ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 7 | July - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

REVISITING THE ROLE OF KASAI'S PORTOENTEROSTOMY IN MANAGEMENT OF EXTRAHEPATIC BILIARY ATRESIA IN THE MODERN ERA OF LIVER TRANSPLANTATION

Hepatobiliary Surgery

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ABSTRACT

Aims: Though portoenterostomy buys time, progressive liver disease is inevitable in Extrahepatic Biliary Atresia. We carried out this study to rethink the role of Kasai's Portoenterostomy (KPE) in the era of Liver transplantation.
Methods: Records of patients who underwent KPE at a tertiary centre in Delhi during 2 years were reviewed. Statistical Analysis of data was done by percentages only.
Results: 28 Patients underwent KPE in 2 years. 2/11(18.1%) who were operated at <90 days were anicteric at 3 months, and 4/17(23.5%) who were operated at >90 days were anicteric. 10(35.7%) developed ascitis, while 13(46.4%) developed recurrent attacks of cholangitis. Majority 23(82.1%) of patients did not benefit irrespective of the age. Survival rate at 1 year was as low as 16/28(57.14%).
Conclusion: Rate of cure by KPE alone is unacceptably low. Most develop complications early in follow up. Except in cases of obvious unavailability of donor, liver transplant could be considered as primary treatment.

KEYWORDS

EHBA; Kasai's Portoenterostomy; Management; Role

INTRODUCTION

Extrahepatic biliary atresia (EHBA), is an important cause of cholestasis in infancy. If unrecognized, death is inevitable from cirrhosis of the liver at a median age of 12 months[1]. It has been more than half a century since Kasai introduced portoentersotomy in 1968 for the treatment of EHBA, and it has been the procedure of choice for long[2]. Since then it had improved the outlook of children suffering from this disease, helped in their further growth, and for a long time was the only ray of hope for children doomed with the disease. In the current scenario, though Kasai's procedure buys us some time, but It is widely assumed that with progressive liver disease, transplant is inevitable, and the long term outcome without transplant is uncertain[3]. Hence, we carried out this study with an objective to rethink about the role of Kasai's Portoenterostomy (KPE) in the era of Liver transplantation.

MATERIALS & METHODS

Our study was retrospective in design. We reviewed the medical records and operative notes of all patients who underwent KPE from January 2017 to December 2018, in the department of Pediatric Surgery at a tertiary care centre located in New Delhi.

Inclusion Criteria were: Portoenterostomy done at our centre and EHBA confirmed by histopathological report of the portal plate or intra operative cholangiogram.

Irrespective of the age in absence of gross clinical signs of Liver Failure, all patients with EHBA underwent standard Portoenterostomy procedure sticking to the fundamental principles of Kasai's operation including the excision of the fibrotic remnant of extra hepatic biliary tree and a 40 cm Roux limb anastomosed End to Side to Porta hepatis. No preoperative Liver biopsy was done for confirmation of diagnosis. A combination of clinical, laboratory findings and imaging were used to reach the diagnosis and proceed with surgery for EHBA, which is portoenterostomy. Portal Plate tissue were sent for histopathological examination which also confirmed the diagnosis of EHBA.

Exclusion criteria were: Pre operative signs of Liver failure such as Ascitis, Lab values: aspartate aminotransferase (AST) >50 IU/L, albumin <3.0 g/dL, International Normalized Prothrombin Ratio (INR) >1.2, and platelet count $<150\times 10^9$/L.

Post operatively all patients were managed with prophylactic administration of oral antibiotics, fat soluble vitamins for atleast 9 months, oral phenobarbitone for 3 months. For each episode of cholangitis identified by fever or jaundice, and also for other complications of portal hypertension and liver failure such as ascitis, patients were admitted and treated with intravenous broad spectrum antibiotics. All patients were followed up for at least one year.

A note was made of the patients' age at surgery, intraoperative signs of liver damage such as hepatomegaly with brown or green discoloration of liver, cholic stools passed during the post operative stay, icteric or anicteric at 3 months follow up, mortality and subsequent admissions required during the following year. The patients were grouped under two brackets: those operated at < 90 days, those operated at >90 days. All patients who passed cholic stools during their post operative stay, showed clearance of jaundice and anicteric with bilirubin levels <2g/dl at 3 months in follow up and did not require repeated admissions during the following year were labeled as improved or benefitted by Portoenterostomy.

RESULTS

Intraoperative liver condition and frequency of complications post surgery in each group <90days at surgery, >90 days at surgery are recorded in Table 1.

Out of 28 Patients who underwent Portoenterostomy, 11 (39.1%) were operated at <90 days of age, while 17 (60.7%) were operated at > 90 days of age due to late referral. Subsequently at the time of surgery, hepatomegaly with or without green or discoloration of liver was seen in 18 (64.2%) patients. 4 of the patients in whom above signs of Liver cirrhosis were seen belonged to <90 days group.

Post operatively, cholic stools were passed by 19 (67.8%) patients. 8/11 (72.7%) of patients who were operated at <90 days passed cholic stools while 11/17 (64.7%) of those operated at > 90 days of age passed cholic stools.

At 3 months follow up, only 2/11 (18.1%) patients who were operated at <90 days were anicteric with bilirubin levels <2 g/dL, and only 4/17 (23.5%) who were operated at >90 days were anicteric with bilirubin levels <2g/dL.

The main post operative complications requiring redmissions were ascitis, Recurrent Cholangitis. Most of these complications occurred within 6 months of Surgery. 23 (82.1%) developed complications. 10 (35.7%) developed ascitis, while 13 (46.4%) developed recurrent attacks of cholangitis.

Patients who never passed cholic stools, remained icteric at 3 months or developed above complications were considered as not benefitted. Majority 23 (82.1%) of patients did not benefit irrespective of the age at which they were operated. 11/23 (47.8%) of patients who did not benefit belonged to <90 days group, while 12/23 (52.2%) belonged to >90 days at surgery group.

Mortality was 5/11 (45.45%) patients in the < 90 days group and 7/17 (41.17%) in the >90 days group. Time of death ranged between 4 months to 10 months post surgery. Survival rate at 1 year was as low as 16/28 (57.14%).

DISCUSSION

EHBA is an idiopathic progressive disease leading to obliterative cholangiopathy starting in the perinatal period, ending up in Liver failure if left untreated. It is a Fatal disease [4] with significant incidence between 1 in 15,000 to 1 in 20,000 [5,6]

Being a progressive disease, Time of intervention has long been considered as a critical factor in the prognosis and outcome of patients with EHBA. Late referrals are a common problem not only in developing but also in developed countries, which delay intervention. Earliest surgery in current study was performed at age of 53 days, while the latest at the age of 240 days. The median age at surgery being 95 days which is relatively higher than those reported in some studies done overseas such as 56 in a study by Kerkar et al in 1997 [7]

In our study, for analysis, we classified our patients into 2 goups of <90 days or >90 days at the time of initial KPE. 11 were operated before 90 days while 17 were operated after 90 days. The median age at which children with EHBA are operated in developing nations is higher due to ignorance and late referrals. Hence we chose age at surgery cut off as 90 days to divide our groups. Out of 11 operated before the age of 90 days, 4 already had liver changes suggestive of fibrosis. Only 8 out of 11 (72.7%) of the patients operated early (<90days) passed cholic stools post operatively while in 3 out of 11 (27.2%) stools remained acholic. Only 2 out of 11 (18.1%) had cleared jaundice and were found to be anicteric at 3 months follow up. 4 of 11 patients developed ascitis, 7 of 11 had cholangitis. As a result, All 11 patients operated at age <90 days were labeled as not benefited by Portoenterostomy. This could be by chance as the sample size of our study is small, but it makes us question whether age at interventions is a significant determinant of prognosis in EHBA. Or may be landmark of poor prognosis according to age can be further extended to 120 days as all 4 of 28 patients labeled as improving or benefitted by KPE in our study were operated before 120 days.

Our jaundice clearance rate, which was 6/28 (21.4%) match more to the first period group from 1981 to 2009 in a study by Andrade WC et al [8]. Although they had much improved jaundice clearance rates in their second group from 2010 to 2016. Not all patients with cleared jaundice had a good outcome. Many worsened due to recurrent cholangitis and a relapse of jaundice, hepatic dysfunction & ascitis. This is also in concordance with the above mentioned study by Andrade WC et al.[8] The overall incidence of Cholangitis in our study is 46.4% (13 of 28). In some previous long term studies, 37% rate of cholangitis at 5 years with most patients having only a single episode have been reported [7]. Similar experience has been reported in other long-term studies [9,10], and recurrent cholangitis has also been described in some long-term survivors [9,11] Interestingly in our study, it was noted that all patients who developed Cholangitis developed within 6 months, while most of them 11 of 28 were admitted for same within 3 months. No new patient developed cholangitis in the following 6 months. Although a longer follow up is essential to see if they require admission further.

Also a long term follow up is essential to monitor growth of children, development of portal hypertension and chronic liver disease. There are no universally accepted criteria for defining long term success in EHBA. Even as per the minimal criteria we used to label the patient as improved or benefitted by Portoenterostomy, which is those who passed cholic stools in post operative period, cleared jaundice and anicteric at 3 months follow up and not requiring readmissions for 1 year in view of complications, only 5 patients were cured. Majority, that is 23 (82.7%) of 28 patients were not cured. Considering same, the role of KPE is to be questioned in treatment of EHBA.

Some may argue that it is unclear whether postoperative cholangitis is a predictor of poor outcome and it is unreasonable to consider these patients as not cured. But we believe if an episode of cholangitis occurs as early as 6 months, it very well demonstrates the ongoing inflammatory process, liver damage and poor outcome. This negative effect of cholangitis on survival and long term prognosis has also been noted by Houwen et al [12] and Vacanti et al [13]

Ascitis is an important sign of Portal Hypertension and liver failure. It was noted in 10 of 28 (35.7%) of our patients. These patients were obviously labeled as not cured by Portoenterostomy. Surprisingly, 3 of these patients developed ascitis during the post operative hospital stay thus delaying oral intake and discharge from hospital. In view of multi genesis of ascitis in patients of EHBA, we checked serum albumin levels in all these patients in the post operative period and found them to be low. These patients were managed with tapping and intravenous albumin administration along with diuretics such as intravenous furosemide or oral spironolactone. We believe early development of ascitis may be due to unmasking of previously existing liver failure. Other 7 patients developing ascitis are attributed to ongoing changes in the liver inspite of establishment of bile flow following portoenterostomy.

In reality, exactly how well a portoenterostomy drains bile into intestines is somewhat unclear as different authors use vague terms such as clearing of jaundice without defining whether this is clinical recovery or biochemical normalization of bilirubin levels. In our series, cholic stools were passed by only 19 (67.8%) patients which was a marker of successful establishment of bile flow. But not all patients who passed cholic stools were anicteric at 3 months follow up. 8/11 (72.7%) of patients who were operated at <90 days passed cholic stools while 11/17 (64.7%) of those operated at > 90 days of age passed cholic stools after surgery. While only 2/11 (18.1%) patients who were operated at <90 days were anicteric and only 4/17 (23.5%) who were operated at >90 days were anicteric at 3 months Follow up.

In the current study, the overall cure rate of EHBA by Portoenterostomy was found to be very low, only 5 of 28 (17.8%). According to previous literature, the operation offers long-term survival for decades without liver transplantation in about 25% of the cases [14]. Contribution of the experience of the surgeon carrying out the KPE to its success cannot be less emphasized. Ours is a centre with wide experience in kasai's surgery as can be expected in a tertiary care centre.

Houwen et al [12] and Vacanti et al [13] have reported survival rate of above 60% after Portoenterostomy with orthotopic liver transplant for impeding liver failure for long term palliation. Houwen et al in 1989 reported 17 survivors at 5 years of a total of 89 patients after Portoenterostomy, in 3 of which orthotopic liver transplant was required [12]. This is a significant number of patients who were saved from Liver transplant at an early age which justifies continuation of Portoenterostomy as the primary treatment for EHBA. But we would like to make a note of the fact that this report dates back to the year 1989. Significant advances have been made in transplant medicine since 1989. We agree that combined treatment of KPE and liver transplantation will promote the success rate remarkably. Repeated surgeries in all circumstances should be avoided as they can not only make the transplant operation more complex and risky, but also will negatively impact child's nutrition, growth and development.

Andrews et al [15] reported a 3-year survival rate of 75% after liver transplantation as the primary procedure. Hall et al [16] noted that first-year survival rates for patients with transplantation for EHBA were 60% to 88%. Except for the obvious unavailability of donor liver for children, in all other situations, the role of KPE can be questioned, and primary transplant in the presence of proper expertise should be considered for better survival, nutrition and growth.

Our study has two main limitations. Firstly, a longer follow up is required to see if recurrent attacks of cholangitis during first year adversely affect prognosis, and to see if any new patients develop complications in future. Secondly our sample size is small due to rarity of the disease.

CONCLUSION

This series shows that age itself is not a major determinant of prognosis after KPE as is preoperative Liver condition. Rate of complete cure by portoenterostomy alone is unacceptably low. Most patients develop significant complications early in follow up cannot be considered as benefitted by KPE. Except in the cases of obvious unavailability of Donor, Liver transplant should be considered as primary treatment in EHBA if proper expertise is available.

Table 1: Intraoperative liver condition and complications post surgery under different groups <90days at surgery, >90 days at surgery

Age at surgery	<90 days	>90 days
Total number of patients	11	17
Liver changes at surgery	4	14
Acholic stools	3	6
Ascitis	4	6
Recurrent cholangitis	7	6
Improving with Portoenterostomy	None	5
Anicteric at 3 months	2	4
Mortality within 1 year	5	7

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