PTBD in the Treatment of Biliary Stricture after Liver Transplantation

Tiangu Yang¹, Yanhua Wang², Xiaowei Sun³, Rui Xu², Hui Zhao²

¹Qingdao University, 308 Ningxia Road, Qingdao, China

²Department of interventional medical therapy, The Affiliated Hospital of Qingdao University, 16 Jiangsu Road, Qingdao, China

³Department of radiology, Qingdao Commercial hospital, 6 Haibo Road, Qingdao, China

Abstract: The purpose is to evaluate effectivity and influence on hepatic function indexes of percutaneous transhepatic biliary drainage (PTBD) in the treatment of biliary stricture after liver transplantation. Twenty-six patients with biliary stricture after liver transplantation were selected as the subjects. Hepatic function indexes such as albumin, direct bilirubin, glutamate transaminase, and γ -glutamyl transpeptidase(y-GT) were compared before and after the PTBD. There was significant difference between pre-procedure and post-procedure albumin value (P < 0.05). Most of patients (21/26) showed improvement of direct bilirubin, glutamate transaminase, and y-GT, and relief of obstructive jaundice symptoms. PTBD shows good effectivity of relieving obstructive jaundice symptoms and reducing hepatic function indexes in patients with biliary stricture after liver transplantation. However, the decrease of albumin should also be concerned.

Keywords: PTBD, Biliary Stricture, Biliary Complications, Liver Transplantation, Hepatic Function Indexes

In recent years, liver transplantation had a great development, and it becomes the most effective treatment method for end-stage liver disease and hepatic benign or malignant tumor. Although its 5-year survival rate is known to be more than 70%, the incidence of biliary complications after liver transplantation is still high, $10\% \sim 40\%$, and its fatality rate is as high as 19%. Therefore, the biliary complications are one of the most important impact on long-term prognosis of liver transplantation (1).

PTBD is one of the main treatment methods for biliary complications after liver transplantation, especially in the treatment of biliary stricture. However, the efficacy and safety of PTBD have not been summarized according to the changes of hepatic function indexes. In this study, the efficacy and safety of PTBD were evaluated by comparing the hepatic function indexes before and after PTBD in patients with biliary stricture after liver transplantation.

Materials and methods: Patient characteristics:

The data of a total of 263 patients in organ transplantation center of our hospital between January 2016 to July 2018, who underwent liver transplantation, were collected. The primary diseases were mainly composed of hepatic malignant tumors, viral hepatitis cirrhosis, alcoholic liver cirrhosis, autoimmune liver disease, acute and chronic liver failure, congenital biliary atresia, malignant tumor of hilar bile duct.

All biliary complications occurred in 39 patients

between 15 days to 3 years after liver transplantation with the incidence of 14.8% (39/263). The kinds of biliary complications included 26 patients of biliary stricture, 6 patients of biliary fistula with infectious peritonitis, 4 patients of gallstones with biliary obstruction, 2 patients of biliary tract infection, and 1 patient of bile duct bleeding. The 26 patients who underwent PTBD for biliary stricture were finally included as the study patients and male to female ratio was 23: 3, and the median age was 54.2 years (between 21 to 71 years old).

All patients presented with jaundice symptoms such as skin yellowing, fever, pruritus and abdominal distension. Some patients (n=25) were hospitalized for changing drainage tubes after PTBD, only the first admission data were collected. All patients signed the informed consent and met the ethical requirements.

Analytic methods and statistics:

All patients were confirmed biliary stricture by imaging examine such as MRCP, ultrasound, CT during admission and follow-up review. Through comparing the changes of hepatic function indexes of the patients in the week before and the week after PTBD, the efficacy of PTBD was analyzed. Specific analysis indexes included albumin, direct bilirubin, glutamate transaminase, γ -GT. Paired-sample T test was applied to test the difference between indexes before and after the PTBD procedure.

This article is published under the terms of the Creative Commons Attribution License 4.0 Author(s) retain the copyright of this article. Publication rights with Alkhaer Publications. Published at: <u>http://www.ijsciences.com/pub/issue/2020-05/</u>DOI: 10.18483/ijSci.2332; Online ISSN: 2305-3925; Print ISSN: 2410-4477



Result:

For a total of 26 patients, liver function indexes which included albumin, direct bilirubin, glutamate transaminase, and γ -glutamyl transpeptidase showed recovery in 19 patients, no obvious changes in 4 patients, while deterioration in the remaining 3 patients.

Albumin level was normal range (n=20), decreased range (n=6) before PTBD. The albumin level showed increase (n=3), no change (n=16) or decrease (n=7) after PTBD. One patient showed a large decrease (from 41.83 to 16.11), which was restored to normal level after human blood albumin supplementation (p <0.05). Table 1 shows a scatter diagram in albumin.

Direct Bilirubin level was normal range (n=13), increased range (n=13) before PTBD. The direct bilirubin level showed no change (n=12), decrease (n=9) and slight increase (n=5) after PTBD (p > 0.05). Although the direct bilirubin kept its level, the biliary obstruction symptoms recovered in most patients. Table 2 shows a scatter diagram in direct bilirubin.

Glutamate transaminase level was normal range (n=17), increased range (n=9) before PTBD. The glutamate transaminase level showed increase (n=5), no change (n=16) or decrease (n=5) after PTBD (p > 0.05). No one showed liver severe damage or liver failure symptoms after PTBD. Table 3 shows a scatter diagram in glutamate transaminase.

 γ -Glutamyl transpeptidase level was normal range (n=20), increased range (n=6) before PTBD. The γ -glutamyl transpeptidase level showed increase (n=3), no change (n=20) or decrease (n=3) after PTBD (p >0.05). Table 4 shows a scatter diagram in γ -glutamyl transpeptidase.

The average duration of carrying the bile drainage tube was 6 months (between 1 month to 27 months). One patient underwent nasobiliary drainage and carried nasobiliary drain tube for one week after removing the drainage tube, and another patient underwent Roux-en-Y anastomosis after removing the drainage tube. The other (n=24) patients did not present with jaundice symptoms after removing the drainage tube. During follow-up, 10 patients changed drainage tube for several times (1 to 8 times) because of drainage tube blockage or malposition.

Four patients died; one of these patients died from acute upper gastrointestinal hemorrhage and shock with widespread tumor recurrence, who underwent splenectomy for reducing portal venous pressure. One patient died from tumor recurrence and multiple organ function failure. Direct bilirubin presented more than 200 umol/L when these two patients died, but their drainage tubes worked and their γ -GT at a slight increasing level. Two patients died from chronic hepatic failure with tumor recurrence, who had severe biliary obstructions with γ -GT of more than 1000 U/L. Table 5 shows the last unsuccessful procedure for

changing drainage tube in one of patient. The data showed that among three patients whose DB was more than 100 umol/L before PTBD, their DB increased after PTBD, two of them died within 6 months after procedure from hepatic failure and tumor recurrence, one of them patient is still carrying drainage tube for more than 3 months in serious condition.

Table 1. Preoperative albumin and postoperative albumin.



Table 2. Preoperative direct bilirubin and postoperative direct bilirubin.







Table 4. Preoperative γ -GT and postoperative γ -GT. _{γ -GT(U/L)}



Table 5. A patient had several times of changing drainage tube who died from chronic hepatic failure.





The last unsuccessful PTBD, γ -GT at a high level as more than 1000U/L

Table 6. A patient with left intrahepatic bile duct stricture, drainage tube was place into left intrahepatic bile duct.



The left intrahepatic bile duct showed no display

Drainage tube passed the part of stricture and placed into left intrahepatic bile duct.



Discussion:

The types of biliary complications after liver transplantation mainly include biliary stricture (anastomotic and non-anastomotic), biliary fistula with infectious peritonitis, stones with biliary obstruction, and Oddi's sphincter dysfunction. The risk factors related with biliary complications include T-tube biliary reconstruction, hepatic artery stenosis or thrombosis, Roux-en-Y anastomosis, cytomegalovirus infection, ischemia-reperfusion injury and primary sclerosing cholangitis. (2-3). Currently, the mainly treatment methods for biliary complications after liver transplantation include ERCP, PTBD, surgery (include resection, laparotomy, secondary liver liver transplantation) and conservative treatment (4-6).

ERCP is considered as the preferred way of dealing with biliary complications for a long time as it has its unique advantages of less trauma and lower complications; better indicated for low degree of obstructive jaundice, especially bile obstructive jaundice caused by bile stones. For the high degree of obstructive jaundice, however, PTBD seems to have higher effectiveness than ERCP (7). From the result of long-term prognosis and survival time, the efficacy is only associated with whether it is anastomotic biliary stricture or not (8). As ERCP plastic stents are prone to extrusion, deformation and secondary obstruction or shedding of plastic stent, it is suggested that PTBD has better curative effect than ERCP in biliary obstruction by compression of tumor recurrence.

PTBD, as one of the mainly methods to treat with biliary complications after liver transplantation, has a significant curative effect. It has a good opening effect for biliary tract obstruction and can effectively relieve obstructive jaundice symptoms, improve hepatic function, and regulate coagulation and immune function (9). The primary purpose of PTBD is to relieve symptoms of biliary obstruction.

From this study, we observed that there was statistical association between PTBD and the decreasing of albumin. On the one hand, most of patients who had obstructive jaundice symptoms, were already in malnutrition before PTBD, one the other hand, continuous external drainage of bile was against lipid and other nutriment absorbing. The lack of albumin would cause problems such as: seepage of puncture point, ascites, slowing would healing. It suggested that a proper albumin supplement and amino acid supplement are necessary, it also can facilitate removing albumin-bound molecules, such as redundant bilirubin.

Direct Bilirubin, which is transformed by liver cells and excrete through bile duct, has a varying degree decrease in most of patients. If drainage tube works, jaundice symptoms would be relieved within a week. This index is the most important evidence to assess the efficacy of PTBD. Although decrease of direct bilirubin after PTBD was not statistically different, biliary obstruction based on jaundice symptom improvement seemed relieved in most patients.

The another index which reflex the degree of biliary obstruction is γ -GT, which produced by liver cells, would countercurrent to blood when biliary obstruction happens. Even before jaundice symptoms present, it would increase more than 10 times above normal. When biliary obstruction relieves, it is also sensitive to decrease (10).

As for Glutamate transaminase, it indicated the damage of liver cells. The mainly increased reason of glutamate transaminase caused by biliary tract obstruction and cholestasis (11). During PTBD, although a part of liver cells would be damaged by puncture. It also requires taking attention to hepatic protection after the procedure. Preoperative planning of puncture route by MRCP before PTBD, reduction of puncture frequency and improvement of puncture success rate are also essential for safety. There was not statistically significant to prove the association(p>0.05), but glutamate transaminase was not increased in most of patients, it helped to recover hepatic function after PTBD from the damage of biliary obstructions.

PTBD has a role of improving liver function indexes in 69.2% (18/26) of the patients in this study. It has a good effect on relieving obstructive jaundice caused by simple biliary stricture after liver transplantation, and a better efficacy on direct bilirubin before reaching a high level (>50 umol/L). γ -GT can also sensitively reflect the degree of biliary obstruction and the effect of jaundice reduction. Therefore, hepatic function indexes should be monitored after liver transplantation, and abnormal indexes indicating possible postoperative biliary obstruction or other complications should be detected as soon as possible (12). Post-procedure

ultrasound should be regularly reviewed to observe whether the biliary tract dilation, biliary tract function and blood flow. If postoperative biliary complications such as biliary obstruction, cholelithiasis and biliary fistula present, the site of the complications should be confirmed, and the optimal treatment method should be selected in combination with the actual situation.

This study has several limitations. First, it is a retrospective study, we cannot observe the long-term results of patients after liver transplantation. Second, sample size is small to draw a meaningful conclusion about liver function indexes to assess efficacy of PTBD.

Conclusion:

In conclusion, PTBD shows good effectivity of relieving obstructive jaundice symptoms and reducing hepatic function indexes in patients with biliary stricture after liver transplantation. However, the decrease of albumin should also be concerned.

Reference:

- 1. The guideline of prevention and treatment for chronic hepatitis B: a 2015 update
- Gursimran Kochhar, Jose Mari Parungao, Ibrahim A Hanouneh, Mansour A Parsi: Biliary complications following liver transplantation. World J Gastroenterol 2013 May 21; 19(19): 2841-2846. https://doi.org/10.3748/wjg.v19.i19.2841
- BARBARA LATTANZI, PETER OTT, ALLAN RASMUSSEN, KAREN RABEN KUDSK, MANUELA MERLI and GERDA ELISABETH VILLADSEN: Ischemic Damage Represents the Main Risk Factor for Biliary Stricture After Liver Transplantation: A Follow-Up Study in a Danish Population. in vivo 32: 1623-1628 (2018). https://doi.org/10.21873/invivo.11423
- 4. Toshitaka Sugawara, Junichi Shindoh, Yujiro Nishioka, Masaji Hashimoto:Total bilirubin amount in drainage fluid can be an

early predictor for severe biliary fistula after hepatobiliary surgery. BioScience Trends. 2017; 11(5):588-594. https://doi.org/10.5582/bst.2017.01208

- Marcos V Perini, Paulo Herman, Andre L Montagnini, Jose Jukemura, Fabricio F Coelho, Jaime A Kruger, Telesforo Bacchella, Ivan Cecconello: Liver resection for the treatment of post-cholecystectomy biliary stricture with vascular injury. World J Gastroenterol 2015 February 21; 21(7): 2102-2107. https://doi.org/10.3748/wjg.v21.i7.2102
- Yuan CH, Xiu DR, Jiang B, Li ZF, Li L, Tao M, Song SB, Zhang TL: Analysis and management of the biliary complications after liver transplantations. Zhonghua Wai Ke Za Zhi. 2013 Jun 1;51(6):499-503.
- Wang L, Wang YY, Zhang Y,Peng W, Zheng PF, Cheng ZB: Two choices of biliary drainage in patients with obstructive jaundice. World Latest Medicine Information (Electronic Version) 2017 Vol.17 No.102.
- Melina Heinemann, Bita Tafrishi, Sven Pischke, Lutz Fischer, Thomas Rösch, Ansgar W. Lohse, Martina Sterneck, Ulrike W. Denzer: ERC and PTCD in biliary strictures after liver transplantation: long-term outcome pre-dictors and influence on patient survival. doi: 10.1111/liv.13995. https://doi.org/10.1111/liv.13995
- Delden OMV, Lameris JS. Percutaneous drainage and stenting for palliation of malignant bile duct obstruction[J]. Eur Radiol, 2008, 18(3): 448-456. https://doi.org/10.1007/s00330-007-0796-6
- Shen B, Luo JF, Pan JG: Effect of Interventional Therapy on Hilar Cholangiocarcinoma and Its Effect on Alpha Fetoprotein,γ-glutamyl Transpeptidase. Medical Innovation of China,2017,14(30):103-106.
- Kwo PY, Cohen SM, Lim JK: ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries. Am J Gastroenterol. 2017 Jan;112(1):18-35. doi: 10.1038/ajg.2016.517. Epub 2016 Dec 20. https://doi.org/10.1038/ajg.2016.517
- Ren XJ, Gao N, Liu WX: Ultrasound in the diagnosis of complications after liver transplantation. Medical Journal of the Chinese People Armed Police Forces.2015 Feb;26(2):205-208.