Biochemical alterations in malignant obstructive jaundice: Effect of pre-operative drainage

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Abstract: The benefit of preoperative biliary drainage in jaundiced patients undergoing pancreaticoduodenectomy for a suspected cancer head of pancreas is still under debate. This study evaluated the postoperative outcomes of preoperative biliary drainage with delayed surgery and immediate surgery. This study conducted on 42 patients who had malignant obstructive jaundice, serum bilirubin level was > 8 mg/dL and < 20 mg/dL, besides 25 healthy subjects. Patients were divided into group (I) was taken initially for preoperative biliary drainage and stent insertion for a period of 3 weeks followed by surgery and group (II) received immediate surgical decompression. We determined liver functions, immunoglobulins (IgA, IgG, and IgM) and cytokines (IL-6, IL-8, and IL-10). Results, mean serum bilirubin in-group (I) was 16.3 mg/dL at admission and fell to 2.7 mg/dL by three week post drainage. While in-group (II), it was 15.9 mg/dL at admission and fell to nearly normal after one week post-operatively in both groups, ALP was significantly reduced after three weeks of drainage and one week post-operative in both groups. Liver enzymes were significantly high at admission and decreased after drainage or surgery. The morbidity and mortality were significantly reduced in-group (I) compared to group (II). The serum immunoglobulin IgA level was significantly increased at admission in both groups (I & II). Its level was significantly decreased in-group (I) three weeks after drainage, and one-week post-operative in both groups. At admission, the circulating IL-8 concentrations were significantly high at admission in both groups (I & II) and reduced significantly after drainage in group (I), and one week post-operative in both groups (I & II). In conclusion, our study point at the clinical significance of the preoperative biliary drainage when major surgery is required in patients with malignant obstructive jaundice, since it improves the overall morbidity and mortality.

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Key words: malignant obstructive jaundice; biliary drainage; liver function; immunoglobulins; cytokines.

1. Introduction

Despite recent advances in perioperative support care, surgery for obstructive jaundice is still associated with significant morbidity and mortality. Jaundice has been considered as a potential risk factor for poor outcome, and pre-operative biliary drainage has been proposed as a method of reversing the pathophysiologic disturbance seen in patients with obstructive jaundice (Wang et al, 2008).

While the postoperative mortality rate after pancreatoduodenectomy has been reduced from around 20% to 1–5% in experienced centers, the morbidity rate has remained virtually unchanged, ranging from 40% to 60% [Balcom et al, 2001; Van Heek et al, 2003]. Many different etiologic factors for development of complications characterized by presence of toxic substances as bilirubin and bile salts, impaired nutritional status, effects of endotoxin, bacterial translocation, modulation of the inflammatory cascade with cytokine release, reduction of cellular immunity and nutritional status. Obstructive jaundice has been reported to be associated with an impaired immune function, including both the systemic and local defense. Alterations have been seen in gut barrier function, as well as the existence of endotoxemia. Biliary obstruction has also been associated with an increase in cytokine release, including TNFα, IL-6 and IL-8, and up-regulation of adhesion molecules (Kimmings et al, 2000).

Preoperative biliary drainage (PBD) was introduced in an attempt to improve the general condition and thus reduce postoperative morbidity and mortality. Early studies showed a reduction in morbidity. However, more recently the focus has shifted towards the negative effects of drainage, such as an increase of infectious complications. In experimental models, PBD is almost exclusively associated with beneficial results: improved liver function and nutritional status; reduction of systemic endotoxemia; cytokine release; and, as a result, an improved immune response. Mortality was significantly reduced in these animal models,

although, human studies showed conflicting results (Mayank and James, 2006).

There are theoretic arguments in favor and against biliary drainage before the pancreatoduodenectomy. Most of the studies failed to show any beneficial effect of this approach whereas others even reported an increased postoperative morbidity related with biliary drainage (Sewnath et al, 2001, Mayank and James, 2006), therefore, the role of preoperative biliary drainage remains controversial. The aim of the study was to study the results of immediate surgical decompression with the endoscopic biliary drainage and delayed surgery for the treatment of malignant obstructive jaundice; a) evaluate preoperative biliary drainage in relation to postoperative outcomes (morbidity & mortality). b) Compare preoperative biliary drainage out come with the out come of traditional surgery.

2. Subjects and methods

The study population consisted of 42 patients who had malignant obstructive jaundice (cancer head of pancreas) recruited from Surgical Department of Banha University Hospital, besides 25 healthy subjects served as control group. All groups were comparable in age distribution and gender. The inclusion criteria are; serum bilirubin level > 8 mg/dL and < 20 mg/dL, CT without evidence of distant metastases or local tumor growth into portal or mesenteric vessels. Exclusion criteria are; cholangitis/infection, previous ERCP and stenting or percutaneous biliary drainage, previous chemotherapy for this malignancy. This study was approved by the research and ethical committees of the Medical Centre of Banha University and written informed consents were obtained from all patients and healthy subjects

2.1 Study design

The diagnosis of patients with cancer head of pancreas was initially based on typical history and the presence of a mass in the head of the pancreas and dilated bile ducts on ultrasound examination or computed tomography. Patients were divided into two groups (21 patients each).

Group (I) was taken initially (21 patients) for preoperative biliary drainage (endoscopic retrograde cholangiopancreatography "ERCP" and stent insertion) for a period of 3 weeks followed by surgery after their general physical condition and biochemical parameters improvement (reduction of bilirubin level and stabilization of liver functions)

Group (II) was randomly assigned (21 patients) to receive the immediate surgical decompression.

2.2 Sampling:

Peripheral blood samples drawn from the patients at admission, 3 weeks after drainage and one-week post-operative. Ten ml of fasting venous blood samples were collected from each subject. Five ml blood put in tubes containing EDTA to separate the plasma after centrifuging for 10 minutes, the other five ml blood was left to clot at room temperature to separate sera after centrifuging for 10 minutes at 3000 r.p.m. Sera were divided into several aliquots and stored at – 70°C until assay. All participants subjected to careful history taking & clinical examination, radiological studies through chest x-ray, abdominal Sonography, abdominal computed tomography [CT] scans and endoscopic retrograde cholangiopancreatography (ERCP) to outline the biliary tree.

2.3 Laboratory investigations:

2.3.1 Hemogram: including hemoglobin concentration, total leucocytic count, platelet count using Coulter counter and examination of Lishman or Wright-stained peripheral blood smears.

2.3.2 liver function tests

1. Determination of serum aspartate transaminase (AST) and serum alanine transaminase (ALT) by using the method recommended by the Committee on Enzyme of the Scandinavian Society for Clinical Chemistry and Clinical Physiology (1974), the test was performed using already commercially available kit from Boehringer-Mannheim Company, Germany.
2. Determination of serum gamma glutamyl transferase (γGT) by using the method recommended by the Committee on Enzyme of the Scandinavian Society for Clinical Chemistry and Clinical Physiology (1976). The test was performed using already commercially available kit from Boehringer-Mannhiem Company, Germany.
3. Determination of the serum total alkaline phosphatase (ALP) enzymatic activity by using optimized standard enzymatic method according to the recommendations of the Committee on Enzyme of the Scandinavian Society for Clinical Chemistry and Clinical Physiology (1974), this a kinetic method utilizing P-nitrophenyl phosphate as substrate in diethanolamine buffer. The test performed using already available kit from BioMerieux, France.
4. Determination of serum bilirubin level by colorimetric method using available kit from Bio-Merieux Company, France (Perry et al, 1983).

2.3.3 Renal function test

Determination of serum creatinine level according to the Jaffe reaction (Husdan and Rapoport, 1968).

2.3.4 Determination of immunoglobulin

Quantitative determination of immunoglobulins levels (IgA, IgM, & IgG) by Single-Radial Immuno-diffusion method of (Mancini et al, 1965) using commercially available tripartigen plates (separate for each immunoglobulin). Each plate contained a pre-prepared solidified agar-gel into which H-chain specific anti-serum (produced by Hoechst Pharmaceuticals Ltd. Bombay) to the respective immunoglobulins (IgG, IgA and IgM) were already incorporated.

2.3.4 Determination of cytokines:

1. IL-6 and IL-8 measured by using a quantitative sandwich enzyme-linked immunosorbent assay according to the kit procedure (R & D Systems, Minneapolis, MN). The limit of detection of the assay was (5ng/1) and lower levels considered undetectable (Le Moineo, 1994).

2. IL-10 was assessed by ELISA, using as coating antibody anti- IL-10 monoclonal cl. three JES3-9D7 (Pharmingen, San Diego, California, USA) (Yamamoto et al., 2000).

3. Statistical analysis

Results expressed as range and mean $\pm$ SD. Statistical differences between haematological, chemical, and cytokine means were analysed using the one-way ANOVA test. Further analysis was carried out using a non-parametric test for two independent samples (Mann-Whitney U test), whereas T-test was used for continuous variables. All statistics carried out using the statistical SPSS for Windows 6.1 software (SPSS Inc., USA). P value <0.05 considered statistical significant.

4. Results

The study was conducted on 42 patients with malignant obstructive jaundice (cancer head of pancreas) (26 male and 16 female) with age range from 55 to 69 years. The mean age of patients who underwent preoperative drainage was almost identical to that of patients who were not drained and the percentage of men in each group was not significantly different. Moreover, weight loss of more than 10%, fever on admission, abdominal pain, jaundice, total bilirubin and creatinine levels showed no significant difference between groups. The clinical parameters in both groups were comparable at the time of admission (Table 1).

Mean serum bilirubin in group (I) patients was 16.3 mg/dL at admission and fell to 2.7 mg/dL after three week post drainage ($p<0.05$), while in-group (II), it was 15.9 mg/dL at admission. After one week post-operatively (pancreatoduodenectomy), the bilirubin levels fell in both groups (I and II) to (1.8 & 5.6 mg/dL respectively) as shown in Table 2 & Figure A. Other parameters of biliary obstruction, such as alkaline phosphatase was significantly reduced after three weeks of drainage (from 364 to 69.5 IUL^{-1}, $p=0.005$), and decreased after one week post-operative in both groups (I & II) (66.5 & 85.8 IUL^{-1} respectively). On the other hand, no effect of drainage was observed on serum creatinine. As regards the liver enzymes (ALT, AST and γGT), they were significantly high at admission and decreased after drainage or surgery (Table 2).

There was no growth from peripheral blood cultures in the studied 42 patients before drainage and curative surgery. After drainage in group (I) six patients had evidence of sepsis while in group (II) in the post-operative period ten patients had evidence of sepsis, with a fever of 38–39°C and/or rigors. Sepsis treated promptly with antibiotics. Only four patients in-group (I) and six patients' in-group (II) had positive blood cultures with a growth of E coli (Table 2).

The duration of postoperative hospital stay in-group (I) (over all stay post-drainage and post-operative) was significantly shorter (7-17 days) as compared to group (II) (11-26 days) (Table 2 & Figure B).

As regards the mortality, in-group (I), three cases died (two case post drainage and one case post-operative), while in-group (II), six cases died in the post-operative period, the cases died from fever and uncontrolled septicaemia (Table 2 & Figure B).

The serum immunoglobulin levels in all patients with obstructive jaundice illustrated in Table (3). There was statistical significantly increased serum IgA at admission in both groups (I & II), with a mean level of 621 mg/100ml & 643 mg/100ml respectively compared to the control group (231 mg/100 ml). Its level was significantly decreased in-group (I) three weeks after drainage, it became 342.5 mg/100 ml, and one-week post-operative in both groups (307.8 & 338.3 mg/100ml respectively). However, both IgG and IgM levels showed no statistical significant difference compared to control group (Table 3).

The plasma concentrations of IL-6 were below the assay detection limit (5pg/ml) in all healthy controls. At admission, IL-6 concentrations in groups

(I & II) were (3.4 & 4.5 pg/ml respectively), three weeks after drainage in group (I) it became 4.3 pg/ml, and one week post-operative in both groups (4.1 & 3.7 pg/ml respectively). while the concentrations of IL-10 at admission in groups (I &II) were (4.5 & 4.1 pg/ml respectively), after three weeks of drainage in group (I), it was 3.6 pg/ml and after one week post-operative in both groups (I & II), it became (3.7 & 3.8 pg/ml respectively).

Finally, circulating IL-8 concentrations were significantly high at admission in both groups (I & II) (106.6 & 110.2 pg/ml respectively) and was reduced significantly after drainage in group (I) to became 17.6 pg/ml; $p<0.001$, and one week post-operative in both groups (I & II), it became 15.3 & 19.5 pg/ml respectively (Table 3).

Table (1) Clinical and biochemical properties of the studied groups at admission to hospital (Data expressed as (%), range & mean ± SD)

Number	**Control (25)**	**Group I (21)**	**Group II (21)**
Age (year)	54-70 56 ± 2.5	58-67 55 ± 3.2	55-69 56 ± 2.1
Sex			
M/F	17/13	13/7	12/9
Duration of illness (days)	----	18	19.5
Clinical presentation			
Fever	-	14 (67%)	16 (76%)
Abdominal pain	-	18 (86%)	17 (81%)
Jaundice	-	21 (100%)	21 (100%)
Weight loss >10%	-	12 (57%)	14 (67%)
HB%	12.8 – 14.3 13.5 ± 1.2	9.5 – 11.8 9.9 ± 1.5	9.2 – 12 10.2 ± 1.6
WBCs X $10^3/mm^3$	5.463-10.875 9.886 ±456	9.856-17.549 16.438 ± 785	10.765-18.654 17.578 ± 674

Table (2) Clinical and laboratory data of the studied groups at different stage of therapy (Data expressed as range & mean ± SD)

	Control	Admission		Pre-operative		Post-operative	
		Group (I)	Group (II)	Group (I)	Group (II)	Group (I)	Group (II)
Number	25	21	21	19	21	18	15
Fever	-	14(67%)	16 (76%)	6 (32 %)	16 (76%)	3(17%)	10 (67%) †
Rigor	-	-	1 (4%)	4 (21%)	1 (4%)	1(5 %)	7 (47%) †
Creatinine	0.5- 0.9	0.6 -1.1	0.7 – 0.98	0.6 – 1.14	0.5 – 0.98	0.8 – 1.04	0.6 – 1
(Mg mL^{-1})	0.8 ± 0.05	0.9 ± 0.13	0.8 ± 0.18	1.01 ± 0.1	0.8 ± 0.18	0.95 ± 0.23	0.93 ± 0.12
+ve culture (E coli)	-	-	-	3 (16%)	-	1 (5.5%)	6 (40 %) †
Hosp. stay	-	-	-	3 - 10	-	4 - 7	11- 26
(days)				5 ± 3		4 ± 2	17 ± 3
Mortality	-	-	-	2	-	1	6 †
Bilirubin	0.65-0.86	13.4 – 18.3	14.3 – 17.97	2.5 – 4.3	14.3 – 17.9	1.9 – 2.5	4.1 – 7.7
(mg dL^{-1})	0.76 ± 0.1	16.3 ± 1.6†	15.9 ± 1.5†	2.7 ± 0.4*	15.9 ± 1.5†	1.8 + 0.9 *	5.6 ± 1.8*
ALT	15-26.1	23 - 44.5	26.3 – 45.8	16.2 - 26.6	26.3 – 45.8	14.6 - 22.6	15.5 – 22.3
(IU L^{-1})	21.24 ± 1.1	36.8 ± 5.4†	37.8 ± 4.6†	22.2 ± 1.2*	37.8 ± 4.6†	18.1 ± 1.4*	21.1 ± 1.6*
AST	16 - 28.4	25.5 – 45.9	29.2 – 49.8	18 – 25.1	29.2 – 49.8	15 – 23.5	20 – 29.5
(IU L^{-1})	21.7 ± 2.6	37.2 ± 4.3†	40.6 ± 4.8†	22.8 ± 1.8*	40.6 ± 4.8†	20.7 ± 1.9 *	25.1 ± 2.3*
γGT	14-19.7	34.4 – 56.9	35.6 – 59.1	16 – 24.4	35.6 – 59.1	14 – 21.6	17 – 22.4
(IU L^{-1})	15.6 ± 1.3	45.5 ± 5.2†	47.4 ± 4.9†	19.6 ± 1.8*	47.4 ± 4.9†	16.9 ± 1.6 *	18.6 ± 1.9*
ALP	45-89	112.3 – 567.8	132.5 - 637.9	52.5 – 93.6	132.5- 637.9	50.5 – 89.6	65 – 101.5
(IU L^{-1})	67.65 ±10.24	346 ± 15.8†	401 ± 16.7†	69.5 ± 8.9*	401 ± 16.7†	66.5 ± 8.1*	85.8 ±9.5*

† P<0.5 = Significant compared to the levels of control,
* P<0.5 = Significant compared to the levels at admission

Table (3): Serum immunoglobulins and cytokines level in the studied groups at different stages of therapy. (Data represented as range & mean ± SD)

	Control	At - admission		Pre-operative		Post-operative	
		Group (I)	Group (II)	Group (I)	Group (II)	Group (I)	Group (II)
IgG	669 – 1454	719.8 – 1464	861 – 1391	738.9 – 1389	861 – 1391	719.9 – 1367	767.5 – 1401
(mg/100ml)	1023 ± 144	1108 ± 122	1109 ± 126	1076.5 ± 132	1109 ± 126	1032.3 ± 149	1088.5 ± 151
IgM	65 – 145	71.2 – 155..3	74.5 – 151.1	75.3 – 149.2	74.5 – 151.1	70.1 – 138.9	72.9 – 152.2
(mg/100ml)	99.7 ± 21	109.5 ± 21	112.5 ± 19.6	110.9 ± 20	112.5 ± 19.6	108.8 ± 18	111.9 ± 21
IgA	101 – 412	456.3 –732.2	460.3 –767.2	198.2 – 465	460.3 –767.2	187.8 – 427.1	118.2 – 457.5
(mg/100ml)	231 ± 70	621.4 ± 75.4†	643.4 ± 74†	342.5 ± 72*	643.4 ± 74†	307.8 ± 67 *	338.3 ± 76*
IL-6	< 5	2.3 – 4.5	2.6 - 4.8	2.5 – 6.2	2.6 - 4.8	2.53 – 5.9	2.1 – 5.3
(pg/ml)		3.4 ± 0.9	4.5 ± 0.8	4.3 ± 1.2	4.1 ± 0.8	4.9 ± 1.2	3.7 ± 0.8
IL-8	< 5	78.5 - 128	82.4 – 132	9.1 – 24.5	82.4 – 132	8 – 25.1	8.5 – 31
(pg/ml)		106.6 ±12.5†	110.2 ± 13.4†	17.6 ± 4.3*	110.2 ± 13.4	15.3 ± 3.4	19.5 + 5.6*
IL-10	< 5	2.1 – 5.8	2.1 – 5.4	1.4 - 4.6	2.1 – 5.4	1.5 - 4.9	1.8 – 5.1
(pg/ml)		4.5 ± 0.8	4.1 ± 1.1	3.6 ± 0.7	4.1 ± 1.1	3.7 ± 0.9	3.8 ± 10.8

† Significant ($p<0.05$) compared to the levels of control
*Significant ($p<0.05$) compared to the levels at admission

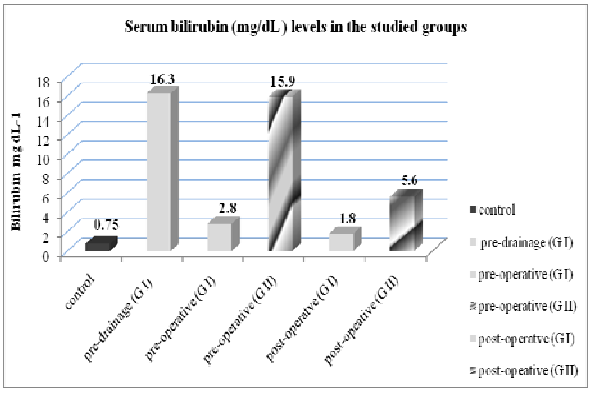

Figure A: Total serum bilirubin in the studied groups at different stages of therapy

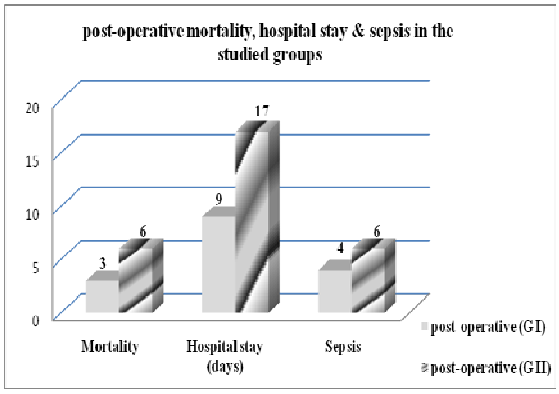

Figure B: Post-operative mortality, duration of hospital stay & sepsis in the studied groups

Discussion

Patients with obstructive jaundice secondary to malignant disease may have increased levels of cytokines as a result of an acute-phase response. Studies have shown that the combination of persistent elevation of cytokines and a prolonged acute-phase response is associated with protein-calorie depletion, leading to higher surgical complications and mortality, especially in patients with cancer (Francisco et al, 2002). Preoperative biliary drainage was introduced in an attempt to improve the general condition and thus reduce postoperative morbidity and mortality. The utility of preoperative biliary drainage for patients with surgical obstructive jaundice is controversial (Van der Gaag et al, 2007; Wang et al, 2008).

Most of the complications in the preoperative and postoperative period in obstructive jaundice have been attributed to hyperbilirubinemia. However, no uniform and universal drop in serum bilirubin has been observed in patients undergoing preoperative biliary drainage. The time taken for achieving a

significant drop in serum bilirubin levels may vary from 4 days to 3 weeks (Kaushik, 2001). Although hepatic function recovery starts immediately after biliary decompression, it may take up to 6 weeks, for complete recovery (McPherson et al, 1982). This agrees to the results of our study. As in our study, in patients with preoperative drainage (ERCP) there was a significant fall in serum bilirubin with returning of the liver enzymes to normal levels 3 weeks post-drainage, while in the patients who performed surgery, the serum bilirubin and liver enzymes showed significant fall but not returning to normal levels one week postoperative. The incidence of sepsis with positive cultures and mortality rate (21% & 16% respectively) reported after preoperative biliary drainage, while the incidence in-group (II) was (40% & 40%). The over all hospital stays in-group (I) was significant lower than in-group (II) (9 & 17 days respectively).

Previous studies supported our results as they evaluated the outcome of preoperative biliary drainage in malignant obstructive jaundice and reported that bilirubin level went to normal values within 12 days, and concluded that percutaneous transhepatic biliary decompression is a safe and potentially helpful procedure (Denning et al, 1981).

Montano-Loza et al, (2005) analyzed a series of 109 patients undergoing pancreatoduodenectomy in order to determine the association between preoperative biliary drainage and postoperative outcome. They concluded that preoperative drainage should not be considered as a routine procedure in patients undergoing pancreatoduodenectomy. While Kapsoritakis et al, (2005) reported that endoscopic stenting for malignant obstructive jaundice is safe, less invasive, and comfortable for the patients, has low cost, high success rate for relief of jaundice, improves comfort and nutritional status of the patients and has a relatively low morbidity and mortality.

Chen et al, (2008) studied the impacts of preoperative biliary drainage, postoperative complications on postoperative liver function and concluded that preoperative biliary drainage can improve liver function effectively. Postoperative complications have adverse effects on the improvement of postoperative jaundice and liver function in a short time after operation. Biliary decompression has no effects on the prognosis.

On the other hand, Karsten et al, (1996) analyzed the outcome of preoperative biliary drainage in patients being operated on for a tumor in the pancreatic head they found that, there was no significant difference in the incidence of postoperative complications between patients who had preoperative biliary drainage and those who did not. In addition, Sewnath et al, in 2001 and 2002 evaluated the preoperative biliary drainage in relation to postoperative outcomes; they found that there was no significant difference in overall morbidity between patients with and without preoperative biliary drainage (50% and 55%, respectively). They concluded that preoperative biliary drainage did not influence the incidence of postoperative complications, and although it can be performed safely in jaundiced patients, it should not be used routinely.

Dos Santos et al, (2005) have reported that presence of an endoscopic biliary drain provokes bacterial colonization, possibly due to combination of residual cholestasis and duodenal reflux to the bile duct, thereby increasing the rate of infective complications during the postoperative period such as cholangitis, liver abscess and pneumonia. Sunpaweravong et al, (2005) reported no significant difference between the two groups (endoscopic and surgery) in terms of the length of hospital stay, survival time, cost, effectiveness, and early complications. However, late complications were significantly more common in the stenting group ($p = 0.007$). They concluded that both techniques are equally effective in biliary drainage, but stenting has a higher rate of recurrent jaundice. They recommend surgery for patients with low surgical risks and endoscopic stent in those with a short life expectancy or those unfit for surgery.

Wang et al, (2008) had a trial comparing pre-operative endoscopic drainage and direct surgery showed no significant difference in mortality, but found higher morbidity in the endoscopic drainage group. The overall hospital stay was 8 to 17 days shorter in the direct surgery group. All these data are in contrast to the results of present study, as the patients managed by preoperative biliary drainage in our series had low morbidity and mortality rates when compared to patients managed by emergency surgical decompression. Although the use of a preoperative biliary stent increases the postoperative wound infection rate by about 5%, there is no overwhelming evidence that it either promotes or protects from the other complications (Velanovich et al, 2008)

As regards to changes in cytokine levels, our results revealed that IL-6 and IL-10 were slightly increased in both groups compared to control and there is no significant reduction of their levels after drainage or surgery. These results were in agreement with Kimmings et al, (2000) who found that both

IL-6 and IL-10, an anti-inflammatory cytokine, were only slightly increased compared with normal, and no significant reduction was observed after drainage.

On the other hand, Shuichi et al, (1998) found the detection rate of IL-6 in pancreatic cancer patients (54.5%) was significantly higher than for healthy controls. Obstructive jaundice potentially modulates the host defense mechanism resulting in perioperative infection. It has been reported that a systemic inflammatory response occurs in patients with obstructive jaundice. The anti-inflammatory response studied by Kimura et al, (2001) found that the Plasma concentrations of IL-10, IL-6 and sCD14 were significantly higher in jaundiced patients than in the controls. After biliary drainage, the concentrations of IL-10, and IL-6 decreased significantly. They concluded that jaundiced patients exhibited an anti-inflammatory immune response that potentially modulates the host defense mechanism and results in anergy and increased susceptibility to infection. Biliary infection may be one of the major stimuli of the immune response.

In the present study, the serum concentration of interleukin-8 was high at admission in both groups and the circulating concentration significantly decreased after drainage and surgery. The finding of increased circulating IL-8 concentrations is of importance in patients with biliary obstruction because this cytokine is involved in activation of neutrophils. High tissue concentrations of IL-8 cause recruitment of neutrophils, whereas high serum concentrations have been reported to cause a reduction in the ability of neutrophils to transmigrate through the endothelium (Baggiolini et al, 1994). Our results matched with that of Honsawek et al, (2005) reported that interleukin-8 (IL-8) is an important mediator of inflammation and immune response in human disease. Serum IL-8 levels were also higher in patients with jaundice compared with patients without jaundice. In vitro chemotaxis of peripheral neutrophils to IL-8 was significantly increased in bile duct ligated rats. In addition, Ljungdahl et al, (2007) found that malignant obstructive jaundice causes increased blood concentrations of endotoxins and cytokines.

Serum immunoglobulin results of the present study showed statistically significant higher IgA levels in both groups compared to the control, however both IgG and IgM showed no statistical significant difference, since immunoglobulin A is the predominant immunoglobulin in the bile. On reviewing the literature through several medical databases, we found few studies dealt with the effects of biliary obstruction on IgA secretion. Biliary obstruction secondary to both calculus and malignancy of the hepatobiliary system causes suppression of bile IgA secretion and elevated serum level of secretory IgA. Bile secretory IgA secretion recovers with endoscopic drainage of the obstructed system (Sung et al., 1995). In rats ligation of the biliary tract induces elevation of serum levels of immunoglobulin A (IgA) and of secretory components. Kloppel et al, (1987) have reported that IgA transport into bile decreased after temporary bile duct clamping. In humans, obstructive jaundice is known to elevate serum levels of IgA, secretory IgA, and IgA-containing circulating immune complexes (Kimming et al, 1995).

5. Conclusion

In conclusion, our study clarify the clinical significant of the preoperative biliary drainage when major surgery is required in-patient with malignant obstructive jaundice, since it improve the overall morbidity and mortality. So biliary drainage is preferred be carried out first for 3-6 weeks, before performing the major surgery, to give time for improvement of overall general condition and biochemical parameters. Hence, if there is a need for delay of a resection surgery, relief of jaundice via drainage may be carried out without fear of increase in postoperative morbidity or mortality.

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