

## Role of Pancreatic Endotherapy in Children

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Received date: May 26, 2021; Accepted date: June 09, 2021; Published date: June 16, 2021

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### Abstract

**Background:** Pancreatic endotherapy with Endoscopic retrograde *cholangio-pancreatography* (ERCP) is used for several indications in adults. However, ERCP experience in children for pancreatic disorders has been limited due to multiple factors. In this study, we have reviewed all patients who underwent pancreatic endotherapy in paediatric patients, to highlight specific indications in addition to procedure safety and long term efficacy in terms of pain relief, hospital admissions and need for surgery.

**Methods:** This was a retrospective study done in Amrita Institute of medical sciences, Kochi. All patients (<18 years of age) who underwent ERCP for pancreatic disorders between January 2009 to December 2016 were studied. Data on patient demographics (Age, gender, and symptoms), indication and details of ERCP (Therapeutics, Number, endoprosthesis) and outcome were recorded in pre-designed proformas. Statistical analysis was carried out using SPSS software version 20.0.

**Results:** A total of 48 patients underwent ERCP for pancreatic disorders (Mean age  $11.71 \pm 4.8$ ). Recurrent acute pancreatitis was the most common indication seen in 28 patients (58.3%). Successful cannulation was achieved in 45 patients (93.8%). Endotherapy success defined as a successful therapeutic procedure after cannulation and was achieved in 41 patients (81.4%). Older age ( $p=0.04$ ) and CCP with pancreas divisum had reduced rates of endotherapy success (58%). Only 2(4.2%) patients had mild post ERCP pancreatitis. A total of 29 patients (70.7%) had pain relief on follow up and only 3(6.25%) patients required surgery.

**Conclusion:** Pancreatic endotherapy with ERCP is safe and efficacious in the pediatric population. CCP with abdominal pain and recurrent acute pancreatitis are the most common indications for ERCP in this population.

### Keywords

Pancreas; Endoscopy; Pediatric; Endotherapy; Chronic pancreatitis; Anomalous bilio-pancreatic junction

### Introduction

Pancreatic endotherapy with Endoscopic retrograde *Cholangio-Pancreatography* (ERCP) is extensively used for therapeutic indications in pancreato-biliary disorders of adults [1]. However, ERCP experience in children has been limited due to multiple factors, including a low incidence of diseases requiring ERCP in this age group, a perception of technical difficulty and inadequate data on safety of ERCP in this population [2]. As a corollary, it has necessitated the adoption of similar risk mitigation strategies as those for procedures in adult patients. Moreover, pancreatic ERCP represents a niche area with specific indications unique to this population. Multiple reports have alluded to safety and efficacy of ERCP in children [2-8]. They have also shown the safety of adult duodenoscopes for pediatric ERCP, thereby precluding the need for the acquisition of specialised equipment for this procedure [9-12]. However, these early reports were predominantly diagnostic with only a limited number of patients with pancreatic indications included. Despite this early data, a careful examination of indications for ERCP as well as the therapeutic scope of the procedure including long term efficacy of pancreatic endotherapy in pediatric population is lacking.

In this study, we have reviewed all patients who underwent a pediatric pancreatic endotherapy at our centre, in an effort to delineate key aspects with regard to indications, safety and long term efficacy in terms of pain relief, hospital admissions and need for surgery [13].

### Methods

This was a retrospective study done in Amrita Institute of medical sciences, Kochi. Patient records were reviewed and all patients who underwent an ERCP January 2009 to December 2016 and were less than 18 years of age at the time of the index procedure were studied [14]. Patients for whom the ERCP was performed for a pancreatic indication (Recurrent acute pancreatitis (RAP), Chronic calcific pancreatitis (CCP), Pancreas divisum (PD), Biliary pancreatitis, Choledochal cyst with Anomalous bilio-pancreatic junction (ABPJ) and traumatic pancreatitis with duct disruption) were then included for analysis, whereas, patients with other indications for ERCP other than those pertaining to pancreatic diseases were excluded. Data on patient demographics (Age, gender), index presentation (pain with/without jaundice, ascites), indication for the procedure, post procedure diagnosis, complications were recorded in pre-designed proformas

[15]. At follow up, pain relief/symptom improvement, the total no. of ERCP, total hospital stay and need for surgery were looked into as outcome measures. Ethical approval for this study was given by the institutional review board.

### Technical considerations of procedure

All ERCPs were performed by an experienced endoscopist under general anaesthesia and the choice of anaesthetic was left to the discretion of a dedicated anaesthetic doctor who was present throughout the duration for all procedures. A standard adult ERCP scope (Olympus TJF Q180V) with an outer diameter of 13.7 mm and channel diameter of 4.2 mm was used. All procedures were performed in the endoscopy suite under fluoroscopic guidance (Flexavision, Shimadzu). Radiation exposure was kept to a minimum by limiting fluoroscopy time, but no special shielding was used to decrease patient radiation exposure. Technical success was defined as selective cannulation of pancreatic duct with an adequate pancreatogram obtained. Endotherapy success was defined as selective deep cannulation of the pancreatic duct with successful therapeutic interventions like stricture dilatation, stone extraction and stent placement as clinically indicated [16]. The patient was observed for a minimum of 24 hours post procedure to look for any complications. Oral diet was resumed 6 hours after the procedure provided the patient was asymptomatic and there was no significant rise in pancreatic enzymes (>3 times upper limit of normal (ULN)).

The pre-procedure diagnosis of Chronic Calcific Pancreatitis (CCP) was made in patients with abdominal pain along with the presence of either typical duct changes on Magnetic Resonance *Cholangio-pancreatography* (MRCP) or pancreatic calcification (including duct stones) on any imaging including plain abdominal x-rays, Magnetic Resonance Imaging (MRI) abdomen or transabdominal ultrasound. Patients of CCP with pain not responding to medical management were considered for endotherapy. Therapeutic interventions included sphincterotomy (Tritome, Cook Medical, USA), stone extraction (Cook Medical, USA), stricture dilatation (Sohendra dilators, Cook Medical, USA) with or without stent placement [17]. Recurrent Acute Pancreatitis (RAP) was defined as more than or equal to 2 documented episodes of acute pancreatitis (AP) as per revised Atlanta criteria; with intervening asymptomatic intervals of varying duration and in the absence of changes of CCP on non-invasive imaging [18]. ERCP was performed in this group after a complete clinical and biochemical resolution of the AP. Anomalous Bilio-Pancreatic Junction (ABPJ) was defined as union of the pancreatic and bile ducts outside the duodenal wall resulting in a long common channel >15 mm on ERCP images.

### Post procedure complications

Post ERCP Pancreatitis (PEP) was defined as new onset of abdominal pain post procedure along with elevation of Serum Amylase/Lipase to >3 times ULN within the first 24 hours of the procedure resulting in extension of hospital stay for at least 2 days. The other complications were as per consensus guidelines [19].

### Follow up

Clinical follow-up was performed using patient records and hospital information system. The follow-up period was defined as the period from the index ERCP at our hospital and the last follow-up visit [20]. At the time of last follow-up, the primary study end-point was

abdominal pain. Other symptoms like jaundice, ascites were also looked at for resolution. The need for repeat ERCPs, surgical interventions and pain medication use were studied. Favourable outcome was defined as resolution of pain and/or other symptoms with no further need for analgesics/endoscopic/surgical interventions [21].

### Statistical analysis

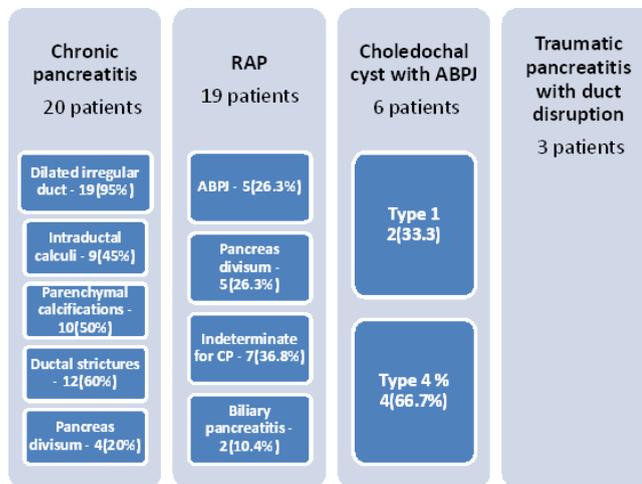
Quantitative data was summarized as mean ( $\pm$  SD) and categorical data was analysed using number (n) and percentages (%). Statistical analysis was carried out using IBM SPSS software version 20.0.

### Results

A total of 83 patients under the age of 18 years underwent ERCP during the specified time period. Of these, 48 patients had pre-specified pancreatic indications for the ERCP and were included in the study. The baseline characteristics of these patients are detailed in (Table 1). The patient population had a mean age of  $11.71 \pm 4.8$  years with a near equal gender distribution (M=26(54.2%), F=22(45.8%)). Pain was the overall predominant mode of presentation (93.8%). 20 patients (52.1%) were diagnosed to have CCP as evidenced by ductal dilatation, intraductal calculi and/or strictures. The ERCP findings with each diagnosis is detailed in (Figure 1).

| Baseline characteristics                      | All patients n=48 |
|---|-------------------|
| Age (Mean $\pm$ SD)                           | 11.71 $\pm$ 4.8   |
| Gender Female (%)                             | 22 (45.8)         |
| Presenting symptom Pain n (%)                 | 45 (93.8)         |
| ERCP intent n (%)                             |                   |
| Diagnostic                                    | 13 (27.1)         |
| Therapeutic                                   | 35 (72.9)         |
| Endoscopic endpoints: n (%)                   |                   |
| Technical success                             | 45 (93.8)         |
| Endoscopic success                            | 41 (81.4)         |
| Post procedure complications n (%)            | 2 (4.2)           |
| Diagnosis: n (%)                              |                   |
| Chronic pancreatitis (CP)                     | 20 (41.6)         |
| Recurrent acute pancreatitis (RAP)            | 17 (35.4)         |
| Biliary pancreatitis                          | 2 (4.2)           |
| Choledochal cyst with ABPJ                    | 6 (12.5)          |
| Traumatic pancreatitis with ductal disruption | 3 (6.3)           |
| Median follow up (months)                     | 8                 |
| Pain relief n (%)                             | 29 (70.7)         |
| Surgery n (%)                                 |                   |
| Drainage procedures                           | 3 (6.3)           |
| Choledochal cyst excision+HJ                  | 5 (10.4)          |

**Table 1:** Baseline characteristics



**Figure 1:** Post ERCP diagnosis and findings

**Technical Efficacy and safety of pancreatic endotherapy**

A total of 63 ERCPs were performed on 48 patients (1.31 procedures per patient). Technical success was achieved in 45 patients (93.8%). A total of 13 patients had an ERCP as a diagnostic procedure; whereas 35 patients had a therapeutic indication for the procedure which, was successfully performed in 30 patients (Endotherapy success rate-85.7%). Two patients (4.1%) had mild pancreatitis post procedure, which was managed conservatively. No major complications of ERCP were seen in this study.

**Clinical end points**

Follow up data was complete for 41 patients (85.4%) with a median follow up period of 8 months. Overall favourable outcome (Pain relief/recurrent pancreatitis/resolution of ascites) was seen in 32/41 patients (78%). Pain relief was seen in 13/18 patients (72.2%) with CCP. No further episodes of recurrent pancreatitis were seen in 10/12 patients (83.3%) who completed follow up. A total of 7/9 patients with pancreas divisum had good pain relief and no further episodes of pancreatitis with minor papillotomy and stenting. All patients with duct disruption and ascites had complete resolution at a median follow up of 5.5 months. Of the 5 CCP patients (27.8%), with no pain relief with endotherapy 3 patients underwent drainage surgery. Five patients (83.3%) with choledochal cyst and ABPJ underwent surgery with good post-operative outcomes (uneventful post-operative period and good quality of life at median follow up of 4.5 months) (Table 2).

| Therapeutic outcome (n=41)                                   | Percentage |
|--|------------|
| Pain relief in CP (n=18)                                     | 13 (72.2)  |
| Recurrent Pancreatitis in RAP (n=12)                         | 10 (83.3)  |
| Pain relief/Recurrent Pancreatitis in Pancreas divisum (n=9) | 7 (77.8)   |
| Complete resolution of ascites (n=2)                         | 2 (100)    |

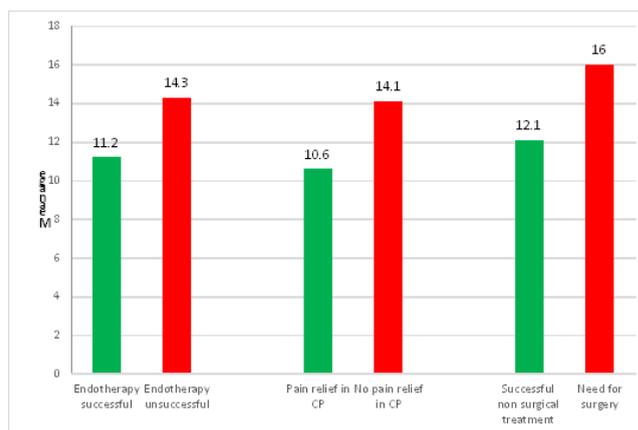
**Table 2:** Clinical end-points of endotherapy

**Anomalous Bilio-Pancreatic Junction (ABPJ)**

A total of 11 patients had anomalous bilio pancreatic junction (ABPJ). 6 patients (54.5%) had an associated choledochal cyst and presented with jaundice ± cholangitis. The remaining 5 patients (45.5%) presented with recurrent acute pancreatitis. The mean age of the patients at presentation was 7 ± 3.5 years. All the patients were successfully cannulated. Pain relief/resolution of symptoms were seen in 10/11 patients (90.9%). No post procedure complications were seen in this subgroup.

**Effect of age**

Age seems to have a significant bearing on endotherapy success as well as clinical end points of pain relief/recurrent pancreatitis and need for surgery. Mean age was significantly lower (p value 0.04) in patients who had endotherapy success, pain relief as well as those who did not need surgery (Figure 2).



**Figure 2:** Difference in Mean age in patients with endotherapy success, pain relief in CCP and need for surgery. (p value-0.04)

**Discussion**

ERCP in the pediatric population has been traditionally viewed as technically difficult especially when using the adult duodenoscopes. The risk related to ERCP in children is not well understood with a wide range of reported rates from 4-33% [2,10,22-27]. The most common adverse event seen post ERCP is pancreatitis. In the largest study done in a similar patient population by Agarwal et al (n=172). Adverse events were seen in 4.7% of patients. Even in our study, ERCP was performed using the adult duodenoscopes in all the children with no major complications observed; only 2/63 procedures (4.1%) had mild Post ERCP pancreatitis which was successfully managed with conservative management. These rates are comparable to adult patient cohorts. In a study comparing the rate of complications of ERCP in 116 children with matched adults, no significant difference in adverse events were noted (3.4% versus 2.5%).

In general, ERCP in children for pancreatic endotherapy, using adult duodenoscopes, is relatively safe. MRCP has largely replaced ERCP over the years for diagnosis of pancreatic disorders in children.

However, the therapeutic value of ERCP has ensured the continued utility of this procedure in the pediatric population. The efficacy of pancreatic duct stenting especially in the setting of chronic pancreatitis has been shown to reduce the need for surgery, reduce analgesic usage and improve patient outcome in the patients with chronic pancreatitis [21]. Pancreatic endotherapy in these patients includes pancreatic sphincterotomy, stricture dilation and stent placement. In some cases, pancreatic ductal stone extraction can also be performed [28]. In a study of 42 children with CP, 37 underwent endotherapy alone and pain relief was seen in 24 patients (64.9%). Only five patients underwent surgery subsequently due to refractory abdominal pain [29]. In the study by Agarwal et al, 147 patients with complete follow up data were studied, of which 91/147 patients (63.6%) had pain relief after endotherapy [22]. In our study 13/18 patients with CP (72.2%) had pain relief. Only three patients required surgery.

When studying different subsets of patients, 7/9 patients (77.8%) of pancreas divisum had good pain relief with minor papillotomy and stent placement. Our study is unique in the relatively large proportion of patients who presented with Anomalous bilio-pancreatic Junction (ABPJ). ABPJ refers to union of the pancreatic and bile ducts outside the duodenal wall resulting in a long common channel (usually >15 mm) [13]. ABPJ is seen in up to 90% of cases of congenital choledochal cysts. Other associations include gallbladder adenomyomatosis, pancreatitis, and pancreas divisum. It is associated with increased risk of pancreatitis and cholangiocarcinoma possibly resulting from biliopancreatic reflux, cholestasis and infection and biliary carcinogens [14,15]. ABPJ is classified into three types depending on morphology of the union [20]. ERCP is indicated for diagnosis and in patients with obstructive symptoms, but surgery is the definitive treatment in these patients. Total resection of the extrahepatic bile duct with hepaticoenterostomy is considered the preferred treatment in children with APBJ with choledochal cyst [16]. A total of 11 patients (22.9%) had ABPJ in our cohort and 9/11 patients (90%) were successfully treated with endotherapy. Five patients (45.5%) presented with RAP and 6 patients (55.5%) had an associated choledochal cyst. Technical success was achieved in all the patients. Patients with ABPJ had a higher rate of endotherapy success with no post procedure complications. The role of endotherapy for pancreas divisum in RAP is controversial. In selected patients, minor papillotomy ± dorsal duct stent placement decreases the rate of RAP, whereas relief of chronic pain is infrequent. Similar results were seen in our study, where 5/5 patients (100%) with pancreas divisum and RAP had no further episodes of pancreatitis; and 2/4 patients (50%) of pancreas divisum with chronic pancreatitis had significant pain relief. It remains to be seen if these results will remain the same with a larger patient cohort and a longer follow up period. Most ERCP in pediatric patients are performed under general anaesthesia. This is because of a higher risk of hypoventilation owing to greater airflow resistance along with dynamic and static airway occlusion in children in conjunction with reduction of chest excursion when placed in the semiprone position [30].

In our center, all therapeutic pediatric endoscopic procedures including but not restricted to ERCP are performed under general anaesthesia with a dedicated anaesthetist present throughout the entire duration of the procedure. In the study by Agarwal et al, at a high volume referral center, all cases were performed under moderate sedation using Midazolam and Ketamine. No anaesthesia related adverse events were reported in this study [21]. In general, ERCP procedures in children can be performed under both general anaesthesia as well as moderate sedation depending on the experience

and expertise of the anaesthetist, GI assistants and endoscopists. The main limitation of the study is the retrospective design of the study which can result in incomplete follow up data. However, 41 patients (85.4%) could be followed up for a median follow up period of 8 months. Long term follow up data of the various sub groups of pediatric patients is required before large scale adoption of endoscopic therapies in children.

## Conclusion

Pancreatic endotherapy (ERCP) with adult duodenoscopes is safe in children; with good efficacy in patients with ABPJ and pancreas divisum. Adverse events are comparable to adult procedures with no added precautions in the pediatric population.

## Authors' Contributions

Harshavardhan Rao B, Priya Nair and Krishnapriya S helped in subject recruitment and data entry of the study. Harshavardhan Rao B and Anoop Koshy were involved with data analysis, interpretation. Harshavardhan Rao drafted the manuscript and Rama P Venu revised the article critically for important intellectual content.

## Institutional review board

The study was reviewed and approved by the Amrita Institute of Medical sciences Research Review Board (Kochi, Kerala, India).

## Conflict-of-interest statement

There are no conflicts of interest to report.

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