in groups A, B, and C, correspondingly. 2, 1, and 5 patients had mild pancreatitis in groups A, B, & C, correspondingly. 1, 0, and 2 patients had moderate pancreatitis in groups A, B, & C, correspondingly. 2, 0, and 3 patients had severe pancreatitis in groups A, B, and C, correspondingly. There was a significant reduction in group B in comparison with other groups as regards the incidence of pancreatitis. There was insignificant variance between studied groups regarding severity of pancreatitis.

Icacan et al. (10) demonstrated that the frequency of ERCP pancreatitis was 3.1 percent in the indomethacin group and 6 percent in the control group. The frequency of endoscopic retrograde cholangiopancreatography pancreatitis has been noted to diminish in the indomethacin group in comparison with the control group. No instances of ERCP pancreatitis were noted in the stent group.

A potential mechanism in the progress of ERCP pancreatitis is an impediment of pancreatic secretion drainage and elevated pressure within the main pancreatic duct. A primary reason is mechanical obstruction resulting from effusion development or spasm of the Oddi sphincter owing to manipulation of the ampulla. The concept of placing a stent into the pancreatic duct for protecting against ERCP pancreatitis was proposed to maintain the continuity of pancreatic secretion flow (**13**). The initial randomized investigation has been carried out by **Tarnasky et al. (14)** The effectiveness of pancreatic stents has been demonstrated in cases with OSD.

Conclusion

The frequency of pancreatitis was significantly reduced in pancreatic stent groups compared to indomethacin and control groups. We concluded that both indomethacin and pancreatic stents are efficient approaches in ERCP pancreatitis prophylaxis. Although indomethacin represents an easy, cheap management, prophylactic pancreatic stent placement remains the improved avoidance approach for post-ERCP pancreatitis.

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