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Percutaneous transhepatic biliary drainage related infectious complications after living donor liver transplantation

Canlı vericili karaciğer nakli sonrası perkütan biliyer drenaja bağlı enfeksiyöz komplikasyonlar

Gökhan Ertuğrul [1], Selda Aydın [2]

[1] Hepatobiliary Surgery and Organ Transplantation Center, Medipol Universty Faculty of Medicine, Istanbul, Turkey
[2] Department of Infectious Diseases, Medipol Universty Faculty of Medicine, Istanbul, Turkey

ORCID ID of the author(s)
GE: 0000-0002-8351-4220
SA: 0000-0002-1913-7774

Abstract

Aim: Biliary complications were the most common cause of morbidity after living donor liver transplantation. Percutaneous transhepatic biliary drainage (PTBD) is performed in this patients. The purpose of our study was to determine the rate of PTBD related infection (cholangitis and sepsis) after living donor liver transplantation.

Methods: This is a retrospective cohort study. Fifty two patients PTBD procedures were performed after living donor liver transplantation. Two main groups were established; Post PTBD infection group and non-infection group. Demographic characteristics, infectious complications and mortality rates were compared.

Results: PTBD procedure related infection (cholangitis and sepsis) rate was 52% (28 patients) and early (thirty days) mortality rate was 17.9% (5 patients).

Conclusion: PTBD related infectious complication and mortality rates are high. In these patients we need to be very careful after PTBD.

Keywords: Living donor liver transplantation, Percutaneous transhepatic biliary drainage, Infectious complications

Öz

Amaç: Biliyer komplikasyonlar canlı vericili karaciğer nakli sonrası en sık görülen morbidite nedenidir. Bu hastalarda perkütan transhepatik biliyer drenaj (PTBD) yapılır. Çalışmamızın amacı canlı vericili karaciğer nakli sonrası PTBD'ye bağlı enfeksiyon (kolanjit ve sepsis) oranını belirlemekti.

Yöntemler: Bu retrospektif kohort bir çalışmadır. Elli iki hastaya canlı vericili karaciğer nakli sonrası PTBD işlemi uygulandı. Hastalar iki gruba ayrıldı. PTBD sonrası enfeksiyon gelişen ve gelişmeyen grup. Bu iki grubun demografik özellikleri, enfeksiyöz komplikasyonları ve mortalite oranları karşılaştırıldı.

Bulgular: PTBD prosedürüne bağlı enfeksiyon (kolanjit ve sepsis) oranı %52 (28 hasta) ve erken (otuz gün) mortalite oranı %17,9 (5 hasta) idi.

Sonuç: PTBD ile ilişkili infeksiyöz komplikasyon ve mortalite oranları yüksektir. Bu hastalarda PTBD'den sonra çok dikkatli olmak gerekir.

Anahtar kelimeler: Canlı vericili karaciğer nakli, Perkütan transhepatik biliyer drenaj, Enfeksiyöz komplikasyonlar

Corresponding author / Sorumlu yazar:
Gökhan Ertuğrul
Address / Adres: Medipol Üniversitesi Tıp Fakültesi, Hepatobilier Cerrahisi ve Organ Nakli Merkezi, TEM Avrupa Otoyolu Göztepe Çıkışı No: 1, 34214, Bağcılar, İstanbul, Türkiye
E-mail: mdgertugrul@gmail.com

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Introduction

The only definitive treatment of end stage liver disease is liver transplantation. In countries where cadaveric liver transplantations are limited, living donor liver transplantation is performed. Percutaneous transhepatic biliary drainage (PTBD) is an effective management of biliary leakage and strıcture after lıvıng donor liver transplantation and it involves sterile cannulation of a peripheral bile duct, cholangiography, determining the location of bile issues, catheter positioning above the bile anastomosis and allowing decompression of the biliary system [1-3]. PTBD is effective at relieving biliary leakage and stricture; however, it has been associated with complications including sepsis, cholangitis and pancreatitis [4].

The aim of the present study was to review PTBDs related infectious complications and mortality rate after living donor liver transplantation.

Materials and methods

Between December 2014 and December 2018 at Medipol University Medical Faculty Hospital Organ Transplantation Department, Istanbul, Turkey, 220 patients with living donor liver transplantation were studied retrospectively. PTBD procedures were performed in 52 (24%) patients.

Two main groups were established; Post PTBD infection group and non-infection group. For each of these groups, the age, sex, etiology, CHILD scores, Model for End-Stage Liver Disease (MELD) scores, rationale of PTBD, infectious complications and early (first thirty days) mortality rates were compared. Also, bacterial and fungal infectious agents and using antibiotic and antifungal types were evaluated.

Patients

For all patients, informed consent was obtained before the procedure. All patients were given pre-PTBD prophylactic antibiotic coverage with 4.5 g of intravenous piperacillin/tazobactam. Patients who were allergic to penicillin or cephalosporin were administered 400 mg of intravenous ciprofloxacin at before 1 hour the procedure.

New developed cholangitis was defined as fever (>38.5°C) that arises within 24 hours after the PTBD. After taking blood for hemoculture (two sets-4 bottles- 40 milliliters blood) and bileculture (10 milliliters bile) at the tıme of fever, the treatment was continued with prophylactic antibiotics (piperacillin/tazobactam or ciprofloxacin).

New developed sepsis includes the criteria for cholangitis as well as the development of hemodynamic instability (heart rate ≥90 beats/minute, respirations ≥ 20/minute) such as a drop in blood pressure requiring intravenous fluid resuscitation, administration of vasopressors within 24 hours of the PTBD. All patients with sepsis were routinely transferred to intensive care unit. Antibiotic treatment was changed according to the hemoculture and bileculture.

Statistical Analysis

SPSS 22.0 (SPSS for Windows, 2007, Chicago) was used for statistical analysis. Continuous variables which have normal distribution were presented as mean ± Standard deviation. Statistical analysis for the parametric variables was performed by the Student's T-test. The qualitative variables were given as percent and the correlation between categorical variables was investigated by the chi-square test and Fisher's exact test. Statistical significance level was defined as $p<0.05$.

Results

Mean age of the infection group was 53.5 (19-71) years; non-infection group was 57.5 (26-69) years, 36 (70 %) of the 52 patients PTBD procedures were male.

Mean CHILD scores of the infection group was 8.5 (6-15); non-infection group was 9 (6-12) respectively. Mean MELD scores of the infection group was 16.5 (8-40); non-infection group was 16.5 (10-30), respectively.

The common etiologic factors of transplantation were HBV in 10 (71.4%) patients (in the infection group), non-alcoholic steatohepatitis in six (46.2%) patients and cryptogenic in six (66.7%) patients (in the non-infection group).

Table 1 shows the comparison of demographic and clinical findings of the infection and non-infection groups. PTBD procedure related infectious complications (cholangitis and sepsis) rate was 52% (28 patients) and early (first thirty days) mortality rate was 17.9% (5 patients). The cause of death in all cases was post-PTBD sepsis.

Table 1: Demographic and clinical data of the groups

		Infection (n=28)	Non-Infection (n=24)	p
Age (Years)		53.5 (19-71)	57.5 (26-69)	0.291
Sex (M/F)		22 (78.6%) / 6 (21.4%)	14 (58.3%) / 10 (41.7%)	0.141
CHILD		8.5 (6-15)	9 (6-12)	0.268
MELD		16.5 (8-40)	16.5 (10-30)	0.847
Etiology		n (%)	n (%)	
	HBV	10 (71.4)	4 (28.65)	0.185
	NASH	7 (53.8)	6 (46.2)	
	Cryptogenic	3 (33.3)	6 (66.7)	
	Autoimmune	2 (50)	2 (50)	
	SBC	3 (100)	-	
	PSC	-	3 (100)	
	HCV	2 (66.7)	1 (33.3)	
	Ethanol	1 (33.3)	2 (66.7)	
Requirement for PTBD				0.022
	Stricture	11 (39.3)	17 (70.8)	
	Leak	17 (60.7)	7 (29.2)	
Early Mortality		5 (17.9)	-	0.038

M: Male, F: Female, HBV: Hepatitis B Vırus, NASH: Non-alcoholic Steatohepatitis, SBC: Secondary biliary cirrhosis, PSC: Primary Sclerosing Cholangitis, HCV: Hepatitis C Vırus, PTBD: Percutaneous Transhepatic Biliary Drainage

Table 2 shows the comparison of bacterial and fungal infectious agents of the two patient groups. The most common cause of bacterial infectious agents was Klebsiella in 15 (53.6%) patients detected in the blood, the most common fungal infectious agents was Candida in 6 (21.4%) patients detected in the blood. All patients were using tacrolimus and mycophenolate mofetil as immunosuppressive therapy after liver transplantation. Table 3 shows the comparison of used antibiotic or antifungal medications. The most commonly used antibiotic was meropenem (42.3%), and the antifungal was anidulafungin (28.8%).

Table 2: Bacterial and fungal agents data of the groups

		Infection	Non-Infection
Klebsiella	Bile	17 (60.7%)	1 (4.2%)
	Blood	15 (53.6%)	-
Enterococcus	Bile	18 (64.3%)	8 (33.3%)
	Blood	9 (32.1%)	-
Pseudomonas	Bile	12 (42.9%)	2 (8.3%)
	Blood	7 (25%)	-
E.coli	Bile	22 (78.6%)	1 (4.2%)
	Blood	7 (25%)	-
Candida	Bile	13 46.4%)	4 (16.7%)
	Blood	6 (21.4%)	-
Acinetobacter	Bile	3 (10.7%)	-
	Blood	5 (17.9%)	-

Table 3: Antibiotics and antifungals used for infection

Antibiotics and Antifungals	n	%
Meropenem	22	42.3
Teicoplanin	18	34.6
Piperacillin/tazobactam	17	32.7
Anidulafungin	15	28.8
Tygacil	7	13.5
Colistin	2	3.8
Imipenem	2	3.8

Discussion

The only definitive treatment of end stage liver disease is liver transplantation. In countries where cadaveric liver transplantations are limited, living donor liver transplantation is performed. In our clinic, 220 patients performed living donor liver transplantation in four years. Patients with living donor liver transplantation carry a higher risk of biliary system complications [5,6] and this complication rate is 20 to 40 % [7-9]. Biliary complications were the most common cause of morbidity after living donor liver transplantation. In addition to biliary complications were shortening graft and recipient survival [10]. In our clinic, there are 52 (24 %) patients with biliary complications (leakage and stricture) in four years.

PTBD is an effective management of biliary complications after living donor liver transplantation [3]. PTBD is performed in patients with biliary leakage and stricture at the earliest. In our clinic, PTBD procedures were performed in all biliary complication patients. PTBD success rate was >95%, but first thirty days significant infectious complications [11]. PTBD related infectious complications (sepsis and cholangitis) have an incidence rate of 34% [12,13]. In our study PTBD procedure related infectious complications (cholangitis and sepsis) rate was 28 (52%) patients.

Pre-PTBD prophylactic antibiotics reduce the incidence of sepsis and cholangitis [14-16]. Making pre-PTBD prophylactic antibiotics to living donor liver transplantation group is more important. Prophylactic antibiotics including coverage for Klebsiella, Escherichia Coli, Enterococcus and Pseudomonas Aeruginosa, decrease risk of potential septic complications [17]. In our study, all patients took pre-PTBD prophylactic antibiotic coverage with 4.5g of intravenous piperacillin/tazobactam. Patients who were allergic to penicillin or cephalosporins were administered 400 mg of intravenous ciprofloxacin. The detected blood culture overgrowth bacteria were Klebsiella 53.6%, Enterecoccus 32.1%, Psodomonas 25%, Escherichia Coli 25%, Acinetobacter 17.9% and fungus was Candida 21.4% in the infection group.

PTBD related infectious complications (sepsis and cholangitis) have an early mortality rate of approximately 20% [18,19]. In our study PTBD procedure related early mortality rate was 17.9 % (5 patients). The cause of death in all cases was post-PTBD sepsis. In our study, the commonly used drugs are meropenem 42.3%, teicoplanin 34.6%, piperacillin/tazobactam 32.7%, anidulafungin 28.8%, tygacil 13.5%, colistin 3.8%, imipenem 3.8%.

Our study has several limitations. First, this study was retrospective. Second, the number of cases in PTBD performed and infectious complications were small.

In conclusion, PTBD is an effective management of biliary complications but infectious complications and mortality rates are high. In these patients we need to be very careful after PTBD.

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