นิพนธ์ต้นฉบับ

Outcomes of Kasai Operation for Treatment of Patients with Biliary Atresia at a Tertiary Care Hospital

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บทคัดย่อ: ผลของการผ่าตัดด้วยวิธีของ Kasai ในการรักษาผู้ป่วยทางเดินน้ำดีตันที่โรงพยาบาลตติยภูมิ

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กลุ่มงานศัลยกรรม โรงพยาบาลขอนแก่น ตำบลในเมือง อำเภอเมือง จังหวัดขอนแก่น 40000

ภูมิหลัง: โรคท่อน้ำดีตัน เป็นโรคที่ไม่ทราบสาเหตุที่ทำให้เกิดการสลายและเกิดเป็นพังผืดของทางเดินน้ำดีภายนอกตับ ซึ่งเกิดการอุดตันของทางเดินน้ำดีในช่วงวัยทารก การผ่าตัดเพื่อแก้ไขให้มีทางเดินของน้ำดีระบายออกจากตับไปสู่ลำไส้เล็กได้ คือวิธีการผ่าตัดของ Kasai หรือการใช้ลำไส้เล็กส่วนต้นต่อเข้ากับขั้วตับ **วัตถุประสงค์:** เพื่อวิเคราะห์ผลลัพธ์ทางคลินิกของผู้ป่วยโรคท่อน้ำดีตันภายหลังได้รับการผ่าตัดด้วยวิธีของ Kasai ในช่วงเวลา 8 ปี **วิธีการ:** เวชระเบียนของผู้ป่วยโรคท่อน้ำดีตันที่ได้รับการผ่าตัดด้วยวิธีของ Kasai ที่โรงพยาบาลขอนแก่นตั้งแต่เดือนมกราคม 2557 ถึงเดือน ธันวาคม 2561 ถูกนำมาศึกษา ข้อมูลทั่วไป ลักษณะทางคลินิก การตรวจวินิจฉัยโรค การผ่าตัดและผลของการผ่าตัดถูกนำมาวิเคราะห์ **ผล:** ผู้ป่วย 26 ราย (ชาย 11 ราย หญิง 15 ราย) ที่ป่วยเป็นโรคท่อน้ำดีตัน เข้ามารักษาในช่วงเวลาที่ทำการศึกษา ผู้ป่วยมีอาการดีซ่านและอุจจาระสีซีด พร้อมกับมีค่ามัธยฐานของค่าบิลลิรูบินรวมอยู่ที่ 9.6 มิลลิกรัม/เดซิลิตร พบ triangular cord sign จากการตรวจด้วยอัลตราซาวด์ 23 ใน 25 ราย (ร้อยละ 92) ผู้ป่วย 17 รายได้รับการตรวจด้วย DISIDA scan ผลแสดงให้เห็นว่าไม่มีการขับของสารกัมมันตรังสีออกไปในลำไส้เล็กในผู้ป่วยทั้งหมดที่ได้รับการตรวจ (ร้อยละ 100) ผู้ป่วยทั้ง 26 รายได้รับการผ่าตัดด้วยวิธีของ Kasai เมื่อค่ามัธยฐานของอายุผู้ป่วย 90.5 วัน (พิสัย 35-171 วัน) ภาวะแทรกซ้อนที่สำคัญหลังผ่าตัดคือปอดบวมที่รุนแรง และการติดเชื้อในกระแสโลหิต ซึ่งเป็นเหตุให้ผู้ป่วยเสียชีวิต 6 ราย (ร้อยละ 23.1) ค่ามัธยฐานของบิลลิรูบินรวมลดลงเหลือ 9.6 และ 5.1 มิลลิกรัม/เดซิลิตร เมื่อตรวจติดตามผลหลังผ่าตัด 2 สัปดาห์ และการตรวจติดตามผลครั้งสุดท้ายตามลำดับ ผู้ป่วย 20 รายที่มีชีวิตรอดยังเป็นปกติดี พร้อมกับมีผู้ป่วย 9 ราย (ร้อยละ 45) ที่ภาวะดีซ่านหายไปอย่างสิ้นเชิง **สรุป:** การผ่าตัดโดยวิธีของ Kasai ยังคงเป็นหัตถการสำคัญที่ช่วยสร้างทางเดินน้ำดี เพื่อให้น้ำดีไหลจากตับลงสู่ลำไส้ ภาวะแทรกซ้อนที่สำคัญหลังการผ่าตัดในการศึกษาครั้งนี้คือ ปอดบวมที่รุนแรงและการติดเชื้อในกระแสโลหิต โดยเฉพาะอย่างยิ่งมักจะเกิดกับผู้ป่วยที่ผ่าตัดเมื่ออายุมากกว่า 3 เดือนขึ้นไป ผู้ป่วยบางรายประสบผลสำเร็จในการระบายน้ำดีลงไปได้ จนกระทั่งภาวะดีซ่านหายไปอย่างสิ้นเชิง

คำสำคัญ: โรคทางเดินน้ำดีตัน การผ่าตัดด้วยวิธีของ kasai, การต่อลำไส้เข้ากับเนื้อเยื่อขั้วตับ

Abstract

Background: Biliary atresia is an idiopathic fibro-obliterative disease of extrahepatic biliary tree that presents with biliary obstruction exclusively in the neonatal period. The operation to restore bile flow from the liver to the small intestine is Kasai operation or hepatic portoenterostomy. **Objective:** The aim of this study was to evaluate the clinical outcomes of patients with biliary atresia after Kasai operation in an 8-year period. **Methods:** Medical records of the patients with biliary atresia underwent Kasai operation at Khon Kaen Hospital during January 2010 to December 2017 were reviewed. Demographic data, clinical presentations, investigation, operative procedure and outcomes were analyzed. **Results:** Twenty-six patients (11 males and 15 females) with biliary atresia were treated during the study period. They presented with jaundice and acholic stool with median level of total bilirubin of 9.6 mg/dl. The

triangular cord sign was revealed from ultrasonography in 23 of 25 cases (92.0%). DISIDA scan was done in 17 cases and showed no excretion of the radionucleotide in the intestine (100%). All of the 26 cases underwent Kasai operation at the median age of 90.5 days (range 35-171 days). Major postoperative complications were severe pneumonia and septicemia that were the causes of death in 6 cases (23.1%). Median level of total bilirubin was decreased to 6.9 and 5.1 mg/dl after 2-week postoperation and the last follow-up respectively. All of the 20 survivors were doing well with jaundice disappearance in 9 cases (45%). **Conclusion:** Kasai operation is the principal procedure for creation of bile flow from the liver to the intestine. Major postoperative complications in this study were severe pneumonia and septicemia, especially occurring in the patients older than 3 months old at operation. Some cases had successful bile drainage until the jaundice was disappearance.

Keywords: Biliary atresia, Kasai operation, Hepatic portoenterostomy

Introduction

Biliary atresia is a condition leads to the most common indication for liver transplantation in children[1-6]. It is an idiopathic fibro–obliterative disease of the extrahepatic biliary tree that presents with biliary obstruction, exclusively in the neonatal period[6]. The operation to restore bile flow from the liver to the small bowel is Kasai operation (hepatic portoenterostomy–HPE)[7]. The overall incidence of biliary atresia is approximately one in 10,000 to 20,000 livebirths[1-5].

Althrough the incidence is low but biliary atresia is the most common indication for liver transplantation in children. Overall survival rate after Kasai operation is approximately 30 to 50% at five years[8]. There are controversies in treatment for this condition which many factors relate to clinical outcomes including the surgeons experience. This study aimed to describe the clinical outcomes of biliary atresia underwent the Kasai operation by young surgeons with experience less than 5 years at Khon Kaen Hospital, one of tertiary hospitals in Thailand.

Materials and Methods

This was a retrospective case review by identification of all medical records of patients with biliary atresia who were surgically treated and followed at Khon Kaen Hospital, Thailand, between January 2010 and December 2017. The protocol of this study was approved by Khon Kaen Hospital Review Board of Human Research (KE61056). All of the patients younger than 15 years old were included in this study without specific exclusion criteria. Demographic data, clinical presentation, investigations, operative procedure and outcomes of treatment were collected. Data analysis was performed by using STATA 14 software application. Categorical variables were summarized by using number and percentage for descriptive statistics. We described non-normally distributed variables by using median and range. Relative risk in this study was used chi square.

Results

Twenty-six patients, 11 males and 15 females, enrolled in the study. Their ages at operation ranged from 35 to 171 days (median 90.5 days). Clinical presentations included jaundice (26 cases), acholic stool (24 cases), dark urine (21 cases) and hepatospenomegaly (21cases), respectively (Table 1). Total bilirubin levels ranged from 3.3-19.2 mg/dl (median 9.6 mg/dl). Of the 26 patients, 16 cases (61.5%) had the evidence of coagulopathy (INR > 1.3). Ultrasonography of the hepatobilary system was performed in 25 cases and triangular cord sign was found in 23 cases (92.0%). Seventeen patients were investigated by DISIDA scan and the results were reported no excretion of the radionucleotide in the gastrointestinal tract in all of 17 cases (100%).

Table 1 Demographic data, symptomatologies and investigation of 26 patients with biliary atresia

Patients' data	(N = 26)
Gender	
Male : Female	11 : 15
Age at operation (days)	
Range (median)	35 – 171 (90.5)
Clinical presentations	
Jaundice	26 (100%)
Acholic stool	24 (92.3%)
Dark urine	21 (80.8%)
Hepatosplenomegaly	21 (80.8%)
Blood chemistry	Range (median)
Total bilirubin (mg/dl)	3.3 – 19.2 (9.6)
Direct bilirubin (mg/dl)	2.6 – 14.7 (8.0)
AST (U/L)	29 – 509 (187.5)
Imaging investigations	
Ultrasonography	25
Triangular cord sign	23 (92.0%)
DISIDA scan	17
No excretion of radio-nucleotide	17 (100%)

Intraoperative cholangiography (IOC) was done in every case with the evidence of complete obstruction of the extrahepatic duct. Hepatic portoenterostomy (HPE) or Kasai operation was performed in all of the 26 patients by using Roux-en-Y loop of the jejunum for anastomosis at the porta hepatis[7] (Figure 1). The median age at operation was 90.5 days or 3 months. None of the patients received steroid therapy after Kasai operation. All of patients underwent Kasai operation got liver biopsy simultaneously but the pathological report usually not described about liver cirrhosis.

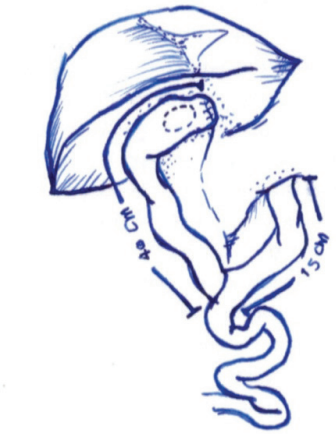

Figure 1 Diagram of Kasai operation (hepatic portoenterostomy)

Major complications included pneumonia, septicemia and ascending cholangitis in 14, 3 and 3 cases, respectively (Table 2). Six cases (23.1%) died after operation 103-171 days (median 150 days) due to severe pneumonia and septicemia (nosocomial infection). All of 6 dead cases were operated at the age over 12 weeks.

Table 2 Outcomes of the patients with biliary atresia after Kasai operation

Results of treatment	(N = 26)
Blood Chemistry examination after Kasai operation	
At 2-week follow-up	Range (median)
Total bilirubin	0.8 – 13.0 (6.9)
Direct bilirubin	0.4 – 10.9 (6.1)
AST	34 – 304 (132.5)
The last follow-up (range 1-36 months, median 4 months)	Range (median)
Total bilirubin	0.2 – 16.1 (5.1)
Direct bilirubin	0.1 – 14.2 (4.6)
AST	45 – 662 (111.5)
Complete jaundice disappearance	9
Recurrence jaundice	11
Complications	
Pneumonia	14 (53.8%)
Septicemia	3 (11.5%)
Ascending cholangitis	3 (11.5%)
Gastrointestinal bleeding	2 (7.7%)
Mortality	6 (23.1%)

Total bilirubin levels were decreased after Kasai operation at the 2-week follow-up (median 6.9 mg/dl) and the last follow-up (median 5.1 mg/dl). AST levels were also improved (Table 2). Complete jaundice disappearance was found in 9 cases (45%) and 11 of the 20 cases had recurrence jaundice again. Liver transplantation was not performed in all of them due to no adequate facilities to provide to these procedures.

Discussion

Biliary atresia is a relatively rare obstructive condition of the bile ducts causing neonatal jaundice. After Kasai HPE procedure had been done in 1959 and reported in 1968[8], some patients survived but results of the most cases were not satisfactory. The liver is progressive damage unit it develops cirrhosis and liver failure at last. Children with biliary atresia are the most common candidate for liver transplantation.

Infants with suspected biliary atresia should be investigated as soon as possible in order to perform HPE or Kasai operation within the age of 8 weeks for prevention of progressive liver cirrhosis. Hepatobiliary ultrasonography will exclude other surgical causes of jaundice such as choledochal cyst and inspisated bile syndrome. The findings of small gall bladder or absent gall bladder are compatible with biliary atresia. In some cases, a well-defined triangular area of high reflectivity is seen at the porta hepatis, corresponding to fibrotic ductal remnants that was called the triangular cord sign by Choi[9] in 1996. Approximately 92% of patients in this

study were noted to see this sign from hepatobiliary ultrasonography. Hepatobiliary scintigraphy by DISIDA scan has a high sensitivity and specificity to biliary atresia[10-12]. All of our 17 cases revealed the radionucleotide uptake in the liver without excretion into the intestine which was suggestive of biliary atresia. However, this special investigation can be done in some institute and takes some more time to do, not suitable for older infants. Erlichman[13] recommended to complete investigations within 6 weeks of age and patients older than 6 weeks old should be investigated within a few days. Patients should have definite diagnosis and undergo Kasai procedure within the age 8 weeks or 2 months. The present study was different from the standard guideline because most of patients were lately transferred from rural hospital to Khon Kaen Hospital. A half of patients in this study underwent IOC and Kasai operation at the age over than 12 weeks (median age 90.5 days or 13 weeks). Because of late HPE procedure in patients with over 3 months of age and progressive liver damage, 6 cases developed severe pneumonia and succumbed at last.

Patients in this study obtained good results of bile drainage after Kasai operation until jaundice was disappearance. However, some cases had complications of ascending cholangitis and developed recurrent jaundice after that. Erlichman[13] reported that ascending cholangitis was the most common complication following Kasai operation in the patients with successful bile drainage. Repeated attacks of ascending cholangitis caused progressive liver cirrhosis and portal hypertension. In this era, at least 50% of children with biliary atresia will undergo liver transplantation by the age of 2 years[13]. The survivors in this study do not have planning for liver transplantation because the follow-up period is short and the late complications of liver failure do not happen.

Conclusion

Kasai operation remains the principal procedure for treatment of biliary atresia and should be done within the age of 12 weeks. Patients with age at operation older than 3 months prone to have complications such as severe pneumonia and septicemia. The 20 survivors in this study are still doing well. Some cases have good results of bile flow and complete jaundice disappearance.

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