

Original Article



Effect of Preoperative Internal Biliary Drainage on Postoperative Outcome Following Pancreaticoduodenectomy for Periapillary Carcinoma

Munsur Miah¹, M Fardil Hossain Faisal², Bidhan C. Das³, Md.Manir Hossain Khan⁴,
Md.Nahid Reza⁵, Riaz Mahmud⁶, Firoz Mahmud⁷, Khandaker Rezaul Hoque⁸.

Abstract

Background: Preoperative biliary drainage before pancreaticoduodenectomy is a controversial issue. Proponents are in favor of preoperative biliary drainage by ERCP with stent to reduce surgical jaundice with an anticipation of better surgical outcome. **Objective:** Compare the outcome with or without pre-operative biliary drainage before pancreaticoduodenectomy. **Materials and Methods:** This observational comparative study was conducted in department of Surgery and Hepatobiliary and pancreatic surgery of BSMMU. Twenty three patients presented with obstructive jaundice due to periapillary carcinoma who subsequently underwent pancreaticoduodenectomy were selected by purposive sampling and finalized by eligibility criteria. **Results:** Patients with preoperative biliary drainage (PBD) group required a longer operative time (mean 4.12 hours versus 3.83 hours) and had more intra-operative blood loss (mean 662 mL versus 495 mL) compared with non PBD group ($P=0.009$ and 0.010). No differences were found with respect to operative mortality (4.3%) and incidence of pancreatic leakage ($P=0.281$). PBD was significantly associated with positive bile culture ($P=0.019$) and high incidence of wound infection ($p=0.029$). **Conclusion:** Preoperative biliary drainage did not increase major postoperative morbidity and mortality but associated with increased operative time, intra-operative blood loss, and incidence of wound infection. Preoperative biliary drainage should be used selectively in patients undergoing pancreaticoduodenectomy.

Keywords: Biliary drainage, pancreaticoduodenectomy, ERCP.

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Introduction

Periapillary carcinoma is one of the leading causes of cancer - related deaths worldwide and the term used to define a heterogeneous group of neoplasm. It has got four components, which include pancreatic adenocarcinoma, cholangiocarcinoma, adenocarcinoma of the ampulla of Vater and duodenal adenocarcinoma. Surgery in the form of pancreaticoduodenectomy is the only form of therapeutic option with curative potential for the disease which is challenging procedure with high postoperative morbidity and mortality.¹ Pancreaticoduodenectomy was performed over 100

years ago. 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%.² 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%.³ Several small steps along with modifications of surgery decreased the mortality rate but no significant improvement regarding morbidity was achieved in recent years.⁴ Preoperative biliary stenting is an important step that is added here before operation to achieve better outcome after

1. Assistant Surgeon, Officer on special duty, Directorate General of Health Services, Government of Bangladesh.
2. Assistant Professor, Department of General Surgery, Khwaja Yunus Ali Medical College & Hospital, Sirajganj, Bangladesh.
3. Associate Professor, Department of Hepato-biliary & Pancreatic Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
4. Associate Professor, Department of Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
5. Assistant Surgeon, Officer on special duty, Directorate General of Health Services, Government of Bangladesh.
6. Assistant Professor, Department of Surgery, Tairunnessa Memorial Medical College Hospital, Tongi, Gazipur, Bangladesh.
7. Assistant Professor, Department of Surgery, Monno Medical College Hospital, manikganj, Bangladesh.
8. Assistant Surgeon, Officer on special duty, Directorate General of Health Services, Government of Bangladesh.

Correspondent: Dr.Munsur Miah, Assistant Surgeon, Officer on special duty, Directorate General of Health Services, Government of Bangladesh. Email: drpolash41@gmail.com, Mobile no: +8801534832460.

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 yet the role of preoperative biliary drainage as an adjunct in patients undergoing surgical resection for malignant biliary obstruction is controversial.⁵ Biliary obstruction alters the normal physiology and affects multiple organ systems that include but are not limited to cardiac, renal, hematologic, and hepatic dysfunction.⁶ 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. Evidence suggests that biliary drainage may improve immune function and nutritional status and reduce the risk of infection.⁷ Recent studies have, however, shown routine preoperative biliary drainage by stenting to offer no benefit over early surgery (within two weeks) without PBD.⁸ 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 stents and subsequent bacterial colonization of the biliary tree may increase the rates of morbidity and mortality.⁹ So, from the different corner of the world confusing decisions are being claimed as results of preoperative biliary drainage in case of malignant obstructive jaundice are different from center to center.

Materials and Methods

This prospective, observational comparative study was carried out in Surgery Department, BSMMU, shahbag, Dhaka over a period of 1 year from June, 2017 to august, 2018. All patients admitted in department of Surgery with diagnosis of obstructive jaundice due to periamplary carcinoma who received preoperative biliary stent were included in Group-I and who were not received stent included Group-II. Data were collected in a predesigned data collection sheet attached here with. Data were processed using computer software SPSS version 23.0.

Results

Patients' medical characteristics:

Total 23 patients, 15 were male and 8 were female. Mean age was 50.35(±10.32).

Table I: Demographic characteristics of patients (n=23)

Variables	Frequency	Percent (%)
Age (years)		
Mean ± SD (Min-Max)	50.35 ± 10.32 (35-75)	
Sex		
Male	15	65.2
Female	8	34.8
BMI (kg/m²)		
Under weight	6	26.1
Normal	11	47.8
Over weight	5	21.7
Obese	1	4.3
Mean ± SD (Min-Max)	21.56 ± 4.22 (14.67 30.05)	
Co-morbidities		
DM	3	13.0
HTN	1	4.3

Clinical characteristics among study groups:

All the patients were presented with jaundice with combination of other different symptoms such as pruritus, fever, melaena, anaemia, weight loss.

Table II: Clinical characteristics between two groups of patients.

	Groups		p value
	Group I (PBD) (n=13) n (%)	Group II (No PBD) (n=10) n (%)	
Jaundice	13(100.0)	10(100.0)	-
Pruritus	10 (76.9)	8 (80.0)	0.999
Fever with chills and	7 (53.8)	7 (70.0)	0.669
Malena	1 (7.7)	2 (20.0)	0.560
Anorexia and vomiti	6 (46.2)	8 (80.0)	0.197
Weight loss	8 (61.5)	7 (70.0)	0.999
Anaemia	3(23.1)	5(50)	0.221

Pre operative biochemical parameters in groups:

Analysis of liver function shows that there were no significant differences of serum total bilirubin, alkaline phosphatase and serum albumin level between two groups of patients.

Table III: Preoperative liver function test between two groups.

Biochemical variables	Groups		p value
	Group I (PBD) (n=13)	Group II (No PBD) (n=10)	
Serum bilirubin	13.00 ± 8.35	10.94 ± 5.48	0.508 ^a
(Min-Max)	(1.80-26.00)	(2.20-16.90)	
Alkaline phosphatase	548.77 ± 252.10	615.10 ± 241.08	0.531 ^a
(Min-Max)	(105.00-908.00)	(217.00-965.00)	
ALT	130.34 ± 104.64	124.90 ± 55.98	
Mean Rank	19.4	15.85	0.017 ^b
(Min-Max)	(32.00-430.00)	(70.00-250.00)	
Prothombin time	15.14 ± 2.75	13.68 ± 2.18	0.018 ^a
(Min-Max)	(12.00-20.50)	(10.90-18.60)	
INR	1.42 ± 0.23	1.17 ± 0.20	0.015 ^a
(Min-Max)	(1.20-1.80)	(0.90-1.58)	
Serum albumin	31.86 ± 3.99	34.50 ± 4.58	0.156 ^a
(Min-Max)	(27.00-41.00)	(25.00-40.00)	

^at test was done to measure the level of significance.

^bMann-whitney U test was done to measure the level of significance

Biochemical parameters of before and after stenting in stented group:

Table IV: Changes of liver function 2 weeks after stenting in group-I patients (n=13).

Biochemical variables	Before PBD	After PBD	p value
Serum bilirubin	13.00 ± 8.35	3.81 ± 3.45	<0.001 ^a
(Min-Max)	(1.80-26.00)	(1.00-12.40)	
Alkaline phosphatase	548.77 ± 252.10	357.23 ± 243.53	0.026 ^a
(Min-Max)	(105.00-908.00)	(80.00-797.00)	
ALT	100.34 ± 104.64	52.80 ± 41.15	
Median	75	37	0.015 ^b
(Min-Max)	(32.00-430.00)	(6.40-131.00)	
Prothombin time	15.14 ± 2.75	12.31 ± 1.01	0.004 ^a
(Min-Max)	(12.00-20.50)	(10.80-14.40)	
INR	1.42 ± 0.23	1.07 ± .16	0.001 ^a
(Min-Max)	(1.20-1.80)	(0.85-1.43)	
Serum albumin	31.86 ± 3.99	35.85 ± 5.43	0.023 ^a
(Min-Max)	(27.00-41.00)	(21.00-41.00)	

^aPaired t test was done to measure the level of significance.

^bWilcoxon signed rank test was done to measure the level of

significance.

Per operative bile culture and growth of organisms:

six patients (46.2%) had positive bile culture in group-I in contrast no organisms were found in group-II.

Table V: Bile culture in two groups.

Bile culture	Groups		p value*
	Group I (PBD) n (%)	Group II (No PBD) n (%)	
Positive	6 (46.2)	0 (0.0)	0.019
No growth	7 (53.8)	10 (100.0)	
Total	13 (100.0)	10 (100.0)	

*Fisher's Exact test was done to measure the level of significance.

Isolated organisms in bile culture:

E.coli was present in 50% patients.

Table VI: Growth of organisms in bile in group-I.

Growth in bile culture	Frequency	Percentage (%)
E.coli	3	50.0
Klebsiella spp	2	33.3
Pseudomonas aeruginosa	1	16.7

Time of procedure and per operative blood loss in groups:

The time required for operation is significantly higher (P=0.009) in group-I than groups-II.

Table: VIII-Differences of per operative blood loss and time of procedure between two groups.

Variables	Groups		p value*
	Group I (PBD) (n=13) n (%)	Group II (No PBD) (n=10) n (%)	
Operation time (hours)	4.12 ± 0.22	3.83 ± 0.26	0.009
(Min-Max)	(3.75-4.50)	(3.50-4.25)	
Blood loss (ml)	662 ± 163	495 ± 104	0.010
(Min-Max)	(430-860)	(410-645)	

*t test was done to measure the level of significance. Data was expressed as Mean ± SD

Post operative outcomes in groups:

Wound infection was common complication.

Table: IX- Differences of post operative outcomes between two groups

Post operative Outcome	Groups		P value*
	Group I (PBD) (n=13) n (%)	Group II (No PBD) (n=10) n (%)	
Morbidity			
Wound infection	8 (61.5)	1(10.0)	0.029
Biliary leakage	1(7.7)	0(0.0)	0.999
Pancreatic leakage	1(7.7)	3(30.0)	0.281
Length of hospital stay(mean± sd) (min-max)	40.08 ±15.82 (26-75)	35.10±10.60 (21-54)	0.402
Mortality	0 (0.0)	1(10.0)	0.435

*Fisher's Exact test was done to measure the level of significance.

Multiple responses.

Discussion

Obstructive jaundice is the most frequent presentation of periampullary carcinoma. For patients with a resectable tumor, surgical resection in the form of pancreaticoduodenectomy is recognized as an only acceptable surgical option for cure. Obstructive jaundice associated with disturbed coagulation, decrease hepatic function and the development of cholangitis which has negative impact on cardiovascular function, leading to hypotension, which predispose to prerenal failure and acute tubular necrosis S. Khurana et al.¹⁰ To overcome these problems, Lygidakis et al¹¹ showed that normalize intra biliary pressures secondary to preoperative biliary decompression were associated with improved liver function, reduced perioperative bleeding and fewer postoperative complications. In several studies such as Koyama K et al¹² and Padillo J et al¹³ reported that biliary decompression result in the reversal of organ dysfunction to variable degrees. Our study also showed a significant reduction of bilirubin, improvement of coagulation and serum albumin level after biliary decompression. In the present study, it also has been showed that more than 50% patient in group-I who underwent biliary decompression whose preoperative serum bilirubin level was more than 10 mg/dl and relatively worse liver function. Although liver function improved with biliary decompression, colonization of bile with various types of bacteria is a common problem. In the present study 46.2% patient had bile infection that underwent biliary decompression before surgery. Whereas none in who did not. Howard et al¹⁴ observed bactibilia in 80% of stented versus 42% of non stented patients (P<0.001), while Jagannath et al¹⁵ found 47% of PBD group had a positive bile culture compared with 31% of those without stent. The possible reason for the high percentage reported in their study could be the period of time between positioning of the biliary stent and surgery. The longer the biliary stent is in place, the longer the reflux of intestinal bacteria into biliary tree and thus the risk of bacterial colonization. In our study 62% of stented patients had a stent in place for over 4 weeks and 38% of stented patients for over 6 weeks. Similar to other studies such as Sudo T et al¹⁶ we found the most commonly micro organisms isolated in bile cultures were Ecoli (50%), Klebsiella spp (33.3 %) and

Pseudomonas (16.7%). These bacteria were sensitive to meropenem, colistin, nitilmicin which are costly antibiotics, they were resistance to ceftriaxon cefuroxime, ciprofloxacin and gentamicine which are low cost and commonly used antibiotics. Gavazzi et al¹⁷ found most commonly isolated organism were Enterococcus spp (75%), E.coli (36.8%) and klebsiella (34%) with higher resistance to ceftazidime which are almost similar to our study. However unlike this study, Howard et al¹⁴ and Karsten et al² found Candida spp. The present study reveals that intra operative blood loss (662 ml vs 495 ml) and operative times(4.12 hours vs 3.83 hours) were higher in patients with stented than non stented group were similar to other studies by Karsten et al² and Hodul et al¹⁸. They found patients in the stented group required a longer operative time (mean 6.8 hours versus 6.5 hours) and had greater intraoperative blood loss (mean 1207 ml versus 1122 ml) compared with unstented group (p=0.046 and 0.018). Possible cause of increase perioperative blood loss and more operative times are due to biliary endoprotheses induced inflammatory changes with considerable fibrosis, ulcerative lesion and bile duct wall thickening. This inflammatory response results increased vascularity of surrounding tissues and induce adhesion formation often making dissection in the area of porta hepatis challenging. The overall morbidity of the present study was 60.86% and mortality was 4.34% due to cardio respiratory failure on 7th post operative day. Preoperative biliary drainage was associated with high morbidity (76.9%) in compare to non stented group (40%). In relation to mortality and morbidity. Some earlier study such as Abdullah et al¹⁹ and S. G. Marcus²⁰ have reported that preoperative biliary drainage could reduce the overall morbidity and mortality due to subsequent correction of the impaired liver function and general condition but other recent studies such as Y Chan et al²¹ showed different results that increased post operative infectious morbidity and sepsis related to mortality. However Hodul et al¹⁸ have shown that postoperative morbidity and mortality for jaundiced patients undergoing pancreaticoduodenectomy were not influenced by preoperative biliary drainage. The other interesting finding of the present study is that the incidence of wound infection is significantly higher in stented group than non stented group (p=0.029). This could be related to increase colonization of bile in stented group than non stented group. Because of wound infection, the duration of hospital stay also increased on stenting group than non stenting group. In some earlier study such as Povoski SP et al⁹ and Pisters PWT et al²² has shown increased infectious complications rate after stenting. But Jagannath et al¹⁵ has shown no such association. In this study other complications including pancreatic fistula, biliary fistula were not significantly different between stented and unstented groups. In comparison to our study Bhati et al²³ found that minor biliary leak was significantly higher in stented group (P<0.043). Shone et al²⁴ also reported the incidence of wound infection and pancreatic fistula to be significantly higher in stented patients. In contrast to other report, Marcus et al²⁰ found endoscopic biliary drainage before pancreaticoduodenectomy to reduce postoperative morbidity.

On the basis of above finding and discussion it can be concluded that preoperative biliary drainage in patients with periampullary carcinoma has many advantages in terms of correction of coagulation abnormalities, improvement of nutrition and serum albumin. But it is strongly correlate with more intraoperative bleeding, prolonged operation time and post operative wound infection which increase the length of hospital stay of patient. Therefore the routine use of preoperative biliary drainage in patients undergoing pancreaticoduodenectomy is not required and it should be reserved for very poor liver function and poor performance status of patient with obstructive jaundice.

Conclusion

Preoperative internal biliary drainage improves the liver function prior to pancreaticoduodenectomy for periampullary carcinoma, but it could causes prolonged operative time, increase preoperative blood loss and bacterial colonization leading to postoperative wound infections and prolonged hospital stay. Therefore, the routine use of pre operative internal biliary drainage was not a good option prior to pancreaticoduodenectomy.

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