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Research Article

Predictors of Outcome of Kasai Operation

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Abstract

Introduction: Kasai procedure is used commonly as the first line for treatment of biliary atresia (BA). Determination of the prognosis of patients with BA remains a significant matter as no single predictor appears to be obviously superior.

Aim: Assessing the predictors of success and failure of Kasai operation.

Patients and Methods: This study included 32 infants with BA divided in to 2 groups: successful Kasai group; 9 cases (28.1%) and failed Kasai group; 23 cases (71.9%). All patients subjected to full history taking, clinical examination, routine investigations. duodenal tube aspiration (DTA), and liver biopsy.

Results: Patients with successful than failed Kasai operation were sex and age matched ($P > 0.05$). Of the pre-operative clinical, laboratory, radiological and histopathological data; the GB contractility was significant higher in patients with successful than failed Kasai operation ($P < 0.001$). Polysplenia, jejunal atresia, positive family history were found only in those with failed Kasai and most of them had positive hepatic subcapsular flow (87%) and they were type III BA (87.0%) but without statistical significance. Most of those with successful Kasai had bile plugs in both bile duct and canaliculi (77.8%) and (8.7%) of those with failed Kasai had no visible bile plugs ($P < 0.05$). Ascending cholangitis were the most frequent post-operative complications (76.2%), followed by growth failure (50.0%), ascites and spontaneous bacterial peritonitis (SBP) (47.4% for each).

Conclusion: Absence of GB contractility and occurrence of ascending cholangitis are warning signs for failure of Kasai operation.

Keywords: *Biliary Atresia; Bile Plugs; Kasai Procedure*

Introduction

Biliary atresia (BA) is a hepatobiliary disorder characterized by obstruction of bile ducts associated with progressive sclerosing cholangiopathy. The etiology of such a cholangiopathy remains elusive, and BA seems to represent more a phenotype than a unique disease [1]. Diagnosis of BA is challenging as there is a high degree of overlap in clinical, biochemical, histological and imaging characteristics of BA and other causes of NC [2].

The disease is difficult to identify in the perinatal period. However, early diagnosis is essential, because hepatoportoenterostomy (HPE; the Kasai procedure), if performed in the first 2 - 3 months of life, could restore bile flow and may prevent deterioration of the liver disease [3].

The Kasai portoenterostomy has been the mainstay of treatment for BA with a success, defined by clearance of jaundice. Kasai procedure is used commonly as the first line of treatment but its long-term efficacy still remains controversial. About half of these children remain jaundiced and suffer from repeated attacks of cholangitis or variceal hemorrhage after HPE. Yet, even with successful HPE, more than 70% of children eventually develop cirrhosis and require liver transplantation [4].

Determining the prognosis of BA patients, remains a significant matter as no single predictor appears to be obviously superior. Early reliable prediction of prognosis of BA patients will be helpful to plan a long-term strategy for BA treatment in each patient: early referral to liver transplant center, optimization of nutritional and medical intervention, educating and counseling of the BA parents, etc [5].

Aim of the Study

The aim of this study was to assess the predictors of the success and failure of Kasai operation.

Patients and Methods

This study included 32 infants with BA admitted to the Pediatric Hepatology department, National Liver Institute, Menoufia University; divided in to 2 groups: successful Kasai group; 9 cases (28.1%) and failed Kasai group; 23 cases (71.9%). The study was approved by the Research Ethics Committee of the National Liver Institute, Menoufia University, Egypt.

All patients subjected to full history taking, clinical examination, routine investigations (liver function tests, complete blood count, abdominal ultrasonography). Duodenal tube aspiration (DTA), and liver biopsy. The diagnosis of BA was confirmed by intraoperative cholangiography (IOC) prior to Kasai operation.

The patients were followed up in the post-operative period and for 2 years post-operative for management of the patients and documentation of the occurred complications.

Statistical methodology

Descriptive results were expressed as mean ± standard deviation (mean ± SD) or number (percentage) of individuals with a condition. For Quantitative data, statistical significance among 2 groups was tested by Mann-Whitney U test. For qualitative data, significance between groups was tested by Chi-square test. Correlation was tested by Spermann test. Results were considered significant if P-value ≤ 0.05 (**, $p \leq 0.01$; and *, $p \leq 0.05$). Statistical analysis was done using SPSS statistical package version 18 on IBM compatible computer.

Results

Patients with successful and failed Kasai operation were sex and age matched ($P > 0.05$). Of the pre-operative clinical and radiological data the GB contractility was significantly higher in patients with successful Kasi than failed Kasai operation ($P < 0.001$), while there were no significant statistically difference between both groups according to other studied parameters. However; polysplenia, jejenoal atresia, positive family history were found only in those with failed Kasai and most of them had positive hepatic subcapsular flow (87%) and they were type III BA (87.0%) but without statistical significance (Table 1). On assessing the preoperative laboratory parameters, LFT and CBC parameters were comparable in patients with failed and successful Kasai (Table 2).

Parameters	Successful Kasai (n = 9)		Failed Kasai (n = 23)		P-value
Sex					0.960
Male	4	44.4%	10	43.5%	
Female	5	55.6%	13	56.5%	
Age of patient admission in days (Mean ± SD)	63.3 ± 19.5		62.47 ± 23.82		0.718
Age at Kasai in days (Mean ± SD)	74.82 ± 19.79		82.55 ± 26.89		0.463
Positive consanguinity	2	29.4%	6	14.3%	0.820
Positive family history	0	00%	2	8.7%	0.493
Polysplenia	0	00%	1	4.3%	0.525
Congenital heart diseases	2	22.2%	1	4.3%	0.119
Other GIT anomalies (jejenoal atresia)	0	0%	2	8.7%	0.361
Liver span (cm) (Mean ± SD)	7.58 ± 1.17		8.06 ± 1.34		0.512
Splenic length (cm) (Mean ± SD)	6.50 ± 1.28		6.16 ± 1.23		0.555
MT (mm) (Mean ± SD)	188.56 ± 73.85		181.94 ± 132.47		0.498
HAD (mm) (Mean ± SD)	709.69 ± 380.6		1114.48 ± 1114.72		0.904
Gall bladder					0.001
Non-contractile	1	11.1%	14	60.9%	
Atretic	5	55.6%	6	26.1%	
Non-visualized	0	00%	3	13.0%	
Contractile	3	33.3%	0	0%	
Positive TC- sign	3	33.3%	4	17.4%	0.327
Positive hepatic subcapsular flow	6	66.6%	20	87%	0.186
Intra-operative cholangiogram					0.149
Type I	1	11.1%	1	4.3%	
Type II	3	33.3%	2	8.7%	
Type III	5	55.5%	20	87.0%	

Table 1*: Preoperative parameters in BA patients with successful vs. failed Kasai.*

Parameters	Successful Kasai (n = 9)	Failed Kasai (n =23)	P- value
	Mean ± SD	Mean ± SD	
TB (mg/dl)	11.86 ± 5.45	11.28 ± 3.02	0.850
DB (mg/dl)	8.96 ± 3.96	8.25 ± 2.3	0.950
TP (g/dl)	5.44 ± 0.59	5.4 ± 0.67	0.721
Albumin (g/dl)	3.62 ± 0.22	3.29 ± 0.51	0.115
AST (U/L)	152.11 ± 54.32	212.35 ± 123.64	0.267
ALT (U/L)	84.33 ± 46.65	105.35 ± 81.45	0.722
ALK.ph. (U/L)	589.11 ± 211.43	509.09 ± 234.78	0.367
GGT (U/L)	1077.33 ± 501.87	748.70 ± 481.55	0.098
PT sec	12.07 ± 0.96	12.165 ± 1.28	0.847
HB (g/dl)	9.54 ± 1.12	9.72 ± 0.98	0.753
PLTs ($x10^3/\mu L$)	485.0 ± 219.59	458.70 ± 171.54	0.769

Table 2: *Preoperative laboratory parameters in BA patients with successful vs. failed Kasai.*

Concerning the preoperative histopathological findings, there was no significant statistical difference between patients with successful vs. failed Kasai as regards the histopathological findings (P > 0.05) except for visible bile plugs where most (77.8%) of those with successful Kasai had bile plugs in both bile duct and canaliculi and (8.7%) of those with failed Kasai had no visible bile plugs (P < 0.05) (Table 3).

Items	Successful Kasai (n = 9)		Failed Kasai (n = 23)		P-value
Hepatocellular multinucleation					0.415
Absent/rare	3	33.3%	12	52.2%	
Present	5	55.6%	7	30.4%	
Prominent	1	11.1%	4	17.4%	
Bile plugs					0.048
Absent	0	0%	2	8.7%	
Visible in bile duct only	0	0%	5	21.7%	
Visible in canalicular only	2	22.2%	0	0%	
Visible in bile duct and canalicular	7	77.8%	16	69.6%	
Degree of ductular proliferation					0.872
No proliferation	0	0%	1	4.3%	
Mild	2	22.2%	4	17.4%	
Moderate	5	55.6%	11	47.8%	
Marked	2	22.2%	7	30.4%	
Steatosis					0.523
Absent/rare	8	88.9%	20	95.2%	
Less 50% of hepatocytes	1	11.1%	1	4.8%	
More 50% of hepatocytes	0	0%	0	0%	
Extracellular hematopoiesis					0.229
Absent/rare	7	77.8%	18	78.3%	
Present	1	11.1%	5	21.7%	
Extensive	1	11.1%	0	0%	
Ductal plate malformation					0.361
Present	9	100%	21	91.3%	
Absent	0	0 %	2	8.7%	
Portal cellular infiltrate					
Absent/minimal	0	0%	3	14.3%	0.609
Mild	6	66.7%	10	47.6%	
Moderate	2	22.2%	6	28.6%	
Marked	1	11.1%	2	9.5%	
Acute cholangitis					
Absent	7	77.8%	18	78.3%	0.568
Present in occasional ducts	2	22.2%	3	13.0%	
Marked	0	5.7%	2	8.7%	
Hepatocellular necrosis					
Absent	1	12.5%	5	22.7%	0.144
Few hepatocytes	3	37.5%	14	63.6%	
Many hepatocytes	4	50.2%	3	13.6%	
Periductular neutrophils					
Absent	2	22.2%	3	13.0%	0.708
Present in occasional ducts	5	55.6%	12	52.2%	

Marked	2	22.2%	8	34.8%	
Mononuclear inflammatory cells in the ducts					
Absent	2	22.2%	5	22.7%	0.401
Present in occasional ducts	5	55.6%	7	31.8%	
Multiple	2	22.2%	10	45.5%	
Pseudorosette formation					
Absent/rare	0	0%	3	13.0%	0.302
Present	3	37.5%	12	52.2%	
Prominent	5	62.5%	8	34.8%	
Hepatocellular swelling					
Absent/rare	4	44.4%	7	31.8%	0.776
Less 50% of hepatocytes	3	33.2%	8	36.4%	
More 50% of hepatocytes	2	22.2%	7	31.8%	
Lobular fibrosis					
Absent	9	100%	21	95.5	0.516
Present	0	0%	2	4.5%	
Prominent	0	0%	0	0%	
Portal fibrosis					
Absent or portal expansion of some portal tracts	0	0%	1	4.3%	0.595
Fibrous expansion of most Portal tracts	3	33.3%	4	17.4%	
Focal porto-portal bridging	3	33.3%	6	26.1%	
Marked Bridging	2	22.2%	11	47.8%	
Cirrhosis	1	11.1%	1	4.3%	
Portal tract edema					
Present	9	100%	20	87.0%	0.225
Absent	0	0%	3	13.0%	

Table 3: *Preoperative histopathological findings in BA patients with successful vs. failed Kasai.*

Short term post-operative complications documented during follow up, were ascending cholangitis (76.2%); the most frequent one, itching (11.1%), Sepsis (43.8%), cholangitic abscess (6.7%), and surgical complications occurred in (12.5%); burst abdomen (6.25%), intestinal obstruction (3.125%) and PVT (3.125%). Long term complications observed were; growth failure (50.0%), ascites and spontaneous bacterial peritonitis (SBP) (47.4% for each), encephalopathy (42.1%), varices (41.9%), GIT bleeding (31.6%), biliary cystic lesions (13.3%), and focal lesions (cirrhotic nodules) (5.6%).

Regarding the outcome of the failed Kasai patients 45% of them still living by their native liver and 55% died.

Discussion

Since its introduction in 1957, HPE has become the primary treatment of choice for BA. Kasai portoenterostomy can achieve complete clearance of jaundice, restore excretory and synthetic liver function, and enable healthy growth and development, although this outcome is neither certain nor predictable from the outset. Success of the Kasai procedure is defined by achieving a total serum bilirubin concentration of less than 2 mg/dl in the first three months post drainage [6].

In the present work, we studied the preoperative parameters to show which of them had any significant impact on Kasai prognosis like age, sex, family history, consanguinity and clinical, laboratories, and ultrasound. We found that there were no significant statistical difference between patients with successful vs. failed Kasai as regards these studied parameters, however the age at kasai in patients with failed Kasai were older than those with successful Kasai but not statistically significant. It appears that age at surgery may not be a significant factor as has been made out in the past with regard to the surgical outcome. It was suggested that the guiding principle for prognostication should be the liver histology rather than the age of the patient [7]. In contrast, Superina., *et al.* 2011 reported that; it is undoubtful issue that age at presentation and operation is the first prognostic factor in success of the procedure. It has been shown that there is a significant decrease in successful bile drainage if HPE is performed after 60 days of life [8].

Regarding the ultrasonographic features contractile GB was present only in those with successful Kasai, while the other radiological findings were unremarkable. Of the preoperative histopathological findings, all patients with successful Kasai had visible bile plug in both bile duct and canaliculi and in Canaliculi only, while absent visible bile plugs was found only in those with failed Kasai. Davenport, 2006 said that, there are many factors, which will influence surgical outcome. Some are unalterable (e.g. degree of cirrhosis or fibrosis at presentation; absence of, or paucity of microscopic bile ductules at the level of section) and some are subject to change (e.g. surgical experience, untreated cholangitis) [9].

The present study reported that; ascending cholangitis was the most frequent post-operative complications, followed by growth failure, ascites and spontaneous bacterial peritonitis. The risk of early death or liver transplantation was significantly higher in BA patients who suffered from early cholangitis within 6 months post-Kasia operation [10]. Higher degrees of cholestasis showed definite correlation with poor surgical outcome and as individual predictor; early cholangitis had 89.0% specificity and 59.3% sensitivity in discriminating survivor BA or no-survivor BA [11]. Although about 60% of patients with BA could achieve complete jaundice resolution after hepatico-jejunostomy, liver failure the most serious complication of BA may continue to progress [12].

The main risks of complications during perioperative or postoperative period may be related to the young age of the infants at the time of operation, the associated hepatic impairment and the ongoing fibro-inflammatory nature of the disease. In addition, granulation tissue at the porta hepatis or growth of bowel epithelium onto the site of biliary tract resection may block the bile outflow [13].

Conclusion

Absence of GB contractility and occurrence of ascending cholangitis are warning signs for failure of Kasai operation.

Authors' Contributions

Mohamed Abdel-Salam El-Guindi, Hatem Abdel-Sattar Konsowa, Alif Abdel-Hakim Allam, Dina Shehata El. Azab, Tahany Abdel-Hameed Salem, Maha Moawad Allam, Haidy Mohammed Zakaria, were involved in the study concept and design, recruitment of patients, clinical management, follow up and data acquisition; Haidy M Zakaria performed the statistical analysis, designed the figures; all the authors reviewed and approved the manuscript.

Conflicts of Interest

None declared.

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