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Pediatric Choledochal Cysts; Hepaticoduodenostomy for Biliary Reconstruction; Is it Time to Get Title of "Gold Standard" from Hepaticojejunostomy? 25 years of Single Centre Experience

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Abstract

Background: Choledochal Cysts (CCs) are a rare entity; especially in the Western world. A complete consensus has not been reached regarding how bile drainage will be provided after the excision. We aimed to evaluate the patients treated with a diagnosis of CC in our clinic and to reveal the results focusing on outcomes of the two hepaticoenterostomy methods.

Method: We reviewed all pediatric patients operated for CC<18 years of age in a pediatric surgery clinic at a tertiary hospital between 1992 and 2017, and excluded treated with internal drainage (ID), ID+ External Drainage (ED) and total Cyst Excision (CE) were excluded from the present analysis.

Results: Of 25 patients with CCs, 7 were male (28%). The mean age was 2.7 years (range between 7 days to 13.6 years). Type I and IVb cysts were diagnosed in 22, and 3 patients, respectively. Total CE+ hepaticoduodenostomy (HD) or Hepaticojejunostomy (HJ) were performed in 10, and 15 patients respectively. Ten HD patients had no long-term complications. However, adhesions (n=1) and anastomotic strictures (n=1) were seen in HJ patients that anastomotic stricture required reoperation. The mean follow-up period was 14 years (range between 6 years and 18 years). We did not observe biliary malignancies during treatment or follow-up.

Conclusion: In our study, patients with total CE+HD have no long-term complications and it was also confirmed by hepatic scintigraphy that there was neither gastric nor hepatic reflux. Despite a limited number of patients but with a long follow-up, our study supports the competition between HD and HJ regarding bile drainage in the literature in favor of HD.

Keywords: Choledochal cysts; Children; Hepaticojejunostomy; Hepaticoduodenostomy

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Introduction

Choledochal Cysts (CCs) are congenital dilatations of extrahepatic and/or intrahepatic bile ducts. Alanso-Lej and his colleagues classified them in 1959, and in 1977, this classification was modified by Todani et al [1]. According to this classification the cyst types are as follows: type I (cystic dilatation of extrahepatic bile ducts), type II (diverticular dilatation of the extrahepatic bile duct), type III (cystic dilatation of the intraduodenal portion of the common bile duct), type IVa (multiple cystic dilatations of extrahepatic and intrahepatic ducts), type IVb (multiple cystic dilatations of extrahepatic ducts), and type V (single or multiple intrahepatic cysts) [2]. It is a rare biliary entity with an estimated incidence of 1:100–150000 live births in Western countries, while the incidence can be as high as 1:1000 live births in the Asian population. CCs are primarily a childhood disease-up to 80% of patients are diagnosed before 10 years of age. Although the etiology is controversial, the main elements in the natural historical emergence of the type I and type IV, which make up the majority of all types, have become clearer. Clinical presentation varies from jaundice in young patients to nonspecific abdominal pain in older, but morbidity increases with complications such as cholangitis, pancreatitis, perforation, hepatitis, liver failure and malignancy in delayed diagnosed patients. External Drainage (ED), Internal Drainage (ID), total Cyst Excision (CE)+ Hepaticoduodenostomy (HD), and total CE+ Hepaticojejunostomy (HJ) were defined according to historical development of treatment [3]. The majority (over 85% to 90%) have satisfactory surgical outcomes. However, 6% to 10% of patients need re-operation [4]. In the present study, we describe results from over 25 years of

experience with CCs from a single institution. Our main focus is on differences in outcomes between HJ and HD as modes of extrahepatic biliary tree restoration.

Material and Methods

This study "Pediatric Choledochal Cysts; Hepaticoduodenostomy for biliary reconstruction; is it time to get title of "gold standard" from Hepaticojejunostomy? 25 years of single centre experience." was conducted at Department of Pediatric Surgery, XXX, after the approval of ethical committee was in conformance with the Declaration of Helsinki. We included all pediatric patients who were operated for CC<18 years of age in a pediatric surgery clinic at a tertiary hospital between 1992 and 2017. Patients who were treated with Internal Drainage (ID), ID+ External Drainage (ED) and only total CE were excluded. Patients' files were evaluated retrospectively in terms of age, sex, application complaints, physical examination findings, family history, diagnostic tests, treatment methods and results. Ultrasound (US), Computed Tomography (CT), Magnetic Resonance Cholangiopancreatography (MRCP), Percutaneous Transhepatic Cholangiography (PTC) and Endoscopic Retrograde Cholangiopancreatography (ERCP) were used for diagnosis. The Todani classification was used for cyst typing

Surgical technique: Via right subcostal incision, cholangiography was performed initially to obtain detailed anatomical information about bile ducts. Dissection of the gallbladder fundus allowed us to reach the CC. Entering under the cysts serosa mostly allowed both the dissection continuing with a more a vascular plan and keeping away from the surrounding tissues. The dissection was advanced to the intrapancreatic region distally and the common bile duct was transected at the level where it merged with the pancreatic canal. Then dissection was advanced to the common hepatic canal level proximally. Before anastomosis, dilated bile ducts were irrigated with heparinized saline to clear the gallstones and checked for stenosis before anastomosis. After the cyst was removed totally, one of the hepaticoenterostomy methods: either hepaticojejunostomy or hepaticoduodenostomy was performed for biliary reconstruction. The anastomosis was performed at the level of the common hepatic canal, except in one patient with type IVb CC, underwent RYHJ, whose cyst was extending to the proximal portion of the common hepatic canal and involving the right hepatic canal. In this patient, the right and left hepatic canals were sutured to each other and anastomosed to the intestine as a single unit. In RYHJ, we replaced the 40 cm jejunal loop in a transmesocolic manner by keeping short (as possible as) in the supracolic region to ensure a straight course. Routinely, hepaticojejunal anastomosis was performed using the end-to-side method with being careful not to leave a blind loop longer than 0.5 cm. The fibrotic wall of the cyst was left and only the mucosa was peeled for safe dissection when necessary. Submucosal dissection was performed to protect the hepatic artery and portal vein around the portahepatis in some patients and to excise the cyst from the distal without damaging the pancreatic channel at the intrapancreatic region in other patients. In HD, anastomosis was performed with full-thickness interrupted sutures between the duodenum second part (2-3 cm distal to the pylorus) and the common bile duct. Mostly the duodenum mobilization was not required. Second part of the duodenum was prepared for the anastomosis with two stay sutures taken over the first part of the duodenum. To obtain a tension free anastomosis the duodenum was anchored to the liver.

The selection of biliary reconstruction procedure (HD or HJ) to perform for the patients with CC did not rely on any criterion (age, sex, type of cyst etc) in this study. All operations were performed by experienced pediatric surgeons and the hepaticoenterostomy procedure was chosen according to the surgeon's personal preference. However, with parallel to the developments in the literature, HJ has been preferred in most reconstruction surgery in latest years. Postoperative complications were classified as early (≤ 30 days) and late (≥ 30 days), according to the Clavien-Dindo classification. Postoperative complications were defined as cholangitis, pancreatitis, wound infection, biliary leakage, intraabdominal abscess, ileus, gallstones, liver abscess, and liver fibrosis [5]. Patients were fallowed up with regular intervals (every 6 months during the postoperative 3 years and then annually). While all patients evaluated to determine liver and bile duct conditions with physical examination, liver function tests, complete blood count, abdominal US and/or hepato-biliary scintigraphy on initial follow-up, on subsequent follow-up, investigations were done only in symptomatic ones. Patients who did not come for visits and discontinued follow-up were contacted by telephone. Complete follow-up results were obtained from 25 patients. Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows version 15 package software (SPSS, Inc., Chicago, IL, USA). Data were expressed as medians (min–max). Categorical variables were analyzed with the chi-square test or, where appropriate, Fisher's exact test. Continuous variables were analyzed with the Mann-Whitney U test. A p value lower than 0.05 was accepted as statistically significant for all analyses.

This study was approved by the Ethical Committee

Results

A total of 25 patients underwent hepaticoenterostomy with the diagnosis of CC. The female/male ratio was 2.5. The ages of the patients ranged from 7 days to 13.6 years, with a median of 2.7 years. Clinical presentation varied and the most common symptom was nonspecific abdominal pain (n=12). Although the classic triad of jaundice, abdominal pain and right upper quadrant mass was not seen in our any patient, a 6-month-old female patient presented with an acute abdomen because of cyst perforation. External drainage was performed promptly and definitive surgery was conducted 3 months later. Additionally,

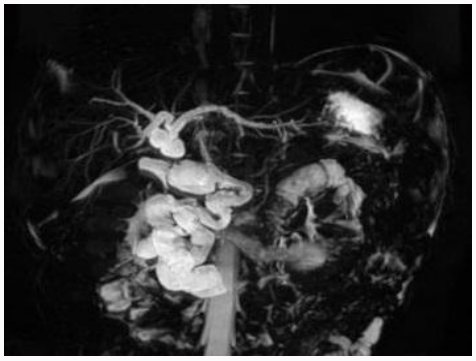

Figure 1: MRCP at the age of 1 year revealed severe stenosis in the hepaticojejunal anastomosis line and dilatation in the intrahepatic bile ducts.

Table 1: Summary of patientssex/age/ surgery/complications/follow-up.

	Sex	Age at operation	Type	Operation	Method	Short-term complications	Long-term complications	Followup (year)
1	M	1,8y	I	CE+HE	HJ	-	-	5
2	M	1,2m	I	CE+HE	HJ	-	-	5
3	F	7,6y	I	CE+HE	HD	-	-	13
4	M	3,6y	I	CE+HE	HJ	-	-	3
5	F	1,9y	I	CE+HE	HD	-	-	6
6	F	8,4m	I	CE+HE	HJ	-	-	7
7	F	1,1y	I	CE+HE	HJ	-	-	6
8	F	6,3y	I	CE+HE	HJ	-	-	6
9	F	1,9y	I	CE+HE	HJ	-	-	8
10	F	4,0y	I	CE+HE	HD	-	-	14
11	M	1m	I	CE+HE	HJ	-	Anastomatic structure	3
12	F	2,7y	I	CE+HE	HJ	Bile leakage	-	8
13	F	7,2y	I	CE+HE	HD	-	-	13
14	F	9,6y	I	CE+HE	HJ	Bile leakage	-	9
15	F	13,6y	Ivb	CE+HE	HJ	-	-	8
16	F	7,9y	I	CE+HE	HJ	-	Ileus	7.5
17	F	6,8y	I	CE+HE	HD	-	-	9
18	M	5,6y	I	CE+HE	HJ	-	-	4
19	F	4,2y	I	CE+HE	HD	-	-	15
20	F	8,7y	I	CE+HE	HD	Gastritis	-	14
21	F	2,1y	I	CE+HE	HD	-	-	14
22	M	2.5m	Ivb	CE+HE	HJ	-	-	9
23	F	2,5m	Ivb	CE+HE	HD	-	-	18
24	M	2,5m	I	CE+HE	HD	-	-	17
25	F	8,5m	I	CE+HE	HJ	-	-	11

y: Year; m: Month; F: Female; M: Male; CE: Cyst Excision; HE: Hepaticoenterostomy; HJ-Roux-en-Y: Hepaticojejenostomy; HD: Hepaticoduodenostomy

we learned ..... the reports that 2 patients had cholangitis and 2 patients had a pancreatitis attack before surgery, while they were asymptomatic at diagnosis. Laboratory findings revealed platelet and white blood cell counts were normal in all patients, but transfusion was required because hemoglobin was 6 gr/dl in one patient. Liver function tests included AST 27–134 mean 51.5 mU/L, ALT 16–125 mean 60 mU/L, and ALP 232–1938 mean 704 mU/L. At the time of admission, the ALP and GGT values were higher in 12 of the patients, even though the AST and ALT values were normal. US (n=25), MRCP (n=15), CT (n=10), ERCP (n=2), biliary scintigraphy (n=1) and PTC (n=1) were used as diagnostic modalities. US was preferred as the first radiological diagnostic method in all patients. While 24 patients were diagnosed correctly, duplication cysts/ hamartoma cysts could not be distinguished in one patient preoperatively by US. US also provided information about stones in the bile ducts (n=9), liver status and dilatation in the intrahepatic bile ducts (n=14). The typing of CCs was conducted by evaluating the surgical results and MR images of the patients. Accordingly, there were type I (n=22, 83%), and type IVb (n=3, 10%) in the patients. All patients underwent surgical treatment. Total CE+ hepatoenterostomy (HD/Roux-en-Y HJ) were performed according to the surgeon's personal preference. However, with parallel to the developments in the literature, HJ has been preferred in most reconstruction surgery in latest years. HD was performed in 10 (40%)and HJ in 15 (60%) patients (Table 1).

Table 2: Post-operative complications.

	HD (10)	HJ (15)	Total (25)	P
Cholangitis	0	0	0	
Pancreatitis	0	0	0	
Biliary Stone	0	0	0	
Intrapancreatic Stone	0	0	0	
Malignancy	0	0	0	
Bile gastritis	1(10%)	0	1(4%)	
Anastomotic Stricture	0	1 (6,6%)	1 (4%)	1.000
Adhesive Intestinal Obstruction	0	1 (6,6%)	1 (4%)	1.000
Bile leakage	0	2 (13,2%)	2 (8%)	1.000

Intrahepatic non-cystic dilatation was found in seven patients (28%) by preoperative imaging. In six patients (24%), numerous gallstones were found inside the cysts during surgery. The size of the removed cysts was ranged from 3 cm to 12 cm, average 6.2 cm in diameter. Operations were completed in average of 4 hours (3- 6.5 hours). The HD duration was shorter than HJ (3.2 versus 5.3 hours) ($p < 0.046$). Patients were fed within 3–10 days, with an average of 5 days. They were discharged in 5–14 days, 8.3 days on average. Postoperative complications were classified as short-term (≤ 30 days) and long-term (≥ 30 days), according to the Clavien-Dindo classification [5].

Table 3: Pre-operative characteristics of the patients in the two groups.

	HD		HJ		Total	
	n	%	n	%	n	P
Sex Female Male	 9 1	 50 14	 9 6	 50 86	 18 7	0.046
Type Type I Type IVb	 9 1	 42.8 33.3	 13 2	 57.2 66.7	 21 3	0.110
Dilatation of intrahepatic bile ducts	2	20	5	80	7	0.648
Preoperative cholangitis	0	0	2	100	2	0.494
Preoperative pancreatitis	0	0	2	100	2	0.494
Biliary stone	2	33.3	4	66.7	6	1.000
Elevated ALT, AST	4	36.4	7	63.6	11	0.500
Direct hyperbilirubinemia	2	33.3	4	66.7	6	1.000
Elevated GGT	4	33.3	8	66.7	12	0.666
Acholic stool	1	20	4	80	5	0.360
Associated anomalies	0	0	2	100	2	0.494

Postoperative complications were defined as cholangitis, pancreatitis, wound infection, biliary leakage, intra-abdominal abscess, ileus, gallstones, liver abscess, and liver fibrosis (Table 2). Bile leakage was found in two HJ patients, and gastritis was seen in one HD patient. All short-term complications were treated medically, with no need for surgery. As far as long-term complications, 10 HD patients had no complications, and there was also no gastric or hepatic reflux shown by hepatic scintigraphy in these patients. However, adhesions and anastomotic strictures were seen in HJ patients. İleus was seen 1 month after surgery and treated medically. Anastomotic stricture at the hepaticojejunal anastomosis line developed in only one patient (6%). This patient had undergone CE+HJ for a type I CC when 41 days old and was found to have preoperative elevations of transaminase, GGT and direct bilirubin together with intrahepatic bile duct dilatation. The serum values and intrahepatic bile duct dilatation improved postoperatively, but the transaminase and GGT levels increased without disturbed bilirubin levels. Intrahepatic bile ducts were dilated up to 4 mm starting from the third postoperative month. The growth and development of patients was normal, and there were no attacks of cholangitis during the follow-up period. The blood levels varied: ALT 49–205 U/L (0–56 U/L), AST 48–131 U/L (<81 U/L), GGT 85–425 U/L (<204 U/L). MRCP at the age of 1 year revealed severe stenosis in the hepaticojejunal anastomosis line and dilatation in the intrahepatic bile ducts (Figure 1). Then, re-exploration was planned. In the operation, we found that the anastomotic line had narrowed down to 2 mm and considered that resection of the stenotic region was necessary. Endoscopy used at operation, via a 7.5F cystoscopy, revealed no significant pathology other than the intrahepatic bile duct dilatation and re-anastomosis was performed. All serum values of the patient returned to normal by the second postoperative week, and the intrahepatic dilatation disappeared. Preoperative clinical, laboratory and demographic characteristics of the patients who underwent HD and HJ surgeries were compared (Table 3). Only the distribution rates of the male and female patients were different in the evaluation conducted, with a significance degree of $p<0.046$. However, no other statistical difference was found between the two groups in terms of the comparison criteria, and the groups were therefore accepted as comparable. Although the mean followed up of all patients was 14 years (range between 6 years and 18 years), it was longer in HD performed patients from HJ performed ones as seen in Table 1.

Discussion

Despite recent advances in surgical techniques and perioperative management, short- and long-term complications are not rare in children, but not common as in adults (6). Complications such as recurrent cholangitis attacks, malignant transformation, intracystic or intrahepatic gallstone formation, cirrhosis development, and pancreatitis are common in patients who do not receive surgery. Complete CE with biliary reconstruction is considered that the gold standard treatment of choice for CCs to avoid complications, but a complete consensus has not been reached regarding how bile drainage will be provided after the excision [7]. The competition between HD and HJ in this regard still continues. We evaluated our patients retrospectively who had undergone HD and HJ in this study, and whether it would support the literature in favor of HD. Preoperative clinical, laboratory and demographic characteristics of the patients who had HD and HJ surgeries were compared and only the distribution rates of the male and female patients were different in the evaluation conducted, with a significance degree of $p<0.046$. However, no other statistical difference was found between the two groups in terms of the comparison criteria, and the groups were therefore accepted as comparable. Anastomotic bile leakage, seen in two patients who underwent HJ (13%, 2/15) in the current study in the early postoperative period, has been reported in the literature that it often develops according the reason of surgical inexperience and severe inflammation (8). Diagnosis is usually made with the drainage of bile fluid from the catheter with US findings as in our patient, but in some cases, it can be difficult and delayed because symptoms are nonspecific (8). Additionally, imaging findings of US and CT cannot be differentiated from other causes of postoperative intra-abdominal fluid collection (8). At that time, gadobenate-enhanced MRCP, suggested by Chavhan et al (7), can be used to diagnose and considered accurately localize the site of bile leakage noninvasively (8). Bile leaks in the hepatoenterostomy line can be self-limited within a few weeks if they can be drained externally (7). Our patients were treated conservatively and recovered spontaneously within 7–14 days and the follow-up period was uneventful. Reoperation is suggested only after the failure of conservative treatment (7), we did not have to. Norayan et al demonstrated that bile leakage rates following HJ and HD were 2.94% (6/204) and 2.1% (7/330), respectively, with no statically significant difference (7). In our study its incidence was higher and compatible with the literature on HJ patients but with no statically significant difference between HD and HJ. Adhesive intestinal obstruction, common seen after intra-abdominal surgery (8), was seen in one patient (6%) in the HJ group as a long-term complication and was not encountered in the HD group. These patients should be closely observed for any sign of deterioration after initial management (8) and, despite the optimal time of surgery has not been clearly defined it should be known that in the absence of clinical improvement, observation longer than 48 h increases the risk of bowel necrosis and bowel resection (9). Our patient did not require surgical intervention and was treated medically. Furthermore, in HJ, it is necessary to pay particular attention to the length and placement of the Roux loop during biliary reconstruction (10). Adhesive intestinal obstruction is a complication that is usually expected in patients who have undergone HJ and is reported at a rate of 3–5.1% in the literature, similar to our series (7, 11). Stricture at the hepaticojejunal anastomosis line developed in only one patient (6%) in this study. MRCP at the age of 1 year revealed severe

stenosis in the anastomosis line and dilatation in the intrahepatic bile ducts (Figure 1). It is reported that the improvement of surgical skills, preservation of blood supply, no or mild cyst wall inflammation, and construction of wide (larger than 1 cm) and tension-free stoma are key factors to reduce anastomosis-related complications [12]. The incidence is reported to be 1.7% to 7.3% in the literature [13-15]. Stricture development can be the result of chronic inflammation and mucosal peeling, and this may be the reason for the higher rates of stricture at advanced age [15]. However, it seems difficul to explain the stricture development in our case with chronic inflammation, as the surgery took place at the age of 41 days. We consider that devascularization in the anastomosis line may be reason. Additionally, it is recommended that there should be no delay in surgical or endoscopic intervention once biliary obstruction develops postoperatively, but a great deal of planning and a thoughtful workup is required. Some investigators recommend that PTC and balloon dilatation in the treatment approach [16]. Whereas, it is considered that recurrent anastomotic strictures may occur due to fibrosis, even after balloon dilatation with PTC, and repeated cholangitis may cause multiple intrahepatic biliary strictures, recurrent hepatic stones and development of biliary carcinoma. Hence, especially in young patients, revision of the HJ followed by ductoplasty is recommended to create a wide stoma for sufficien bile drainage [12]. We operated on the patient, resected the stenotic region and made a wider re-anastomosis for the biliary reconstruction. The intrahepatic dilatation disappeared by the second week postoperatively. The next follow-up of the patient was uneventful. Although the belief that the postoperative ascending cholangitis rate will be higher in patients who undergo HD causes most surgeons to prefer HJ, there is little data to support this notion [13]. Postoperative cholangitis is reported at a rate of 1.7% to 4.9% and is said to be caused by bile stasis, stenosis in the bile duct or anastomosis line, a small anastomosis, or reflux of intestinal content into the biliary ducts [11,17]. Cholangitis was not seen in any of our patients, especially in the HD group in which it was thought and expected to occur. Another point of comparison between the two methods is postoperative duodeno-gastric reflux. Bile reflux is not expected to develop in patients who undergo HJ due to the nature of the surgery. Gastritis due to bile reflux into the stomach is reported in up to 33.3% of HD patients [18,19]. Besides, Santaro et al. [13] reported that HD did not cause symptomatic bile gastritis, as their anastomosis is sufficientl far from the pylorus and not tense thanks to their use of the wide Kocher manoeuvre. Unlike Santore however, we performed the anastomosis close to the second part of the duodenum to avoid excessive duodenal dissection in our patients with an adequate common hepatic canal length. Gastritis was seen in the early postoperative period in only one patient who was non-compliant with long-term follow-up, a lower incidence compared with the literature (6% of HD patients. The incidence of the development of biliary malignancy following CC excision is reported as 0.7% to 5.4%. The time to onset after primary surgical intervention is reported to be 1 to 34 years. The total excision of the cyst in the extrahepatic bile ducts significantly decreases the probability of a malignancy, although it does not eliminate it completely [20]. Malignancy was not found in the cyst material that was resected or during follow-up in any of the patients in this series. Even though there were two patients that only the mucosa could be excised by leaving the posterior wall of the cyst while performing CE+HJ. In our study in patients with total CE+HD, there were no long-term complications and also it was confirmed by hepatic scintigraphy that there was neither gastric nor hepatic reflux

Although, no statistical difference was found between the HD and HJ groups in terms of the above stated complications in our series, the only significant statistical difference was found in operation times ($p<0.039$). The main limitations of our study are patient number and retrospective format. So, apart from randomized trials, studies with long-term follow-up are also necessary to explore the benefits of HD or HJ in the management of CCs.

Conclusion

HD surgery has advantages such as being more physiological, taking a shorter time, having a lower risk of adhesive intestinal obstruction and allowing the evaluation of bile ducts by endoscopy when necessary. The disadvantages are the theoretical possibility of ascending cholangitis and duodeno-gastric reflux, which were not seen in our series in long-term follow-up periods. The basic advantage of HJ surgery is the lack of duodenal content reflux into the bile ducts and bile reflux into the stomach. The disadvantages are it is more complicated, takes longer, and there is a higher possibility of adhesive intestinal obstruction together with duodenal ulcer development and fat malabsorption. Based on this information, we consider that our study strongly supports that HD can be replace HJ for surgical treatment of CCs.

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