Kasai Hepatoportoenterostomy for Biliary Atresia in Children: Technical Notes and Details of Perioperative Therapy

Alessandro Boscarelli*

Paediatric Surgery Unit, Giannina Gaslini Children's Hospital and Research Institute, Genoa, Italy

Abstract: Biliary atresia is a progressive obliterative cholangiopathy of neonates, which causes jaundice and can lead to end stage liver disease. Despite recent improvements, Kasai hepatoportoenterostomy remains the standard surgical procedure to re-establish bile flow in these patients to date. Nevertheless, the majority of children with biliary atresia ultimately undergo liver transplantation. Herein, technical notes and perioperative therapies in children undergoing Kasai operation are reported.

Keywords: Biliary atresia, Kasai hepatoportoenterostomy, Jaundice, Children, Liver transplantation.

INTRODUCTION

Biliary atresia (BA) is a neonatal cholangiopathy, which leads to progressive fibrosis and obliteration of the extrahepatic and intrahepatic bile ducts and may hesitate in end stage liver disease within the first year of life [1]. The incidence rate is approximately 1 per 10000 live births, and it is highest in Pacific Area [2, 3]. First hepatoportoenterostomy (HPE) for treatment of BA was accomplished by Japanese surgeons Kasai and Suzuki in 1959. To date, Kasai HPE remains the first treatment choice for BA in the liver transplantation era [4].

TECHNICAL NOTES

Under general anesthesia, the patient is positioned in dorsal decubitus with a small transverse roll under the back. After appropriate surgical site preparation, a right subcostal incision is performed extending from the costal margin to the lateral border of the left rectus muscle ("Chevron incision"). If the diagnosis is not immediately obvious by inspection of the liver and biliary tract, an intraoperative trans-gallbladder cholangiography should be executed using a small feeding tube (4Fr) secured by a non-absorbable purse-string suture. A "bulldog" clamp on the common bile duct could be necessary to allow proximal passage of contrast into intrahepatic ducts. Other concomitant anomalies, which may alter the surgical approach, must be excluded. An open or tru-cut liver biopsy is usually performed at this stage, and it is sent for histological examination to confirm the diagnosis and assess the stage of liver disease. Liver mobilization is then accomplished by section of the falciform, coronary, and right and left triangular ligaments. A progressive dissection starting from the remaining gallbladder is performed to expose and isolate the extrahepatic bile duct. Hepatic arteries (right and left) and the portal vein are identified, carefully isolated and dissected till to their entrance into the liver. The distal common bile duct is ligated and divided, and the proximal part elevated to continue a gradual dissection toward the porta hepatis. Once the porta hepatis is reached, biliary remnant is removed and porta hepatis is now incised using scissors or surgical scalpel to obtain a bile extravasion. Notably, the transection of the fibrous tissue should be extended to the level of the posterior wall of the portal vein. Moreover, hemostasis by cauterization should be avoided but eventual perforating branches of the portal vein can be ligated with 5/0 non-absorbable suture. The porta hepatis is then packed and the liver replaced into the abdominal cavity. The jejunum is divided using a linear stapler approximately 10-20 cm distal to the ligament of Treitz. A Roux loop is constructed at about 40 cm along the anti-mesenteric border with 5/0 absorbable suture and the distal end is brought up to the porta hepatis through a right-sided window in the transverse mesocolon. Notably, to avoid an eventual internal hernia, the mesenteric defect should be obliterated with absorbable interrupted sutures. The end-to-end or end-to-side anastomosis at the porta hepatis is then made with running or interrupted 5/0 or 6/0 absorbable suture (Figure **1**). The mesocolic window is secured around the Roux loop with absorbable interrupted sutures, and the liver is finally relocated into the abdominal cavity. A drain through the foramen of winslow can be left or not. The abdomen is closed in layers [5-7].

*Address correspondence to this author at the Paediatric Surgery Unit, Giannina Gaslini Children's Hospital and Research Institute Via Gerolamo Gaslini 5, 16147 Genoa, Italy; Tel: +39 010 56362217/2392;
Email: tboscar@hotmail.it

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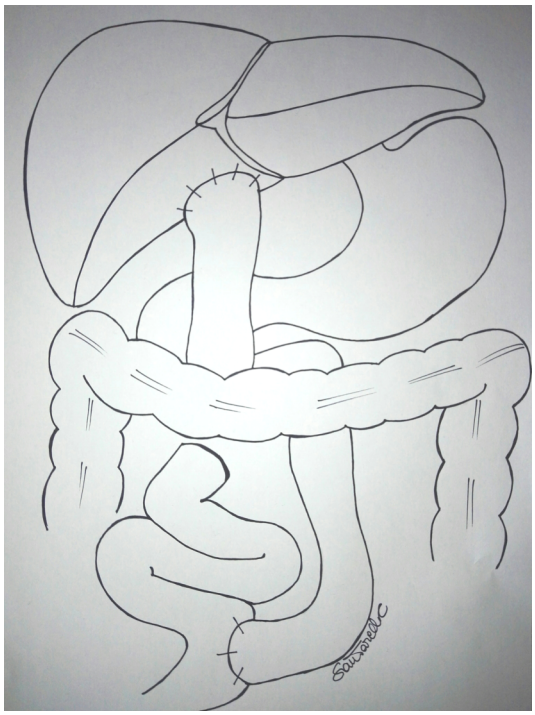

Figure 1: Schematic representation of Kasai hepatoportoenterostomy.

PRE-OPERATIVE THERAPY

- **Nutrition:** Pregestimil or Pepti-Junior
- **Oral fat-soluble vitamins:**
  - Vitamin A 2500-5000 UI daily
  - Vitamin K 1-2 mg daily
  - Vitamin D 30-50 ng/kg/day
  - Vitamin E 100 mg daily

* *ensure vitamin doses are regularly adjusted according to growth and vitamin levels*

INTRA-OPERATIVE THERAPY

- **Antimicrobial prophilaxis:**
  - intravenous Cefazolin 30 mg/kg/dose, continued six hourly for 72 hours
- **Intravenous fluid management**

POST-OPERATIVE THERAPY

- **Oral fat-soluble vitamins:** see pre-operative therapy
- **Long-term oral cholangitis prophylaxis:**
  - co-trimoxazole 2mg/Kg/day as trimethoprim component

* *ensure co-trimoxazole dose is regularly adjusted according to weight*

- **Steroid therapy:**
  - intravenous methylprednisolone 20 mg daily, decreasing by 2.5mg daily until 5 mg/day then stop
  - oral prednisolone 5 mg daily for one further week
- **Complementary therapies:**
  - oral ursodeoxycholic acid 20mg/kg/day in divided doses
  - oral esomeprazole 0.4-0.8 mg/Kg daily

Figure 2: Pre-, intra-, and post-operative therapy in children undergoing Kasai procedure for biliary atresia.

DETAILS OF PERIOPERATIVE THERAPY

Neonates undergoing investigation for cholestatic diseases such as BA should commence a specific nutritional (with an increased percentage of medium chain triglyceride) and fat-soluble vitamins support as soon as possible. In particular, Pregestimil or Pepti-Junior which contain 40-50% of fat as medium chian triglyceride is recommended. Notably, oral fat-soluble vitamins are commonly continued following Kasai HPE for at least 3 months after the resolution of jaundice. Intraoperatively, an intravenous (IV) antimicrobial prophylaxis is usually started and continued six hourly after surgery for 72 hours. Moreover, although refeeding is rapidly initiated after the operation, an initial IV fluid therapy is also necessary. Current evidence for post-operative management of children with BA supports the idea that steroid therapy has a significant benefit in reduction of bilirubin levels and resolution of jaundice with a positive impact on outcomes. Thus, a high-dose steroid therapy with IV methylprednisolone, and then oral prednisolone is administered in the post-operative period. On completion of antibiotic coverage, a long-term oral cholangitis prophylaxis with co-trimoxazole is commonly prescribed before discharge from hospital and continued for 12 months. Lastly, ursodeoxycholic acid seems to have beneficial effects on cholestasis [8, 9]. Specific therapeutic details are reported in Figure **2**.

DISCUSSION

Biliary atresia (BA) is a congenital progressive obstructive cholangiopathy which can lead to end stage liver disease if not corrected. Even if several studies have been carried out to determine the underlying pathogenesis of BA, the effective etiopathogenesis remains still unknown [10, 11]. Three macroscopic forms of BA have been described. In particular, type I affecting the distal common bile duct (5%), type II affecting only the common hepatic duct (2%), and type III affecting the right and left hepatic ducts and the gallbladder (>90%) [1]. The diagnosis of BA might be suspected at prenatal ultrasound (US) scan and confirmed after birth if a typical clinical triad characterized by conjugated hyperbilirubinemia, pale stools, dark urine, and hepatomegaly at US imaging are present. Nonetheless, intraoperative trans-gallbladder cholangiography and a liver biopsy are mandatory to confirm the diagnosis of BA and assess the exact stage of liver disease [12].

The standard corrective operation for BA in children is Kasai HPE. The objective of this procedure is to re-establish bile flow by an intestinal Roux-en-Y limb anastomosed to the porta hepatis. Current evidence suggests that pre-operative prognostic predictors of negative outcome are a greater degree of liver fibrosis and later age at Kasai HPE. On the other hand, the

best results are obtained if the Kasai HPE is performed before three months, and particularly in toddlers operated before two months of life [6, 13]. Several surgeons tried to refine and improve outcomes of this technique over the years. For instance, in 1997 Hashimoto and colleagues performed a modification of Kasai HPE using cavitron ultrasonic suction aspirator (CUSA) to isolate biliary remnants and simplify enteric anastomosis, thus obtaining a complete and persistent biliary drainage [14]. In 2006, Kobayashi and colleagues tried to further ameliorate the surgical procedure placing interrupted 5-0 absorbable mattress sutures horizontally in the surface of the liver posterior to the remnant fibrous mass, concluding that a careful posterior anastomosis is crucial to improve the outcome expressly for less experienced surgeons [15]. Moreover, with the dawn of minimally invasive surgery, laparoscopic HPE is increasingly being performed with results and mid-term outcomes comparable with open HPE. A robot-assisted approach for Kasai HPE has also been reported in the literature. Despite this, the minimally invasive approach does not seem to improve the prognosis of these patients [16-18]. Interestingly, Kasai HPE does not adversely affect outcomes in terms of graft survival rates or general complications after liver transplantation (LT), and it could be useful to perform a redo-HPE in designated cases. Furthermore, while redo-HPE may increase the morbidity of an eventual LT, laparoscopic approach for redo-HPE could instead reduce the influence of reoperation on LT [19, 20]. In terms of post-operative complications, ascending bacterial cholangitis is the most frequent (70-90%), and can lead to serious liver damage. As already mentioned, current literature strongly supports the theory that high-dose steroid therapy may have a positive impact on post-operative outcomes. On the other hand, there is no study in literature to date providing adequate evidence regarding the benefit of prophylactic antibiotics in preventing post-operative cholangitis and consequently ameliorating HPE outcomes [21]. Even though, a recent study found out that Gram-positive bacteria account for almost half of the causative pathogens of cholangitis, and therefore the use of antimicrobials with activity against gram-positive pathogens is indicated for the empiric antimicrobial treatment of cholangitis in children with BA [22].

BA is actually the most common indication for pediatric LT due to the low 4-year survival rate (42%) after Kasai HPE. Children with BA typically require LT in case of severe malnutrition, portal hypertension and infection following Kasai procedure. However, the best timing of LT after Kasai operation for BA is not yet well-defined [23-25].

In conclusion, sixty years after the first hepatoportoenterostomy, the Kasai HPE remains the standard non-transplant operative treatment for BA in children. Although Kasai HPE increases survival of the native liver, it is usually the first-line of management and the majority of these patients ultimately requires liver transplantation.

CONFLICTS OF INTEREST

None to declare.

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