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Outcome of Removal of Biliary Stent Prior to Pancreaticoduodenectomy

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ABSTRACT

Background: Obstructive jaundice is the commonest manifestation in patients with periampullary carcinoma. Pancreaticoduodenectomy is the only curative procedure for resectable tumor. But raised serum bilirubin level may cause the postoperative events. For that reason, preoperative biliary drainage is an important step to reduce the overall postoperative complications. The main aim of this study is to assess the rate of post-operative complications, length of hospital stays and death between patients undergoing pancreaticoduodenectomy with or without removal of biliary stent. **Methodology:** This prospective cross-sectional study was conducted into department of Surgery and Hepatobiliary, pancreatic and liver transplantation Surgery of BSMMU from July,2017 to June 2018. Initially all the patient diagnosed as periampullary carcinoma and underwent preoperative biliary drainage were enrolled in the study by purposive sampling. Surgery was planned 4-6 weeks after stenting. The analysis was done by student's t test here. Cross tabulation and chi square test were done to analyze the categorical data. p value was considered as significant at <0.05. Data analysis was done using the software statistical package for social science (SPSS-23). **Results:** Patients with biliary stent in situ till pancreaticoduodenectomy was significantly associated with positive bile culture (P=0.025) and, E. coli (45.45%) is the most common organism. Post-operative woundinfection was significantly high (p=0.035) in Group A than Group B. From the

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point of view of postoperative morbidity Group B showed better results than Group A. Microscopic findings of bile duct showed disruption of mucosal epithelium in all 11 (100%) patients in Group A in contrast it was in 3 (33.33%) patients in Group B, which was statistically significant (P value <0.05). **Conclusion:** Removal of biliary stent before surgery who already underwent preoperative biliary decompression for improvement of liver function showed relatively better outcome after surgery in comparison to those patients in whom pancreaticoduodenectomy was done with keeping stent in situ.

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INTRODUCTION

Periampullary carcinoma may obstruct the distal part of hepatobiliary-pancreatic duct resulting in obstructive jaundice. Hepatobiliary pancreatic malignancy causes obstruction in 70–90% of patients, causing jaundice, hepatocellular dysfunction, biliary cirrhosis, pain, pruritus, and cholangitis. [1] Prior to the use of stents, the primary treatment for biliary obstruction was surgery, such as cholecystojejunostomy or choledochojejunostomy. [2] The endoscopic placement of biliary stents was first introduced in the early 1980s. [2] There was a rapid shift from surgery towards endoscopic retrograde cholangiopancreatography (ERCP) stent placement because of its better mortality and morbidity profile. [3] Pancreaticoduodenectomy (PD) is a challenging surgery with high postoperative morbidity and mortality. The operation is commonly performed due to neoplasm in the head of the pancreas, distal common bile duct or in the periampullary region. [4] Pancreaticoduodenectomy was performed over 100 years ago. Initially both mortality and morbidity were intolerably high. Over the years, mortality has diminished in high volume centers (1 - 5%), but morbidity remains high at 18-58%. [5] It has been reported that the mortality rate due to surgical treatment of malignant obstructive jaundice ranges from 5% to 27% and that the morbidity rate is approximately 50%. [6] Several small steps along with modifications of surgery decreased

the mortality rate but no significant improvement regarding morbidity was achieved in recent years. [7] Preoperative biliary stenting is an important step that is added here before operation to achieve better outcome after operation. In 1960s and 1970s preoperative biliary stenting was frequently advocated in an effort to improve surgical outcomes in pancreatic cancer patients undergoing curative-intent resection. This was considered to correct physiologic disturbances induced by hyperbilirubinemia secondary to malignant obstruction, theoretically optimizing patients' condition prior to operation and improving perioperative morbidity and mortality. But still yet the role of preoperative biliary drainage as an adjunct in patients undergoing surgical resection for malignant biliary obstruction is controversial. [8] Biliary obstruction alters the normal physiology and affects multiple organ systems that include but are not limited to cardiac, renal, hematologic, and hepatic dysfunction. [9] It is associated with impaired hepatic function, coagulation disturbances, and development of cholangitis. Hyperbilirubinemia is a potential risk factor that might be associated with poor surgical outcomes. Now days, ERCP with biliary stenting has become standard practice in patients with pancreatic head cancer. [10] In a recent, multicenter, randomized trial, patients who underwent preoperative biliary drainage had a 74% rate of complications compared with 39% for those who directly underwent surgery. [11] In addition, it has been shown

that the systemic inflammatory response continues to be intense after internal biliary drainage, a fact that may be attributable to bacterial colonization. Results of recent retrospective studies have suggested that the placement of biliary drains and subsequent bacterial colonization of the biliary tree may increase the rates of morbidity and mortality. [12] But to the best of our knowledge, there is no such consensus regarding the comparison between the outcome after pancreaticoduodenectomy in patients having biliary stents and patients being removed biliary stent 2 weeks prior surgery. This is a new arena that should be discovered in the field of hepatobiliary surgery specially in our perspective.

MATERIALS AND METHODS

This prospective cross-sectional study was conducted into department of Surgery and Hepatobiliary,pancreatic and liver transplantation Surgery of BSMMU from July,2017 to June 2018. Initially all the patient diagnosed as periampullary carcinoma and underwent preoperative biliary drainage were enrolled in the study by purposive sampling. Surgery was planned 4-6 weeks after stenting .

RESULTS

All the patients were divided into 2 groups. In one group pancreaticoduodenectomy without removing biliary stent were categorized and labeled as Group A . On the contrary, the subsequent group participants underwent pancreaticoduodenectomy with removing biliary stent prior to surgery and labeled as Group B. Liver function test were done prior stenting and after removal of stent as well as prior surgery and after surgery. Bile duct was collected from the resected specimen for checking biliary epithelial condition. Early post-operative outcome were recorded. Data were collected by a peer reviewed, pre structured, interview and observation-based data collection sheet. Data were edited, managed, analyzed and plotted in tabular and figure form. Data analysis was done using the software statistical package for social science (SPSS) version 23 (IL,Chicago, USA). Quantitative data were expressed as mean and standard deviation (SD).The analysis were done by student's t test here. Cross tabulation and chi square test were done to analyze the categorical data. p value was considered as significant at <0.05.

Table-1: Distribution of the study according to demographic data(n=20)

Demographic variable	n=20	%
Age		
Mean±SD	51±8.61	
Range	36-75	
Sex		
Male	13	65
Female	7	35
BMI		
Mean±SD	18.40±1.9	
Range	15-24	
Presentation		
Jaundice	20	100
Fever	12	60
Abdominal pain	12	60
Melaena	1	5

Table-1 shows the mean age of these patients was 51 ± 8.61 (age range: 36-75). Among 20 patients 13(65%) were male and 7(35%) were female. Mean BMI of patients were 18.40 ± 1.9 (range: 15-24). Out of 20 patients all are (100%) presented with jaundice, 12(60%) cases each presented with fever and abdominal pain and only 1(5%) patient presented with

melaena. Regarding to co-morbidities 7(35%) and 5(25%) cases presented with HTN and DM respectively. Among them 12(60%), 6(30%) and 2(10%) cases suffered from carcinoma head of pancreas, ampullary carcinoma and distal cholangiocarcinoma respectively.

Table-2 Changes of liver function after stenting (n=20)

Biochemical parameter	Before stenting	After stenting	p-value
	Mean \pm SD	Mean \pm SD	
Serum bilirubin	13.00 \pm 8.35	3.81 \pm 3.45	<0.001 ^a
Alkaline phosphates	548.77 \pm 252.10	357.23 \pm 243.53	0.026 ^a
ALT	100.34 \pm 104.64	52.80 \pm 41.15	0.015 ^b
PT	15.14 \pm 2.75	12.31 \pm 1.01	0.004 ^a
INR	1.42 \pm 0.23	1.07 \pm 0.160	0.001 ^a
Serum albumin	31.86 \pm 3.99	35.85 \pm 5.430	0.023 ^a

^aPaired t-test was done to measure the level of significance. ^bWilcoxon signed rank test was done to measure the level of significance.

Table-3: Differences of Liver Function Test before surgery (n=20; 11 in Group-A and 9 in Group-B)

Biochemical parameter	Before surgery		p-value
	Group-A (n=11)	Group-B (n=9)	
Serum bilirubin	2.41 \pm 1.5	3.36 \pm 1.8	0.08 ^{NS}
Alkaline phosphates	233.22 \pm 134.625	265.8 \pm 177.59	0.07 ^{NS}
Prothombin time	12.31 \pm 1.01	12.92 \pm 1.03	0.101 ^{NS}
INR	1.21 \pm 0.11	1.26 \pm 1.2	0.89 ^{NS}
Serum albumin	28.33 \pm 11.11	30.4 \pm 1.67	0.09 ^{NS}

P-value was calculated by student's t-test, S: Significant, NS: Not significant, P-value was significant at <0.05

Table-3 depicts that there was no significant difference of liver function tests between two groups before surgery.

Table-4: Differences of Liver Function Test after surgery (N=20; 11 in Group-A and 9 in Group-B)

Biochemical parameter	Before surgery		p-value
	Group-A (n=11)	Group-B (n=9)	
Serum bilirubin	1.4 \pm 0.3	1.85 \pm 1.1	>0.05NS
Alkaline phosphates	97.78 \pm 68.15	135.4 \pm 78.11	
Prothombin time	12.92 \pm 1.03	13.92 \pm 1.33	
INR	1.26 \pm 1.2	1.36 \pm 1.2	
Serum albumin	29.11 \pm 1.1	29 \pm 2.82	

P-value was calculated by student's t-test, S: Significant, NS: Not significant, P-value was significant at <0.05

Table-4 Shows that liver became nearly normal in both groups after surgery with no significant difference.

Table-5: Differences of bile culture and growth of organisms between groups (n=20; 11 in Group-A and 9 in Group-B)

Variable	Group-A (n=11)		Group-B (n=9)		p-value
	n	%	n	%	
Growth positive	7	63.6	3	33.3	0.025
Type of organism					
E. coli	5	45.45	1	11.11	0.039
Klebsiella	1	9.09	1	11.11	
Pseudomonas aeruginosa	1	9.09	1	11.11	

Table-5 shows that 7 of 11 patients (63.6%) had colonization of bacteria in Group A in contrast 3 of 9 patients (33.3%) had colonization of bacteria in Group B, and the difference was statistically significant. The type of organisms were E. coli, Klebsiella and

Pseudomonas aeruginosa. E. coli was in 5 of 7 patients (45.45%) in Group A and only 1 patient (11.11%) in Group B, and this difference was significant. Klebsiella and Pseudomonas aeruginosa was found in 1 case in each group.

Table-6: Differences of postoperative outcome between groups (N=20; 11 in Group-A and 9 in Group-B)

Postoperative morbidity	Group-A (n=11)		Group-B (n=9)		p-value
	n	%	n	%	
Wound infection	6	54.54	2	22.22	0.035
Wound dehiscence	2	18.18	1	11.11	0.262
Biliary leakage	1	9.09	0	0.0	0.999
Pancreatic leakage	1	9.09	0	0.0	0.999
Septicemia	1	9.09	0	0.0	0.999
Postoperative mortality	1	9.09	0	0.0	0.999
Length of hospital stay (Mean±SD)	40.08±15.82	35.10±10.60			
(Min-Max)	26-75	21-54			

Table-7: Differences of microscopic findings of resected bile duct between groups (N=20; 11 in Group-A and 9 in Group-B)

Microscopic findings	Group-A (n=11)		Group-B (n=9)		p-value
	n	%	n	%	
Mucosal disruption					<0.05 ^s
Present	11	100	3	33.33	
Absent	0	0.0	6	66.66	
Mucosal hyperplasia					
Present	6	54.5	4	44.44	
Absent	5	45.5	5	55.55	
Inflammatory infiltrate					

	Present	9	81.8	5	55.55
	Absent	2	18	4	44.44
Presence of Fibrosis					
	Present	11	100	8	88.88
	Absent	0	0.0	1	11.11

P-value was calculated by student's t-test, S: Significant, NS: Not significant, P-value was significant at <0.05.

DISCUSSION

Biliary decompression is an option for improving liver function prior to definitive procedure in patients with obstructive jaundice. However there are many controversies with the final outcome of this procedure. A study showed that obstructive jaundice associated with disturbed coagulation, decrease hepatic function and the development of cholangitis which has negative impact on cardiovascular function, leading to hypotension, and predispose to prerenal failure and acute tubular necrosis. [13] To overcome this problems, Lygidakis's study showed that normalize intra biliary pressures secondary to preoperative biliary decompression were associated with improved liver function, reduced peroperative bleeding and fewer postoperative complications. [14] Some study reported that biliary compression result in the reversal of organ dysfunction to variable degrees. [15-16] The present study also showed that a significant reduction of bilirubin, improvement of coagulation and serum albumin level have occurred after biliary decompression. Although the liver function improved after preoperative biliary drainage, many studies revealed that stent related complications such as wound infection, cholangitis, sepsis are quite common. In 2010 Van der Gaag et al published the result of a randomized controlled trial with patients of bilirubin level below 250 $\mu\text{mol/l}$ who underwent biliary drainage prior to surgery with plastic end prosthesis versus early surgery. The RCT showed that a higher proportion of patients in the preoperative drainage group suffered postoperative and drainage related

complications compared to patients in the early surgery group without preoperative drainage. [17]

In the present study all(n=20) patients underwent biliary decompression prior to surgery. Liver function improved significantly in all patients 10-15 days after decompression. Considering the evidence of stent related complications in other studies published in literature [18] The stent was removed 7 -10 days prior to surgery in 9 patients and stent kept in 11 patients till surgery. Our observation is that post operative outcome was significantly better in patients in whom stents removed prior to surgery than who did not. Incidence of wound infection wound dehiscence, biliary leakage, pancreatic leakage and septic complications were more when stents kept in situ. till surgery. The reason of more incidences of wound infection, wound dehiscence, biliary leakage, pancreatic leakage and septic complications possibly due to colonization of bacteria in presence of stents in situ. The other important observation of the present study that increased disturbance of mucosal integrity due to presence of stents in side biliary tree. Because of mucosal disruptional changes has shown in present study may lead to more complications like biliary leakage, cholangitis and septic complications.

On the basis of above discussion and our observation it is summarized that removal of stent prior to surgery provides a relatively good post operative outcome in view point of wound infection, other septic complications and biliary anastomotic leakage. As the number of cases are small and duration of

study is short in the present study ,any prospective study with large number of cases will provide appropriate result in future.

Limitations of the study

The present study was conducted in a very short period due to time constraints and funding limitations. The small sample size was also a limitation of the present study.

CONCLUSION

Removal of stent 7-10 days prior to definitive surgery who underwent biliary decompression for improving liver function provides better post operative outcome in obstructive jaundice.

RECOMMENDATION

This study can serve as a pilot to much larger research involving multiple centers that can provide a nationwide picture, validate regression models proposed in this study for future use and emphasize points to ensure better management and adherence.

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DECLARATION

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