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Correlation between Percutaneous Biliary Drainage and Decrease in Serum Bilirubin

César Hayashi-Mercado[1], Miguel González-Urueta[2], Gabriel Luna-López[3], Abelardo Aguilar-West[4]

[1]ISSSTE Hospital 1° de Octubre, Mexico City.

[2]UABC, Baja California, México.

[3]ISSSTE Hospital 1° de Octubre, Mexico City.

[4]Hospital Militar Escuela Dr. ADB 2254, Managua, Nicaragua.

ABSTRACT

Background: Obstruction of the bile duct, whether caused by a tumor or a surgical injury, will cause: jaundice, elevated liver enzymes, and eventually, liver failure. The primary goal of percutaneous management is draining bile into the small intestine and achieving a drainage that is the most similar to the normal physiologic drainage, maintaining normal enterohepatic circulation. The present study aims to make a correlation between percutaneous biliary diversion and the decrease in serum bilirubin in pre- and post-procedure studies (24 hours).

Methods: We did a retrospective review of the database of the Interventional Radiology service of Hospital Regional 11° de Octubre, México. The time study was between years 2017 and 2022. We analyzed 75 patient's clinical records who underwent percutaneous management with a diagnosis of bile duct dilation due to an obstructive origin. The population was divided in three groups benign, malignant and post-surgical based on the ethiology of the bile duct obstruction. Total serum bilirubins, liver enzymes, coagulation tests and platelets of each patient were obtained from the clinical record prior to percutaneous biliary diversion and 24 hours after procedure.

Results: 75 patient records were explored, of which 26 (34.7%) were men and 49 (65.3%) were women The mean age was 62.3 years. A statistically significant decrease in total serum bilirubin was observed 24 hr after the procedure with a p value of 0.009. A statistically significant decrease after the procedure was also observed in liver enzymes with a value of: GGT with p: 0.002, GOT with p: 0.003 and LDH with p: 0.005

Discussion: There was a decrease in total serum bilirubin and liver enzymes after an effective biliary diversion, regardless of the cause of obstruction.

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INTRODUCTION

Primary pancreas, gallbladder, bile ducts, and liver tumors account for 80,000 cancer new cases and about 58,000 deaths each year in the United States; of which, in advanced stage disease, they generally result in biliary obstruction. They have poor prognosis and surgical treatment, generally, is not resolving [1]. Bile duct injury incidence after open cholecystectomy is 0.1% to 0.2%.. In laparoscopic cholecystectomy, it increases to 0.4%-0.7%, in both, the surgeon's technique and experience are involved. [2]. In a retrospective study conducted by David Martin et al. from 2000 to 2011, the main causes of bile duct injury reported were: anatomical misinterpretation (confusion of the common bile duct with the cystic duct), injury during intraoperative cholangiography, cicatricial stenosis due to poor clip placement, dehiscence of the cystic stump and direct injury during dissection. Primary bilary colangitis (PBC) incidence ranges from 0.33 to 5.8 per 100,000 population/year [3].

Bile duct obstruction, whether caused by a tumor or by a surgical injury will cause: jaundice,elevated liver enzymes, and eventually, liver failure [2]. In malignant origin cases, relief of the obstruction is a useful palliative treatment and can improve life quality and survival [1].

Historically, biliary-enteric shunts were the only solution for this obstruction type, but with recent technological advances, percutaneous transhepatic biliary drainage (PTBD) and endoscopic retrograde cholangiopancreatography (ERCP) have been introduced as less invasive alternatives [4].

Percutaneous management of malignant biliary disease includes external biliary drainage, external-internal biliary drainage, and plastic or metal stents placement ,being safe and effective techniques to alleviate patients' obstructive symptoms with unresectable tumors. The primary goal of percutaneous management is draining the bile into the small intestine and achieving a drainage that is the most similar to the normal physiologic drainage, maintaining normal enterohepatic circulation [5].

Postoperative bile leaks usually occur as a complication of laparoscopic cholecystectomy or enterobiliary anastomosis. Bhavesh Popat et al. conducted a study and the main causes of bile leakage are said to be: bile duct injury during a laparoscopic cholecystectomy, hepaticojejunal anastomosis, common bile duct-to-common bile duct anastomosis associated with liver transplantation, and liver lobectomy. Treatment will depend on t lesion type and may include endoscopic, percutaneous and open interventions. In some cases, surgical repair and/or endoscopic management is impossible or unsuccessful, particularly in patients with large postoperative bile duct defects. In such cases, bile flow can easily be diverted from the bile duct defect through percutaneous transhepatic biliary drainage [6].

Perihilar cholangiocarcinoma, also known as Klatskin tumor, is a common malignant tumor of the biliary system. Due to extensive ductal spread of this tumor from the hepatic hilum to the inferior bile duct and its close relationship to the portal vessels, surgical treatment with conventional approach, generally, cannot achieve complete resection[7]. Currently, the diagnostic classification method for hilar cholangiocarcinoma is the one proposed by Bismuth and Corlette in 1975 and complemented in 1988. In clinical practice, a clear understanding of cholangiocarcinoma classification will guide surgeons on planning decisions, ensuring negative surgical margins and increasing patient survival to the greatest extent possible [8]. In 2014, the American Hepato-Pancreato-Biliary Association established that treatment of patients with hilar cholangiocarcinoma requires a coordinated multidisciplinary approach to optimize the chances of long-term survival and effective palliation. A proper diagnosis and staging study includes high-quality imaging; ideal treatment for patients with resectable hilar malignancy is resection of the intrahepatic and extrahepatic bile ducts, as well as resection of the ipsilateral involved liver. Preoperative biliary drainage shows greater efficiency when percutaneous transhepatic technique is used and may be indicated in patients with cholangitis, malnutrition, or liver failure [9].

Postoperative bile leakage is a rare but serious complication of some surgical procedures, including cholecystectomy, pancreaticoduodenectomy, liver resection, and liver transplantation [10]. The older classifications are based on peripheral leaks, central leaks and biliary strictures, Siewert et al. described type 1 lesions as peripheral leaks and included immediate biliary fistulas. In contrast, central leaks consist of tangential lesions without structural loss of the bile duct and correspond to type 3 lesions. Type 2 lesions occur when late stenosis are diagnosed without obvious intraoperative trauma. Among the most used classifications are: Corlette-Bismuth, Strasberg and more recently Starwart-Way [11]. Timely biliary decompression and drainage are the cornerstone of acute cholangitis treatment. The mortality rate of acute cholangitis is extremely high when interventional procedures or open drainage were not available [12]. In 2018, the Tokyo guidelines began being used for acute cholangitis criteria, as well as for the evaluation of acute cholangitis severity. When endoscopic biliary drainage is not feasible, percutaneous transhepatic drainage is an effective option, with generally relative contraindications. In a systematic review and meta-analysis conducted by Feng Duan et al. Percutaneous bile duct drainage was found to be superior to endoscopic biliary drainage in relation with therapeutic success rate, incidence of general complications, intraperitoneal bile leakage, 30-day mortality, sepsis, and duodenal perforation. . Percutaneous bile duct drainage demonstrated a significantly lower incidence of cholangitis and pancreatitis than the endoscopic approach, with an OR of 0.48 (95% CI, 0.31 to 0.74) and 0.16 (95% CI, 0.05 to 0.52) for cholangitis and pancreatitis, respectively. However, the incidence of bleeding and tube dislocation in the percutaneous approach was significantly higher than the endoscopic approach, with an OR of 1.81 (95% CI, 1.35 to 2.44) and 3.41 (95% CI, 1.35 to 2.44). 95%, 1.10 to 10.60) for hemorrhage and tube dislocation, respectively [14]. With the widespread application of ultrasound, the classic puncture with fluoroscopic control has gradually fallen into disuse. Currently, a puncture of the intrahepatic bile duct is performed with ultrasonographic guidance, using the Seldinger technique and 18 to 22 G diamond-tipped needle, confirming the reflux of bile, later with a 0.018 metal guide, a triaxial exchange catheter, 0.035 Teflon guide and dilators, it is possible to install a biliary drainage catheter. According to quality guidelines developed by American radiologists, drainage success rates are 95% in patients with biliary dilatation and 70% in those without biliary dilatation [15]. In a study, conducted by Aleksandar N. Filipovic et al., was observed that transhepatic biliary drainage guided by ultrasound and fluoroscopy was a safe and effective procedure. Initial ultrasound-guided puncture and biliary tree entry at a 30° angle was an operator-dependent factor impacting on reducing total fluoroscopy time during the procedure [14]. In another study by Wonho Lee et al, it was observed that patients without bile duct dilatation, the use of

 Corresponding Author: César Hayashi-Mercado

ultrasound and fluoroscopy for percutaneous drainage of the bile duct proved to be effective in 100% of patients [16]. Among the indications for percutaneous drainage of the bile duct are: cholangitis, structural biliary dilatation, lower serum bilirubin before starting chemotherapy, and biliary access prior to stent placement. The relative contraindications are: anomalies in coagulation tests and ascites. In a study conducted by Andreas Weber et al. It was observed that 39 of 419 patients had complications (9.31%) related to the procedure, such as bleeding (2.86%), acute cholangitis (1.67%), sepsis (1.43%), acute pancreatitis (0 48%), bilioma (0.48%), intrahepatic bile, hematoma (0.48%), biliovenous fistula (0.48%), biliopleural fistula (0.48%), pneumothorax (0.24%), peritonitis (0.24%) and perforation (0.24%). In patients with dilated and non-dilated intrahepatic bile ducts, the overall percentage of procedure-related complication rates were 6.94% vs. 14.5%, respectively [17].

METHODS

This study is observational, analytical, longitudinal, retrospective and quantitative. The time study was between the years 2017-2022. This study studied a single-center population, in the International Radiology Service of Hospital Regional 1º de Octubre, México. We included records of patients diagnosed with biled obstruction and records of patients treated by the Interventional Radiology service. We excluded files of patients who did not have a laboratory and clinical follow-up and files of patients with a history of obstructive process and have only attended for catheter replacement . Sampling method was non-probabilistic for convenience. We analyzed the medical records of a total of 75 patients with a diagnosis of bile duct obstruction who underwent percutaneous biliary drainage. The population was divided in three based on the ethiology of bile duct obstruction which were: benign, malignant and post-surgical. Total serum bilirubin, liver enzymes, coagulation tests and platelets of each patient were obtained from the clinical record prior to percutaneous biliary diversion and 24 hours after procedure. Descriptive statistics were performed for the qualitative variables and will be summarized as frequency and percentages: age, gender, imaging method used for the procedure, bile duct obstruction classification (malignant, benign, postoperative), degree of cholangitis of each patient and percutaneous management used (external shunt, mixed, ballooning and stent placement) as descriptive statistics.

The information collected was processed with SPSS, and reported with P values in graphs and tables. The chi-square test was used to explore the procedure as successful or otherwise. For the quantitative variables, Student's T of paired data was used; the direction was explored and summarized with P values. The following variables were used: serum bilirubin 24 hours after the procedure, as well as liver function tests (GGT, GOT and LDH), hoping to find a correlation coefficient of at least 0.5.

RESULTS

75 patient records were explored, of which 26 (34.7%) were men and 49 (65.3%) were women. The mean age was 62.3 years, median 63 years and mode 63 years, with a standard deviation of SD: 12.861. Cholangitis was present in 27 patients (36%), pericholangitic abscesses in 8 patients (10.7%), and jaundice in 58 patients (77.3%). Mean hyperbilirubinemia was 6.14 g/dl, median 5.7 g/dl, and mode 5.7 g/dl. Benign obstruction was observed in 31 patients (41.3%), malignant obstruction in 36 patients (48%) and post-surgical origin in 8 patients (10.7%). Total serum bilirubin pre-procedure showed a mean of 6.1 g/dl and post-procedure 3.3 g/dl. Grade 1 cholangitis was observed in 72 patients (96%), grade 2 in 3 patients (4%), and grade 3 was not identified. Liver function tests showed a mean pre-procedure of: GGT of 96.4 U/l, GOT of 92.4U/l and LDH of 645 U/l; and post-procedure of: GGT of 82.2 U/l, GOT of 74.3 U/l and LDH of 455 U/l. The imaging methods used for biliary bypass were: fluoroscopy in 14 patients (18.7%) and fluoroscopy + ultrasound in 61 patients (81.7%). (Figure 1-2, Table 1)

A correlation was made with the chi-square test of the percutaneous drainage of the bile duct versus the improvement of the PFH, using a CI of 95% and a significance level of 5% (0.05); Since the bilateral asymptotic significance is 0.045 less than 0.05, the hypothesis that there is a relationship between percutaneous biliary drainage and improvement in liver function tests is accepted. Therefore, we can affirm that there is a statistically significant value that suggests that the mixed or external shunt is associated with a decrease in liver enzymes. We explored if there is a statistically significant association between a successful mixed or external biliary bypass and a decrease in serum bilirubin in obstructive processes with a malignant etiology, obtaining a p value of 0.004. However, there is no statistically significant value that suggests an association between biliary diversion (mixed or external) in obstructive processes (benign or post-surgical) and the decrease in serum bilirubin, showing a value of p: 0.739 and p: 0.465 respectively. (Table 2)

Student's T test was performed for related samples, comparing total serum bilirubin before the procedure and total serum bilirubin after the procedure (24hr), observing a statistically significant decrease with a p value: 0.009. The same statistical test was performed to compare means in liver function tests, observing a statistically significant decrease in all examinations, values: GGT with p: 0.002, GOT with p: 0.003 and LDH with p: 0.005. (Table 3)

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TABLES

Table 1.		
POPULATION (N: 75 PATIENTS)		
SEX		
Male	**N: 26**	**34.7%**
Famale	**N: 49**	**65.3%**
AGE		
Mean	**62.3 years**	**DS: 12.861**
Median	**63 years**	
Mode	**63 years**	
COLANGITIS		
Presence	**N: 27**	**36%**
Ausence	**N: 48**	**64%**
PERICHOLANGITIC ABSCESS		
Presence		
Ausence	**N: 8**	**10.7%**
	N: 67	**89.3%**
JAUNDICE		
Presence	**N: 58**	**77.3%**
Ausence	**N: 17**	**22.7%**
HYPERBILIRUBINEMIA		
Media		**DS: 1.8**
Mediana	**6.14 g/dl**	**Percentile 25: 4.5 mg/dl.**
Moda	**5.7 g/dl**	**Percentile 50: 5.7 mg/dl.**
	5.7 g/dl	**Percentile 75: 8 mg/dl.**
TYPE OF OBSTRUCTION		
Benigne		
Malignant	**N: 31**	**41.3%**
Post-surgical	**N: 36**	**48%**
	N: 8	**10.7%**
IMAGING METHOO		
Fluoroscopy	**N: 14**	**18.7%**
Ultrasound + Fluoroscopy	**N: 61**	**81.3%**
TOTAL SERUM BILIRUBIN	**Pre-surgical**	**Post-surgical**
Mean		
Median		**3.3 g/dl**
Mode	**6.1 g/dl**	**3.2 g/dl**
	5.7 g/dl	**4.1 g/dl**
	5.7 g/dl	
CHOLANGITIS GRADE		
Grade 1 (mild)		
Grade 2 (moderate)	**N: 72**	**96%**
Grade 3 (severoe	**N: 3**	**4%**
	N: 0	**0%**
LIVER ENZYMES (MEAN)	Pre-procedural	Post-procedural
GGT		
GOT		82.2 U/l
LDH	96.4 U/l	74.3 U/l
	92.4 U/l	455 U/l
	645 U/l	

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Tabla 2. PERCUTANEOUS BILIARY DRAINAGE: COMPARISON BETWEEN DIFFERENT OBSTRUCTIVE PROCESSES PRE-PROCEDURAL VS POST-PROCEDURAL		
Biliary Drainage.	Liver enzymes improvement	P: 0.045
Biliary bypass in benign obstructive processes.	Decrease in serum bilirubin in benign processes.	P: 0.739
Biliary bypass in malignant obstructive processes	Decrease in serum bilirubin in malignant processes.	P: 0.004
Biliary bypass in post-surgical obstructive processes	Decrease in serum bilirubin in post-surgical processes.	P: 0.465

Tabla 3. LIVER ENZYME TESTS: COMPARISON PRUEBAS DE FUNCIÓN HEPATICA: MEAN COMPARISON PRE-PROCEDURAL VS POST-PROCEDURAL		
Total serum bilirubin pre-procedural	**Total serum bilirubin post-procedural**	**P: 0.009**
GGT pre-procedural	**GGT post-procedural**	**P: 0.002**
GOT pre-procedural	**GOT post-procedural**	**P: 0.003**
LDH pre-procedural	**LDH post-procedural**	**P: 0.005**

DISCUSSION

Bile duct obstruction, whether benign, tumor or surgical procedure associated, will cause: jaundice, increased liver function tests and finally liver failure. The primary goal of percutaneous management is draining the bile into the small intestine and achieving a drainage that is the most similar to the normal physiologic drainage, maintaining normal enterohepatic circulation [5]. In a study, conducted by Aleksandar N. Filipovic et al., was observed that transhepatic biliary drainage guided by ultrasound and fluoroscopy was a safe and effective procedure. Initial ultrasound-guided puncture and biliary tree entry at a 30° angle was an operator-dependent factor impacting on reducing total fluoroscopy time during the procedure [14]. In another study by Wonho Lee et al, it was observed that in patients without bile duct dilatation, the use of ultrasound and fluoroscopy for percutaneous biliary drainage reported an effectiveness of 100% of the patients [16]. The results of this study are consistent with what has been reported in the literature, observing that most of the population studied decreased liver enzymes and jaundice after an effective biliary diversion, regardless of the cause of obstruction [10]. The fact that malignant type obstructions benefit more from a mixed shunt may be related to the fact that this type of process leads to complete bile duct obstruction, while benign and post-surgical obstruction leads to partial obstruction[14].

CONCLUSIONS

In our study, statistically significant p values were observed in liver enzymes decrease 24 hours after the percutaneous bypass procedure of the bile duct, likewise, we observed that there is no statistically significant value if an external shunt is used versus mixed, with the exception of malignant processes, which they benefit from a mixed type procedure. However, we emphasize that despite the fact that a decrease in live enzymes were observed in the different obstructive processes, the external shunt does not promote use of bilirubins since they do not pass the digestive tract, due to its excretion towards the outside. This conditions other problems related to fat metabolism and other micronutrients. We need more studies and more in-depth investigation with larger populations with different comorbidities for us to observe the behavior of these pathologies after biliary diversion in different clinical scenarios.

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