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Factors Affecting the Success Rate of Kasai Portoenterostomy

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Abstract

Introduction. Surgical repositioning of biliary drainage to the intestine (jejunum) through an artificial fistula (portoenterostomy) following surgical removal of extrahepatic residual biliary duct in biliary atresia, which is first proposed by Kasai has never been evaluated in our center. Thus, we run a study aimed to find out the success rate.
Method. We run a cohort study retrospectively enrolled subjects with biliary atresia consecutively. A review of histopathology was carried out, and focused on degree of fibrosis as well as cirrhosis. Obtained data were subjected to statistical analysis using Fischer test and logistic regression.
Results. Out of 15 subjects enrolled in the study, we found success management in five subjects based on three months of icteric free period. Using Fischer test, we found a significant correlation (p = 0.04) between degree of fibrosis and outcomes in 1-year period with relative risk of 4 (CI 95% 1.5–10.65).
Conclusion. Affecting factors in success rate of portoenterostomy remains unclear; degree of fibrosis might be the one. Different center reports different outcome as the histopathology characteristics varies in different center.

Keywords: *biliary atresia, portoenterostomy*

Introduction

The primary treatment in biliary atresia is surgical repositioning biliary drainage to the intestine (jejunum) through an artificial connection (portoenterostomy) following surgical removal of extrahepatic remnants residual biliary duct. This portoenterostomy which is a hepato-porto-enterostomy proposed in 1957 by Kasai and furthers attributed according to his contribution.
Among factors affecting, the success rate of this procedure is thought to be related to the prime time of surgery. A study in Japan concluded that baby with such a procedure carried out in less than 30 days of the early life and those with 30–90 days showed no significance, but should the procedure be carried out in more than 90 days period lasts with poor outcome.[16] Whilst in Europe, the success rate of Kasai portoenterostomy has been reported as much as 80% in subjects aged 60 days and influenced by the experience of surgeon in the establishment of biliary drainage to achieve a normal bilirubin level. The successes of Kasai portoenterostomy in the establishment of biliary drainage reaches only 20–30% should the surgical procedure is carried out in babies of more than 60 days old.[15]

Published studies in US and UK aimed to find out a correlation of the degree of fibrosis with the success of portoenterostomy concluded that the degree of hepatic fibrosis is just increased with increasing age. Hepatic fibrosis referred not solely to be the universal and primary problem encountered in biliary atresia, but played a role as the predictor in the success of Kasai portoenterostomy. With no Kasai portoenterostomy, the progress of hepatic fibrosis is just faster. Such a condition is reflected by the process of cirrhosis which has been observed in weeks of the early life. Yet the aetiologia of this fibrosis remains unclear. Immune and non–immune factors were thought plays a role in the pathogenesis of biliary atresia, leading to cholestasis and oxidative stress that induces the hepatic fibrosis in biliary atresia.

Achievement of the goal of portoenterostomy is observed by reduced bilirubin serum level back to normal, 15 years success is found in 90% of case and even up to fourth decade of life. Should postoperative level of serum bilirubin remain high and there is progressive hepatic cirrhosis, then the baby is not survived up to the first 2 years in the early life. It is known that should there a partial biliary drainage, then the hepatic destruction is found up to the puberty or adult life. Finally, 70–80% case following a success portoenterostomy requires liver transplantation as there is hepatic damage. Hence, such a procedure of Kasai portoenterostomy is then referred to a surgical procedure should be instituted to achieve optimal condition prior to liver transplantation.

Kasai portoenterostomy has never been evaluated in our center. Thus, we run a study aimed to find out the success rate and to find a guidance prior to such a procedure portoenterostomy to achieve the optimal condition.

Method

We run a cohort study retrospectively enrolled subjects with biliary atresia consecutively who treated in dr. Cipto Mangunkusumo General Hospital during period of January 2008 to May 2013 and Mitra Keluarga Kelapa Gading hospital during period of August 2012 to April 2013. Target population is subject diagnosed as biliary atresia in those two hospitals who met the inclusion. We used consecutive sampling method and 36 calculated subjects were

enrolled. We took data from medical record, prime the age of subject representing the time of surgery, pre– and three-month postoperative serum direct bilirubin level, preoperative histopathology findings focused on degree of fibrosis (according to Weerasooriya) and degree of cirrhosis (according to Laennec classification) were variables subjected to statistical analysis. The analysis was then instituted using unpaired categorical analysis with type 1 error was set to 5% and type 2 error was set to 20%. Ethical committee of FMUI and research bureau of RSUPN dr. Cipto Mangunkusumo General Hospital approved the study (No. 620/H2.F1/ETIK/2013, 7 October 2013).

Results

Twenty subjects who met the inclusion were enrolled in the study. Among these subjects, five was then excluded further as there were no paraffin block available. Such a procedure carried out in period of less than 90 days in nine subjects, whilst the next six in period of more than 90 days of life.

From histopathology point of view, grade II found in three subjects and grade III in twelve subjects. Cirrhosis grading with classification 0 found in three subjects, grade 4a in two subjects, grade 4b in two subjects, and grade 4c in eight subjects. The success rate of a procedure is seen in table 1 and 2.

Table 1 Subjects' characteristic

	n	Success rate	
		Success [n=5]	Failed [n = 10]
Prime time of surgery			
<90 days	9	3	6
>90 days	6	2	4
Degree of fibrosis			
Grade II	3	1	2
Grade III	12	4	8
Degree of cirrhosis			
0	3	1	2
4a	2	1	1
4b	2	0	2
4c	8	3	5

Table 2. Characteristic of serum bilirubin in subjects with biliary atresia

	n	Success rate	
		Success [n=5]	Success [n=5]
Bilirubin direct (mg/dL)	8.6 (±1.9)	8.0 (±2.2)	8.9 (±1.8)
Bilirubin total (mg/dL)	10.87(±2.3)	10.33(±1.43)	11.14(±2.66)
Gamma GT (U/L)	966 (±418)	1161 (±556)	868 (±321)

Using univariate analysis, we found no p value of each variable less than 0.25, thus no further multivariate analysis is carried out.

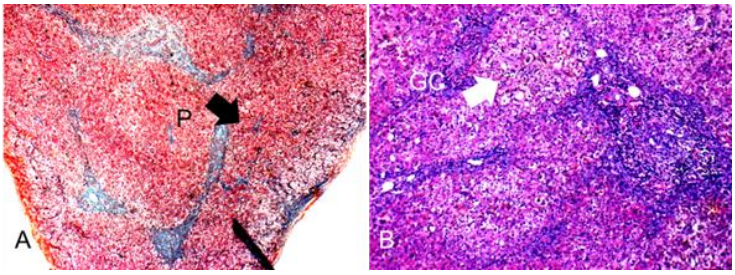

Figure 1. Histopathology findings A. using trichrome staining with objective lens magnification of five times and B. using hematoxylin and eosin with objective lens magnification of ten times; showing degree of fibrosis of the second grade with giant cell (GC). No nodule and bridging fibrosis found.

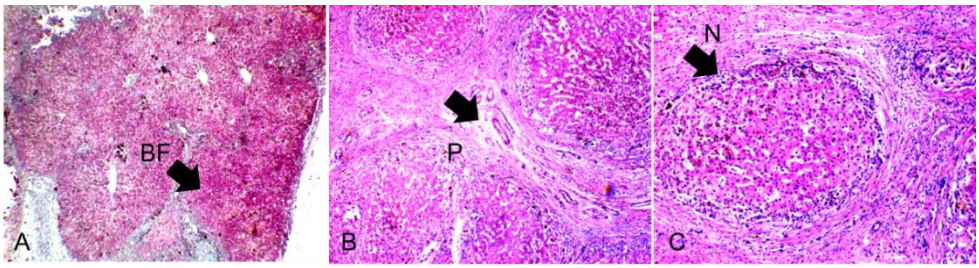

Figure 2. Histopathology findings A. using trichrome staining with objective lens magnification of five times and B. using hematoxylin and eosin with objective lens magnification of ten times; showing degree of fibrosis of the third grade with cirrhosis bridging fibrosis crossing portal vein (P) with cirrhotic nodule (N), bridging fibrosis (BF).

Table 3. Correlation between degree of fibrosis and outcome

	Outcome, mortality <1 year		
Degree of fibrosis	Survived in 1 year	Not survived in 1 year	Total
<Third degree	3	0	3
Third degree	3	9	12
	6	9	15

To find out the probability of a correlation between degree of fibrosis with the outcome which, is survival in first one year of life, we used Fischer test and found RR = 4, p value of 0.04 and 95% confidence interval 1.5–10.65 with power of 20% as seen in table 3. Fibrosis of the second degree found in three subjects, whilst third degree found in twelve subjects (see figure 1 and 2).

Discussion

The incidence of biliary atresia in 250 million Indonesian population with 2.5% of life birth is projected to 300–450 population per annum. Whilst in Jakarta with 10 million population the incidence is about 25 population per annum. We noted there were 10 biliary atresia admitted to dr. Cipto Mangunkusumo hospital annually. Based on data, there were babies with this kind of anomaly has been unmanaged due to lack of health referral system.

In the study we found out of fifteen managed with such a procedure, ten were baby girls; nine managed in less than 90 days old period. Three months icteric free which is representing the success of Kasai porto-enterostomy found in five subjects, or roughly up to 30%.

The success rate reported in Europe is 80% of babies managed in less than first 60 days of life. In contrast, the success rate for those who managed more than first 60 days is up to 30%.[16] Study of Weerasooriya and his coworkers in Washington University found that the success rate of Kasai portoenterostomy is up to 30% in babies less than 49 days. However, in our center we found 5/15 or roughly up to 33.3 %. Another study of Scoen and his collaborates found the success rate of those babies who managed with this Kasai portoenterostomy in less than first 75 days life period as much as 83% whilst in our center we found of roughly 27%. Scoen and his coworkers concluded that Kasai portoenterostomy might be done in more than 120 days period.

Tagge and his collaborates reported that those who managed more than 84 days period were found anicteric. Suruga and his collaborates also reports a better outcome of 40% babies who were managed in more than 90 days period.[8-11] These data shows that the different outcomes found in those studies lead to a simple thought that the prime time of surgical procedure influences the outcome.

Table 3 showing that the risk of death in babies aged less than one year with degree of fibrosis of the third grade is four times higher than those who had degree of fibrosis less than third grade. In the outcome analysis, we found those who survive in one year postoperatively with degree of fibrosis of the second grade is three out of three who were managed with Kasai portoenterostomy. Whilst, those with third grade of fibrosis shows nine of twelve subjects were not survives prior to one year postoperatively.

Though in the study we assumed that degree of fibrosis might influence the success of Kasai portoenterostomy, unfortunately we could not have concluded it as the power of the study is quite low due to insufficient number of samples enrolled. A published study of Schoen et al in Atlanta who review histopathology samples of Tan et al, found that there was no correlation between the prime time of surgery with the patency of portal duct or inflammatory response to success of Kasai portoenterostomy.
After Laennec, Scoen et al who reviews histopathology findings focused on fibrosis found that fibrosis of the first degree, inflammatory response found predominantly as fibrosis is not visible yet. However, in the study, we found mostly showed fibrosis of the third grade whereas bridging fibrosis found in >50% samples in addition to cirrhotic nodules. With this difference of histopathologic features represents information that degree of fibrosis might be contributed to the different success of Kasai portoenterostomy of biliary atresia in our center with study of Scoen et al. Further, study of Weerasooriya and colleagues who found that subjects with Kasai portoenterostomy that carried out in period ranged of 60–90 days showed fibrosis of third grade reach up 11 of 30 subjects, whilst those with fibrosis of second degree showed and managed in period ranged of 30–60 days reach up 14 of 30 subjects and fibrosis of the first grade showed and managed in period of less than 30 days reach up 5 of 30 subjects. However, in our study subjects with Kasai portoenterostomy that carried out in period ranged of 60–90 days showed fibrosis of third grade reach up 9 of 11 subjects and those who showed the second-grade fibrosis reach up 2 of 11 subjects. Should it be compared to study of Weerasooriya and colleagues, fibrosis of the third grade takes the first place. With the different of success rate to other studies in centers abroad with the perspective degree of fibrosis, then we could find that the nature of disease of biliary atresia cases managed in our center shows a progressivity of emerging fibrosis. This is seen in 9 of 15 subject with fibrosis of the third grade. Hence, is was thought that biliary atresia in Indonesia requires an earlier period to have Kasai portoenterostomy to be carried out.

Finally, we find a conclusion that biliary atresia in Indonesia should be detected earlier. This detection preferable to be carried out by liver biopsy when the icteric unresolved by 30 days, and prepared for Kasai portoenterostomy in less than 60 days period.
Another interesting focus in our study is fibrosis of the second grade with giant cells that might be related to the possible intra uterine infection. Somehow this was just an assumption that must be proven. Further study might be required to find out whether this giant cell influencing the success of Kasai portoenterostomy.

In their study, Weerasooriya and his coworkers found, that the outcome represented by the survival within a year following such a procedure in those with fibrosis of the second grade is 2 of 11 subjects, whilst in our center we found out 3 of 12 subjects. This was lead to a thinking about the possibility of fibrosis influencing the outcome; in one-year survival. Other studies showed that the prime time of surgery is not a factor influencing the success rate of surgery, but fibrosis influencing the outcome.

Subjects in our study were treated with ursodeoxycholic acid aimed to improve biliary drainage. Three times daily of 10mg/kg each commencing a day prior to Kasai portoenterostomy and continued postoperatively in addition to administration of prophylactic antibiotic an hour prior to surgery and continues five days postoperatively. Based on the Strategic to improve the outcome of biliary atresia from Dutch National Database, the Kasai portoenterostomy Kasai were performed prior to 60 days, referred to the first group; where those who treated in more than 60 days were classified as a group with delayed treatment found no difference between the two groups. Post Kasai portoenterostomy treatment is aimed to prevent ascending cholangitis spreads from microorganism of gut origin with the use of antibiotic. The administration of ursodeoxycholic acid following Kasai portoenterostomy with 20mg/kg/daily aimed to maintain biliary drainage results in reduction of serum bilirubin direct in a month postoperative. Should the reduction be less than 50%, the administration is then discontinued to minimize the complication that might be found. Other treatment has been reported is the administration of corticosteroid which, requires a further investigation to be treated as a protocol.

Conclusion

Finally, we resumed that the success of Kasai portoenterostomy is represented by the reduction of serum bilirubin level to normal in three-month period postoperatively. Degree of fibrosis is thought as an influencing factor that might be related to the outcome. Unfortunately, we could not find the evidence in the study as there were limitations in the study.

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