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Pre-operative single dose Dexamethasone in reducing the incidence and severity of post-ercp pancreatitis: a prospective study.

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Abstract

Acute pancreatitis is the most common and potentially fatal complication of endoscopic retrograde cholangiopancreatography (ERCP). The aim of this study was to find out the effectiveness of pre-procedure usage of single dose of intravenous dexamethasone in reducing the incidence and severity of post-ERCP pancreatitis (PEP).

Keywords : endoscopic retrograde cholangiopancreatography (ERCP), post-ERCP pancreatitis (PEP), dexamethasone.

1. Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a technique that combines the use of endoscopy and fluoroscopy to diagnose and treat certain problems of the biliary or pancreatic ductal system. One of the most frequent and feared complication after endoscopic retrograde cholangiopancreatography is post-ERCP pancreatitis (PEP) [1]. According to Cotton et al., post-ERCP pancreatitis (PEP) is defined as a “new onset of upper abdomen pain, an elevation in pancreatic enzymes of at least three times the upper limit of the normal range 24 hours after the procedure and hospitalization for at least two nights”. Grading of severity of post-ERCP pancreatitis is mainly depends upon the length of hospital stay [8]. Mild post-ERCP pancreatitis (PEP) is defined as a hospitalization for 2-3 days, moderate post-ERCP pancreatitis (PEP) is defined as 4-10 days of hospitalization whereas severe post-ERCP pancreatitis (PEP) is defines as a hospitalization of greater than 10 days post-ERCP, or development of a complication (e.g. pseudocyst or necrosis), or need for intervention (drainage or

surgery). The overall incidence of post-ERCP pancreatitis (PEP) is about 1%-10% [2-4]; however this can rise to 30% in presence of certain risk factors. Post-ERCP pancreatitis (PEP) is often mild, but in around 10% of the cases (0.4%-0.6% of the procedure performed) it is severe with mortality rates of 0.2% to 0.6% [5-7] Furthermore, asymptomatic hyperamylasaemia occur in 35%-70% of patients undergoing ERCP [9].

Risks factors for developing post-ERCP pancreatitis includes previous history of pancreatitis, cannulation attempts for >5 times, manipulation and injection of contrast into the pancreatic duct, biliary balloon sphincter dilatation, pancreatic acinar opacification, sphincter of oddi hypertension (SOH) and precut or needle-knife sphincterotomy [6,7,10-12].

The pathological mechanisms of post-ERCP pancreatitis (PEP) are multifactorial and these includes : mechanical trauma to ampulla of vater or pancreatic sphincter leading to oedema and transient obstruction to outflow of pancreatic juices, pancreatic parenchymal injuring secondary to increased hydrostatic pressure

in the pancreatic duct caused by injection of contrast or saline and bacterial or chemical insults to pancreatic parenchyma. All these factors either independently or in combination, leads to autodigestion of pancreatic parenchyma because of premature activation of pancreatic proteolytic enzymes and the release of inflammatory cytokines. Phospholipase A2 (PLA2) is believed to play a key role in the initial inflammatory cascade of post-ERCP pancreatitis (PEP) by regulating a numbers of pro-inflammatory mediators, including prostaglandins, leukotrienes, and platelet-activating factor [20].

The incidence and severity of post-ERCP pancreatitis (PEP) can be prevented by breaking this initial cascade of inflammation. The results of several single dose usage of chemo prophylactic agents like glucagon [13], calcitonin [14], nifedipine [15], octreotide [16], somatostatin [17], interleukin10 [18] and indomethacin [19] have been disappointing.

Dexamethasone is a glucocorticoid. It was first made in 1957 and was approved for medical use in 1961 [20]. It has anti-inflammatory and immunosuppressant effects [21]. It is used in the treatment of many conditions including rheumatic problems, a number of skin diseases, severe allergies, asthma, chronic obstructive lung disease, croup, brain swelling and along with antibiotics of tuberculosis [21]. The effects of dexamethasone are frequently seen within a day and last for about three days [21]. It is more potent inhibitor of phospholipase A2 (PLA2) than NSAID (indomethacin or diclofenac) which is thought to play a critical role in early inflammatory cascade. Dexamethasone is a cheap, widely available, with easy method of administration and with few side effects with single use, can be used for reducing the incidence and severity of post-ERCP pancreatitis (PEP) in both low risk and high risk patients.

2. Material and method

This prospective single centre study was conducted in Swagat Superspeciality Surgical Institute and Research Hospital, Guwahati, Assam, India from December 2018 to October 2019. Total number of patients studied were 40. These patients underwent history and general physical examination, routine blood investigation serum amylase and lipase level, Ultrasonography (USG) and Magnetic Resonance cholangiopancreatography (MRCP) at the time of admission.

Inclusion criteria includes: patients with history of choledocholithiasis with or without jaundice or gall

stone, patients with previous history of pancreatitis, patients with low and high risk of developing post-ercp pancreatitis (PEP) and patients with all age group. Exclusion criteria includes: patients who were already on steroids in the previous week, patients with acute pancreatitis, or hyperamylasaemia and hyperlipasemia at the time of ERCP, diabetic and immunocompromised patients and patients with previous history of ERCP or sphincterotomy or biliary stenting and patient having obstructive jaundice with sepsis were also excluded.

ERCP was performed under sedation with intravenous propofol and in some patients with general anaesthesia. Intravenous dexamethasone (8mg) injection was given 30 minutes prior to the procedure. Timing of procedure (> or < 20 minutes), shape of ampulla of vater (flat or protuberant), difficult cannulation (attempts >5 times), precut, biliary sphincterotomy, pneumatic balloon dilatation, number of pancreatic duct cannulation (> or <2 times), impacted stone at the lower distal end of common bile duct (CBD), single or multiple stones in CBD, large or small stones in CBD, diameter of CBD and pancreatic duct, biliary stenting and abnormal anatomy of duct of Wirsung all were recorded. Patients were put on intravenous fluid, antibiotics and antispasmodic 30 minute before and also after the procedure.

All these patients were assessed for pain upper abdomen and back, nausea and vomiting and serum amylase and lipase level 24 hours after the ERCP procedure. Serum amylase level of 350 U/L and serum lipase level of 1100 U/L were taken as upper limit of the normal range. Assesment of whether patients developed post –ERCP pancreatitis (PEP), defined as a new onset of pain in the upper abdomen with elevation in pancreatic enzymes of at least three times the upper limit of the normal range 24 hours after the procedure and hospitalization for at least two nights.

3. Results

Total number of patients studied were 40. Out of which 22 (55%) were females and 18 (45%) were males. In 28 (70%) cases, time of procedure was >20 minutes and in 12 (30%) of cases it was <20 minutes. Ampulla of vater was flat in 16 (40%) cases and protuberant in 24 (60%) cases. In 18 (45%) cases it was difficult cannulation (>5 attempts). Precut was done in 3 (7.5%) cases. Biliary sphincterotomy was done in all 40 (100%) cases. Hydrostatic CRE balloon dilatation (Boston Scientific USA) was done in 7 (17.5%) cases. Accidental pancreatic duct cannulation (>2 times) was done in 8 (20%) of cases. 12 (30%)

cases had impacted stone at the lower end of common bile duct. 25 (62.5%) cases had multiple calculus whereas 15 (37.5%) cases had single calculus. 32 (80%) cases had large calculus (>10mm) in the common bile duct (CBD) whereas 8 (20%) cases had

small calculus (<10mm) in the CBD. Biliary stenting was done in 28 (70%) cases. Diameter of common bile duct (CBD) was >10mm in 26 (65%) cases and in 14 (35%) cases it was <10mm.

Risk Factors for Post-ERCP Pancreatitis

Characteristic	Number of Cases
1. Sex	
a) Females	22 (55%)
b) Males	18 (45%)
2. Time of procedure	
a) > 20 minutes	28 (70%)
b) < 20 minutes	12 (30%)
3. Ampulla of Vater	
a) Flat	16 (40%)
b) Protuberant	24 (60%)
4. Difficult Cannulation	
a) > 5 attempts	18 (45%)
b) < 5 attempts	22 (55%)
5. Biliary sphincterotomy	40 (100%)
6. Pneumatic Balloonic Dilation	07 (17.5%)
7. Number of Pancreatic Duct Cannulation	
a) > 2 times	08 (20%)
b) < 2 times	32 (80%)
8. Impacted Stone in Distal CBD	12 (30%)
9. Number of Calculus	
a) Multiple	25 (62.5%)
b) Single	15 (37.5%)
10. Size of Calculus	
a) Large >10mm	32 (80%)
b) Small <10 mm	08 (20%)
11. Diameter of CBD	
a) > 10mm	26 (65%)
b) < 10mm	14 (35%)
12. Biliary Stenting	
a) Done	28 (70%)
b) Not Done	12 (30%)

In our study, only 1 (2.5%) cases out of 40, had mild post-ercp pancreatitis (PEP). In this cases, time of procedure was >20 minute, there were large and multiple calculus in the CBD, CHD and intrahepatic ducts, CBD was >2cm, biliary sphincterotmy and hydrostatic balloon dilatation was done. Furthermore, asymptomatic hyperamylasaemia was seen in 13 (32.5%) cases whereas hyperlipasemia was seen in 12(30%).

4. Discussion

The objective of this prospective single centre study was to find out the effectiveness of pre-procedure usage of single dose of intravenous dexamethasone in reducing the incidence and severity of post-ERCP pancreatitis (PEP) in both low risk and high risk patients. Dexamethasone (8mg) was given prior to ERCP to reduce the oedema of biliary and pancreatic sphincter and to break the initial cascade of inflammation by inhibiting the phospholipase A2 (PLA2). In our study, incidence of post-ercp pancreatitis was 2.5% which is lower than the other

pharmacological agents used for the prevention of post-ercp pancreatitis and only 2.5% of the patients had mild post-ERCP pancreatitis (PEP). None of the patients had developed moderate or severe post-ERCP pancreatitis. These patients were discharged within 48 hours of post ERCP. The incidence and severity of post-ERCP pancreatitis is strogly influenced by numbers of factors such as the number of cannulation attempts, degree of filling of the pancreatic duct with contrast material, precut sphincterotomy, balloon dilatation of the sphincter, young age, non-dilated common bile duct etc. The pre-procedure use of dexamethasone seems to reduce the incidence and severity of post-ercp pancreatitis remarkably compared to the usage of other pharmacological drugs seems to be exciting option and need to be studied further.

5. Conclusion

In our study, we found that prophylaxis with preoperative dexamethasone in ERCP patients significantly reduces the overall incidence and severity of post-ERCP pancreatitis (PEP).

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