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The Patterns of Postoperative Liver Dysfunction and Its Outcomes in Open Heart Surgery Patients: An Observational Study

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Abstract

Background: The use of cardiopulmonary bypass (CPB) in open heart surgery is frequently associated with organ dysfunction. We evaluated the patterns of serum bilirubin, enzymes level and early clinical outcomes of postoperative liver dysfunction in open heart surgery patients. *Methods*: In our study, we assessed the parameters of postoperative liver dysfunction (serum bilirubin, enzymes levels) and their impact on early clinical outcome after open heart surgery of 97 patients from May 2016 to January 2017. Postoperative hyperbilirubinemia was defined as serum total bilirubin >2.0 mg / dl. *Results:* The patients were divided into two groups: Group A; CPB time ≤ 120 minutes (37.11%), Group B; CPB time >120 minutes (62.88%). Mean total CPB and cross clamp time in group A (96.30 & 65.30 minutes respectively) and in group B (176.06 & 139.49 minutes respectively). High inotropic support, ventilation time, ICU stay, blood transfusions and complications were more in group B. The serum total bilirubin reached its maximum level on the first, second and third postoperative day in 17%, 43%, and 34% in group A and 7%, 64%, 44% in group B patients and hyperbilirubinemia came mainly from indirect bilirubin. The pattern of raised liver enzymes mainly AST on the first, second and third postoperative day in 86%, 86%, and 40% in group A and 87%, 98 %, 64 % in group B patients. Hospital mortality was higher in group B (16.33%) than in group A (5.55%). *Conclusions:* Postoperative hyperbilirubinemia and significantly raised enzyme mainly aspartate aminotransferase is common in patients undergoing cardiopulmonary bypass on second postoperative day and is predictor of mortality.

Keywords: Cardiopulmonary Bypass; Blood Transfusion; Hyperbilirubinemia; Liver Function Tests; Organ Dysfunction.

Introduction

Inspite of advances in anaesthesia, surgical and perfusion techniques, postoperative liver dysfunction is still common and compromises standard care of cardiac surgery patients. Early transient hyperbilirubinemia after heart surgery is very common. In the various studies, incidence is reported to be 10%–40% and is often associated with postoperative morbidity and mortality, while some studies showed that CPB time less than two hours is not associated with compromised liver function test. An elevation of serum liver enzymes after uncomplicated CPB has been reported in some studies. In our study aimed to identify pattern and safe levels of the serum bilirubin, enzymes and their impact on clinical outcome of postoperative liver dysfunction after CPB.

Objective

1. To identify the pattern of serum bilirubin, enzymes levels and early clinical outcomes after

cardiopulmonary bypass.

2. To identify the safe levels of serum bilirubin and enzymes in postoperative liver dysfunction.

Material and Methods

In our observational study, we assessed the serum bilirubin, enzymes level and clinical outcome of postoperative liver dysfunction in 97 patients after heart surgery from May 2016 to January 2017. The patients were divided into two groups: Group A; CPB time ≤ 120 minutes (n=36 cases), Group B; CPB time >120 minutes (n=61 cases). After anaesthesia, standard median sternotomy was performed, followed by routine aortic and atrial/ bicaval cannulation. CPB was established using membrane oxygenator, non-pulsatile blood flow and moderate systemic hypothermia. Myocardial protection was achieved by cold blood cardioplegia and topical cooling with iced slush. Indication for packed red blood cells includes: (1) haemoglobin <8.0 g/dl, (2) excessive mediastinal bleeding more than 200 ml/ hour in three consecutive hours. The serum bilirubin and enzymes levels were measured preoperatively, after CPB, postoperative day 1, 2 and 3. Postoperative hyperbilirubinemia was defined serum total bilirubin more than 2 mg/dl in any measurement. Exclusion criteria- cyanotic heart disease and patients died on day of surgery. Both groups analyzed in terms of preoperative, intraoperative, postoperative variables including study parameters.

Results

We assessed the serum bilirubin, enzymes level and clinical outcome of postoperative liver dysfunction in 97 patients after open heart surgery. The patients were divided into two groups: Group

Table 1: Comparison of patient's characteristics between two groups

Patients variables (Total =97 cases)	Group A CPB time =<120 minutes (n = 36 cases)	Group B CPB time >120 minutes (n = 61 cases)
Age (range & mean in years)	7-59 (28)	12-71 (35.55)
Sex		
• Male	8(22.22 %)	32(52.45%)
• Female	28(77.77%)	29(47.54%)
Body surface area (mm2in mean)	1.33	1.50
Left ventricular ejection fraction (% in range)	38-60%	40-60%
Preoperative Hemoglobin (gm /dl mean)	12.3	13.02
CBP time (range & mean in minutes)	54-120 (96.30)	121-310(176.06)
Aortic cross clamp time (range & mean in minutes)	34-94 (65.63)	66-260(139.49)
Procedure (= n cases)		
• MVR	20(55.55%)	32(52.45%)
• AVR	01(2.77%)	09(14.75%)
• DVR	00(00%)	15(24.59%)
• ASD	14(38.88%)	04(6.55%)
• Others	01(2.77%)	01(1.6%)
High inotropic support-	06(16.66%)	13(21.31%)
Blood product(PRBC) transfusion (range in units)	00-04	03-06
Ventilation time (= n cases)		
• Within six hours	31(86.11%)	42(68.85%)
• More than six hours	05(13.88%)	19(31.14%)
ICU stay (range in days)	2-3	4-17
Complications-		
• Re-exploration for bleeding	01(2.77%)	03 (4.91%)
• Respiratory infections	02(5.55%)	07 (11.47%)
• Wound infections	01(2.77%)	04 (6.55%)
• Neurological complications		
➢ Confusion	01(2.77%)	03 (4.91%)
➢ Deep comatose	01(2.77%)	04 (6.55%)
• Renal failure	02(5.55%)	06 (9.83%)
• Mortality	02(5.55%)	10 (16.33%)

CPB= cardiopulmonary bypass, MVR= mitral valve replacement, AVR= aortic valve replacement, DVR= double valve replacement (both aortic and mitral), ASD= atrial septal defect, CABG= coronary artery bypass, PRBC=packed red blood cell, ICU= intensive care unit

Table 2: Effect of CPB time on postoperative liver function test between two groups

Value	CPB TIME ≤120 minutes (total n= 36)					CPB time >120 minutes (total n=61)				
	T.B.	D.B.	AST	ALT	A.P.	T.B.	D.B.	AST	ALT	A.P.
Preoperative =n (%)										
*Normal range	35	33	34	33	32	57	52	55	56	55
	(97.2)	(91.6)	(94.4)	(91.6)	(88.8)	(93.4)	(85.2)	(90.1)	(91.8)	(90.1)
*Above normal range	01	03	02	03	04	04	09	06	05	06
	(2.7)	(8.3)	(2.7)	(8.3)	(11.1)	(6.5)	(14.7)	(9.8)	(8.1)	(9.8)
Postoperative Day1=n (%)										
*Normal range	30	19	05	33	32	57	23	08	58	60
	(83.3)	(52.7)	(13.8)	(91.6)	(88.8)	(93.4)	(37.7)	(13.1)	(95.0)	(98.3)
*Above normal range	06	17	31	03	04	04	38	53	03	01
	(16.6)	(47.2)	(86.1)	(8.3)	(11.1)	(6.5)	(62.2)	(86.8)	(4.9)	(1.6)
Postoperative Day2=n (%)										
*Normal range	20	08	05	29	33	21	07	01	45	58
	(57.1)	(22.8)	(14.2)	(82.8)	(94.2)	(35.5)	(11.8)	(1.6)	(76.2)	(98.3)
*Above normal range	15	27	30	06	02	38	52	58	14	01
	(42.8)	(77.1)	(85.7)	(17.1)	(5.7)	(64.4)	(88.1)	(98.3)	(23.7)	(1.6)
Postoperative Day3=n (%)										
*Normal range	23	21	21	33	34	32	20	20	41	57
	(65.7)	(60)	(60)	(94.2)	(97.1)	(56.1)	(35.0)	(35.0)	(71.9)	(100)
*Above normal range	12	14	14	02	01	25	37	37	16	00
	(34.2)	(40)	(40)	(5.7)	(2.8)	(43.8)	(64.9)	(64.9)	(28.0)	(00.0)

The normal range of study parameters is - Total bilirubin (T.B. = <2 mg/dl) and Direct (D.B. = < 0.8 mg/dl), Aspartate aminotransferase (AST = 0-50 U/L), Alanine aminotransferase (ALT = 0-50 U/L), Alkaline phosphatise (A.P. =50–140 U/L), Above normal range (TB = >2mg/dl , D.B. = >0.8mg/dl, AST & ALT = >50 U/L, AP = >140 U/L), CPB= cardiopulmonary bypass.

A; CPB time ≤ 120 minutes (37.11%), Group B; CPB time >120 minutes (62.88%). The operative technique was similar in all patients. There was no significant difference in age, body surface area, left ventricular function in both groups. Haemoglobin was > 12 gm% in both groups. Mean total CPB and cross clamp time in group A (96.30 & 65.30 minutes respectively) and in group B (176.06 & 139.49 minutes respectively). High inotropic support, ventilation time, ICU stay, blood transfusion and complications were more in group B than group A. Hospital mortality was higher in group B (16.33%) than in group A (5.55%, Table 1). The serum total bilirubin reached its maximum level on the first, second and third postoperative day in 17%, 43%, and 34% in group A and 7%, 64% and 44% in group B patients and hyperbilirubinemia came mainly from indirect bilirubin. The pattern of raised liver enzymes mainly AST on the first, second and third postoperative day in 86%, 86%, and 40% in group A and 87%, 98 %, 64 % in group B patients (Table 2.)

Discussion

In the modern era, inspite of progress in technology of oxygenators, techniques of surgery, CPB and cardiac anaesthesia variability in incidence of post operative jaundice still persists. Collin et al [1] did study in 248 consecutive patients undergoing cardiopulmonary bypass surgeries and found that early postoperative post pump jaundice (PPJ) developed in 20% cases and is strongly associated with bad outcome, 25% of jaundice patients died in postoperative period. They also noticed that jaundice was conjugated hyperbilirubinemia and detectable in 48 out of 49 patients by postoperative day 2 and suggested that PPJ was caused by defect in hepatic excretion of bilirubin. Hypotension, hypoxia, hemolysis, heart failure and hypothermia were not associated with the development of PPJ, although post operative jaundice was significantly associated with multiple valve replacement, higher transfusion requirements and longer CPB. The mortality of patients is related to the time of postoperative jaundice occurrence and was significantly increased in patients whose total bilirubin concentration reached to its peak level on the seventh postoperative day [2]. The high incidence of postoperative jaundice in Abha study [3] related to prolonged pump time. F sabzi et al [4] carried out a prospective study in 400 patients scheduled to undergo first time coronary artery bypass grafting (CABG) but only two hundred patients fulfilled the criteria and randomly were included in the study. There were 60% women and 40% men, with a mean age of 58±5 years. The preoperative TB was increased up to 20% in third postoperative day but there was no significant differences between preoperative value and first and second postoperative day. The preoperative AST and ALT was increased up to 7.3% & 4% in third

postoperative day. There was significant relation between prolonged pump time (>100 minutes) and quantity of AST in the second postoperative day but prolonged pump time has not effect on others postoperative liver function test. Wang MJ etal[5]studied prospectively in 302 consecutive patients who had undergone cardiac operation for various cardiac lesions and found that overall incidence of postoperative hyperbilirubinemia was 35.1%. In patients with postoperative hyperbilirubinemia, 70% of the increase of total bilirubin on the first postoperative day came about from an increase in unconjugated bilirubin. Olsson et al [6] observed in 93 patients up to nine months for hepatic dysfunction after open-heart surgery. On the first postoperative day almost all of the patients showed abnormal aspartate aminotransferase (AST) activity and AST/ ALT (alanine aminotransferase) greater than 1, and about 25% had hyperbilirubinemia. They suggested that early postoperative leakage of enzymes not only from the myocardium, but also from the liver. Iqbal et al [7] did a non randomized prospective study of 100 patients, selected for on pump CABG with normal liver function. Their result showed that there is no significant effect of aortic cross clamp time on postoperative liver enzyme (AST & ALT) levels. However there were significant differences between pre and post operative values of bilirubin and ALP. An Y et al [8] noticed high incidence of postoperative hyperbilirubinemia (25.3%) after extracorporeal circulation surgery.

In postoperative hyperbilirubinemia, 56.2% reached peak total bilirubin concentration on the first postoperative day, 33.5% on the second day and 10.3% on the seventh day. Their study also showed that postoperative hyperbilirubinemia occurred more frequently in patients receiving valvular replacements than in patients undergoing CABG or operation for CHD. Sharma et al [9] conducted observational studies in 476 patients who underwent cardiac surgical procedures. The overall incidence of postoperative hyperbilirubinemia was 25%. Patients undergoing valve repair or replacement had the highest incidence of hyperbilirubinemia (36.2%), followed by coronary artery bypass grafting with concomitant valve surgery (34.1%), congenital heart surgery (23.1%), and coronary artery bypass alone (12.7%). Postoperative hyperbilirubinemia was associated with increased duration of inotropic support, mechanical ventilation, intensive care unit stay, hospital stay, and mortality.

In contrast to above studies, we assessed the serum bilirubin, enzymes level and clinical outcome of postoperative liver dysfunction in 97 patients after open heart surgery. The patients were divided into two groups: Group A; CPB time ≤ 120 minutes (37.11%); Group B; CPB time >120 minutes (62.88%). There was no significant difference in age, BSA, left ventricular function in both groups. Mean total CPB and cross clamp time in group A (96.30 & 65.30 minutes respectively) and in group B (176.06 & 139.49 minutes respectively). High inotropic support, ventilation time, ICU stay, complications were more in group B than group A. The serum total bilirubin reached its maximum level on the first, second and third postoperative day in 17%, 43%, and 34% in group A and 7%, 64%, 44% in group B patients and hyperbilirubinemia came mainly from indirect bilirubin. The pattern of raised liver enzymes mainly AST on the first, second and third postoperative day in 86%, 86%, and 40% in group A and 87%, 98 %, 64 % in group B patients The mortality was higher when hyperbilirubinemia reached to peak level on the second postoperative day. Hospital mortality was higher in group B (16.33%) than in group A (5.55%).

Conclusion

Postoperative hyperbilirubinemia and significantly raised enzyme mainly aspartate aminotransferase is common in patients undergoing cardiopulmonary bypass on second postoperative day and is predictor of mortality. The increased preoperative bilirubin level, valvular heart disease, cardiopulmonary bypass time, aortic cross clamp time and blood transfusion units were common factors for persistent hyperbilirubinemia which is associated with a grave clinical outcome than early transient hyperbilirubinemia. All measures should be taken to prevent prolong CPB to avoid persistent postoperative hyperbilirubinemia resulting in impending liver failure, sepsis, or multi organ failure.

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