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Research Article

Changes in Liver Enzymes in the Patients Undergoing Open Cardiac Surgery and Related Factors

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ABSTRACT

One of the most important gastrointestinal complications following cardiac surgery is hepatic dysfunction. This prospective study was evaluated the incidence and significance of liver dysfunction after open cardiac surgery.

This study was conducted on 150 patients who were candidates for heart surgery. Liver tests including bilirubin (total and direct), alkaline phosphatase, AST, ALT were measured before the operation and on the first, third, and seventh postoperative days. Out of 150 patients, 80 were men (53.3%) and 70 were women (46.7%) with mean age of 62±12.5. Level of AST, ALT and bilirubin total has increased significantly after surgery (P<0.05). There were significant relationship between AST, ALT and alkaline phosphatase on first day after surgery and hypothermia less than 32 ° C (P<0.05), blood transfusion more than 6 units (P<0.05), intraoperative hypotension (P <0.001), duration of the pump over 100 minutes (P <0.001) and smoking (P<0.05).There was significant difference between two groups in length of ICU stay (7.14 ± 9.17 days in patients with liver enzyme changes VS. 4.11 ± 2.17 days in patients without liver enzyme changes, p-value< 0. 05) . Patients with changes in liver enzyme had a longer hospital stay (25.2 ± 6.48 in patients with liver enzyme changes VS. 9.23 ± 5.3 in patients without liver enzyme changes, p-value< 0. 05). Four deaths occurred among patients with changes in liver enzyme level but there was no death in patients without changes in liver enzyme levels that this difference in mortality rate was statistically significant (< 0.005).The results of this study showed that there is a significant relationship between and changes in liver enzymes and hypotension during the, hypothermia, the pump duration, blood transfusion, and the type of the pump.

Keywords: liver enzymes, open cardiac surgery, liver dysfunction

INTRODUCTION

Open heart surgery can be viewed as one of the greatest medical advances of the 20th century. It has been estimated that about 397,000 patient undergone cardiac surgeries in the United States in 2010 and > 80% of routine cardiac surgical procedures are performed using cardiopulmonary bypass (CPB)(1). Gastrointestinal complications following cardiac surgery are associated with high morbidity and mortality rates, prolonged hospital stay, and increased cost of hospitalization(2,3,4). Open cardiac surgery requires using cardiopulmonary bypass (CPB) which takes over

the function of the heart, lung, and circulatory system. The pump or extracorporeal circulation has important effects on body organs, including liver, due to activation of coagulation system and complement system, hemodilution, decreased tissue perfusion, neuroendocrine abnormalities, hypothermia, and existence of non-pulsatile perfusion. The most important complication of the pump is disturbance of oxygen transport, metabolism, and hepatic blood flow (5, 6,7). The pump-induced disturbed hepatic blood flow is in the form of contracted arteries and decreased oxygen consumption which leads to a 50% decrease in hepatic blood flow compared to the normal state; decreased blood circulation is more observable during cooling and warming patients during the pump (8,9,10). Liver is a strong organ which resists for many years against biochemical toxins and for hours against hypoxia. However, despite these excellent and significant abilities, cardiac surgery imposes degrees of liver failure on 2.3% of patients. As liver failure happens, mortality rate significantly increases too. The most important factors causing postoperative liver failure after open cardiac surgery are pharmaceutical factors for anesthesia, primary heart failure, and cardiopulmonary pump (11,12,13). Despite the advances made in the areas of anesthesia, extracorporeal circulation, surgery techniques, and postoperative cares, the rate of hyperbilirubinemia is still high following the surgery. According to the studies, postoperative jaundice after open cardiac surgery is associated with 25% of deaths (14). Given the importance of liver function for health, an increase in liver enzymes' levels introduces the damage to hepatocytes which leads to longer hospital stay of patients and more costs (15). This study aims at investigating changes in liver function tests after open cardiac surgery and identifying the factors related to these changes.

MATERIAL & METHODS

In this prospective study, 150 adult patients who underwent to valvular or coronary artery bypass grafting (CABG) in Rajaie cardiovascular Medical and research center fromJanuary to April 2014 were studied. Exclusion criteria including patients having complicated and combined surgery, patients with a clinical history of Gilbert's syndrome, history of cardiac arrest and CPR, history of severe and diagnosed chronic obstructive pulmonary disease (COPD), preexisting liver disease, renal failure, severe tricuspid regurgitation, severe pulmonary hypertension, hepatitis B and C, postoperative compressive pneumothorax and/or difficult intubations, EF< 25%, Redo surgeries , and patients who were reluctant to participate in the study. Liver tests including bilirubin (total and direct), alkaline phosphatase, AST, ALT, albumin, and blood lipids including LDL, HDL, and cholesterol were checked before the operation and on the first, third, and seventh postoperative days. Other information including age, sex, the type of anesthesia, the type of operation, a history of alcohol use and cigarette smoking, BMI, the type of the pump (centrifugal or roller), the amount of blood transfusion (more than 6 units), hypothermia (less than or equal to 32°C), duration of the pump (more than 100 min) and duration of aortic cross-clamp (more than 60 min) and hypotension during the surgery (mean blood pressure lower than 50 mmHg) were collected from patients' records. Quantitative data were expressed as Mean±SD and qualitative data as number (%). Qualitative data were compared with Chi2 or fisher exact test. Mann Whitney U or T-student test was used to compare quantitative variables. Repeated measure ANOVA was used to study the trend of liver enzyme changes during time. The statistical analyses were performed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). A value of $P<0.05$ was considered statistically significant.

RESULTS

Out of 150 patients, 80 were men (53.3%) and 70 were women (46.7%) with mean age of 62±12.5. Demographic and clinical characteristics of all patients are shown in table 1. Liver enzyme levels before surgery and 1, 3 and 7 days after surgery

are shown in Table 2. Trend of changes in AST level was statistically significant during time (P=0.03).Means of AST level has increased significantly on the first postoperative day (P<0.05). The mean of AST has decreased on the third and seventh postoperative day compared to before the surgery, which is not statistically significant (P>0.05). Trend of changes in ALT level was statistically significant during time (P=0.001). Means of ALT level has increased significantly on the third postoperative day (P<0.05) but it had no significant changes at first and seventh days after surgery (p>0.05).

Trend of changes in total bilirubin level was statistically significant during time (P=0.02). Means of Bili-T level has increased significantly on the third postoperative day compared to before surgery (P<0.05) but it had no significant changes at first and seventh days after surgery (p>0.05).

ALP and direct bilirubin level had no statistically significant changes during this period of time (P>0.05).The association between liver enzymes and demographic or clinical factors were assessed. Liver enzyme levels had no association with age and sex (P: 0.06, P: 0.09 respectively). There were significant relationship between AST, ALT and alkaline phosphatase on first day after surgery and hypothermia less than 32 ° C (P<0.05), blood transfusion more than 6 units (P<0.05), intraoperative hypotension (P <0.001), duration of the pump over 100 minutes (P <0.001) and smoking (P<0.05). There were no relationship between liver enzyme levels and type of surgery P>0.05).The mean ICU stay time was 7.14 ± 9.17 days in patients with liver enzyme changes and 4.11 ± 2.17 days in patients without liver enzyme changes. There was significant difference between two groups in length of ICU stay (p-value< 0. 05) (Table3).

Patients with changes in liver enzyme had a longer hospital stay (25.2 ± 6.48 in patients with liver enzyme changes VS. 9.23 ± 5.3 in patients without liver enzyme changes, p-value< 0. 05) (Table3).Any death that happens from the time of surgery until discharge was defined as hospital mortality. Four deaths occurred among patients with changes in liver enzyme level but there was no death in patients without changes in liver enzyme levels that this difference in mortality rate was statistically significant (< 0.005) (Table3).

Table 1: Demographic and operative characteristics of all patients

Variables		N (%)
Sex	Male	80(53.3%)
Female		70(46.7%)
Alcohol use		7 (4.3%)
Cigarette smoking		42 (28%)
Pump	Ruler	139(92.7%)
Centrifugal Pump		11(7.3%)
Pump time	>100 min	45(30%)
Clamp time	>60 min	89(59.3%)
Type of surgery	CABG	70(46.7%)
MVR		40(26.7%)
AVR		33(22%)
PVR		7(4.7%)
Blood transfusion	>6 unit	14(9.3%)
Hypothermia	≤32° C	60(40%)
Hypotension	MAP<50 mmHg	115(76.7%)

CABG: coronary artery bypass grafting, MVR: mitral valve replacement, AVR: aortic valve replacement , PVR: pulmonary valve replacement

Table 2: Comparison of the means of liver tests before the surgery and on the first, third, and seventh postoperative days

Test	Before the surgery	First postoperative day	Third postoperative day	Seventh postoperative day	P-Value
	mean±SD	mean±SD	mean±SD	mean±SD	
AST	48±32	49±32*	23.6±10	23.7±28	0.03
ALT	19.5±11	21.1±8	24.6±10.8*	24±15	0.003
ALP	121±65	128±77	124±92	178±90	0.324
Total Bilirubin	0.4±0.6	1.3±0.8	1.1±0.6*	2.2±1.2	0.02
Direct Bilirubin	0.6±0.5	0.6±0.4	0.33±0.4	0.3±0.2	0.467

SD=Standard Deviation, ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase

* There is a significant change in liver enzyme in comparison with before surgery (P<0.05)

Table 3: Mortality, ICU stay and hospital stay in patients with change liver enzyme in comparison with patients without change liver enzyme

	With liver enzyme change	Without liver enzyme change	P-Value
In hospital mortality	4 (3.7%)	0%	< 0.005
ICU stay (days)	7.14 ± 9.17	4.11 ± 2.17	< 0.05
hospital stay (days)	25.2 ± 6.48	9.23 ± 5.3	< 0.05

DISCUSSION

Gastrointestinal complications after open cardiac surgery in patients are about 2-3% (16). One of the most important gastrointestinal complications is hepatic dysfunction. Due to non-pulsatile blood flow, the pump or extracorporeal circulation causes decreased tissue perfusion and disturbed liver tissue oxygenation (17).

In Current study, changes in liver enzyme level during time in patients who underwent open cardiac surgery were evaluated. Our findings showed AST one day after surgery, ALT and Bilirubin Total three days after surgery were increased significantly in comparison with preoperative levels. Although the ALP in one, three and seven days after surgery were increased, this increase was not statistically significant. Akhlaghi S H et al studied the changes in liver enzymes and bilirubin after CABG using acute normovolemichemodilution in their study. They showed that the changes in bilirubin (total and direct) had significant increased (p<0.0001), while the changes in ALP, AST, and ALT enzymes were not significant compared to those before the surgery (18). Sabzi F et al, found significant AST level increase one postoperative day (p<0.05) in their study which is in line with our results (19).A major cause of damage to liver cells and enzymes increase during open heart surgery is anesthetic drugs. One of them seems to be the oxidative transformation of anesthetics drugs to toxic metabolites. Toxic metabolites increase intracellular calcium concentration (Ca ++ i) and decrease hepatic blood flow during anesthesia lead to liver blood flow changes. The incidence of hepatotoxicity is directly contributed with catabolized metabolites of anesthesia by cytochrome P450 2E1 to liver proteins that lead to antigens formation which cause antibody-mediated immune response. Factors such as blood products transfusion, shock due to decreased blood volume, and other surgical stress are associated with hepatic inflammation and dysfunction (20). In our study, we found significant relationship between type of pump, pump time over 100 minutes, blood transfusions more than 6 units, hypothermia less than 32 ° C and hypotension with changes in liver enzymes after surgery, but There were no significant relationship between age, sex, weight, type of

surgery, cross clamp time, history of smoking and alcohol and liver enzymes level .Mastoraki A et al. studied postoperative jaundice after cardiac surgery. They found that there is a significant relationship between duration of cardiopulmonary bypass, duration of aortic cross-clamp, and insertion of intra-aortic balloon pump and postoperative bilirubin level. The surgeries which are heterogeneous leads to long operation, pump, and aortic cross-clamp time, increasing damage to liver and in turn increasing enzymes (21).Chetty G et al. concluded that anesthesia has no effect on liver blood flow but hypothermia decreases liver blood flow (13). Increased peripheral blood flow and increased oxygen uptake in certain parts of the body may cause a mismatch between the visceral organs and metabolic needs, but this mismatch was not associated with disturbed liver function (22). Collins et al. showed that amount of blood transfusion during open heart surgery is one of the most important factors in liver dysfunction tests (23).

CONCLUSION

In conclusion, our study showed that AST, ALT and bilirubin levels had transient increase after open heart surgery. On the other hand there is a significant relationship between changes in liver enzymes following the open cardiac surgery andthe type of the pump, the duration of pump, smoking, number of blood transfused unit, hypotension and hypothermia during the operation.

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