IS OXIDATIVE STRESS INJURY RELATED WITH AORTIC CROSS TIME DURATION AFTER OPEN HEART SURGRY?

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Abstract: It is well none that open heart surgery and use of Cardiopulmonary bypass (CPB) is associated with damaging effects in almost all organs in human body. Multiorgan damage is caused by the systemic inflammatory response due to CPB and ischemia – reperfusion over myocardium and other organs. [1-5]. Myocardial injury and dysfunction are caused by the production of radical oxygen species (ROS) [6]. Sources of ROS are mitochondrial cytochrome oxidase, the arachidonic acid cascade, the xanthine oxidoreductase system, and neutrophil granulocytes. Isoprostanes are products of the arachidonic acid and are produce with oxidation of tissue phospholipids. Increased levels in blood and increased excretion of 8-isoprostane (8-iso-PGF2α) in urine have been found in several pathological situations and levels of 8-isoprostane have been measured previously during coronary reperfusion in patients with on-pump coronary artery bypass graft surgery (CABG). [7–13]
Malondialdehyde (MDA) is a very reactive metabolite with multiple reports indicating its role in carcinogenesis, liver and renal toxicity, diabetes mellitus, cardiovascular and neurovascular diseases, and various effects on nucleic acids [14]. Barrera et al. discussed its effect on osteoporosis, sarcopenia, immunosenescence, and myelodysplastic syndromes [15]. MDA is metabolized by mitochondrial aldehyde dehydrogenase and decarboxylation to acetaldehyde, which is then oxidized to acetate and further to water and CO2 [16,17]. MDA is a metabolite from lipids degradation, which include at least one methylene group. The main MDA precursors are arachidonic, docosahexaenoic, and linolenic acids [21].
Keywords: oxidative stress, aortic cross time, open heart surgery

1. INTRODUCTION

The aim of this study is to determine the correlation between the aortic cross clamp duration and oxidative stress marker levels in systemic blood of patients undergoing valve surgery with the help of CPB. The levels of oxidative stress markers were measured five times over a period of 48 – hour time course: T0 (15 minutes before skin incision); T1 (5 minutes after CPB); T2 (1 hour after starting CPB); T3 (12 hours after starting CPB); T4 (24 hours after starting CPB) and T5 (48hours after starting CPB).

2. MATERIALS AND METHODS

Forty patients with valvular heart diseases were included in this study for a period of two years. Average age of the patients was 68 year and all of them were operated in elective manner. Surgery included open heart surgery with single, double or triple valve disease treatment. Ten patients underwent aortic valve replacement, twenty patients underwent aortic valve replacement and mitral valve reconstruction, five underwent mitral and tricuspid valve reconstruction and five aortic valve replacement mitral and tricuspid valve reconstructions. Patients with severe hepatic disease, severe renal failure, severe chronic obstructive pulmonary disease, preoperative antioxidant therapy, pregnancy and infective endocarditis were not included in this study. None from the patients suffer from coronary artery diseases and they were divided in two groups. First group included patient with cross clamping time <50 min. and second group included patients with cross clamping time > 50 min. Plasma levels of malondialdehyde and 8 – isoprostane were measured five times over a period of 48 – hour time course: T0 (15 minutes before skin incision); T1 (5 minutes after CPB); T2 (1 hour after starting CPB); T3 (12 hours after starting CPB); T4 (24 hours after starting CPB) and T5 (48hours after starting CPB).

Anesthetic and surgical management

Anesthesia was induced intravenously and maintained with an inhalatory mixture (air, oxygen with FiO2 0.5 and 2% sevoflurane) in all patients. Muscle relaxation was obtained with doses repeated when needed. Patients were

ventilated with a volume-controlled mode (tidal volume: 7–8 ml/kg, respiratory rate 12–14 and a positive end-expiratory pressure: 5 cm H2O) to maintain normoxia and normocapnia.

Cardiopulmonary bypass

After systemic administration of heparin (300 UI/kg body weight), CPB was initiated in a standard manner with cannulas placed in the ascending aorta and right atrium or bi-caval canulation. CPB was maintained at a flow rate of 2.4 l/minute/m2. Mild and Moderate hypothermia was used (32–34°C), and local hypothermia for myocardial protection was achieved by anterograde infusion of a cool cardioplegic solution administered intermittently (every 20–25 minutes average) during clamping.

3. RESULTS

Our study showed positive correlation between the aortic cross-clamp times and the blood plasma levels of 8-isoprostane and MDA in the times T1 and T2. We found a significant increase of 8- isoprostane and MDA at each time point after CPB (T1–T4), with the greatest increases in the early time points (T1 and T2). And we found significant differences in oxidative stress marker levels in T1 and T2 between the two groups (<50 minutes vs. >50 minutes), with higher levels in favor for the second group.

Table 1: Patient's clinical characteristics and operative data

Characteristic	Groupe 1 (< 50 min) Total 20 patients	Groupe 2 (>50 min) Total 20 patients
Age (yr.) mean	65	69
Sex	12/8 m/f	11/9 m/f
Diabetes (n)	10	14
Smoking (n)	15	12
Hypertension (n)	20	20
BMI (kg/m2) mean	27.6	28.4
Cardiopulmonary bypass time (min)	67 (35–80	117 (91–162)
Aortic cross-clamp time (min)	<50 min	>50 min
Left ventricular ejection fraction (%)	57 (48–67)	48 (36–60)

4. DISCUSSION

Several studies have demonstrated that cardiac surgery with CPB is associated with ischemia-reperfusion injury associated with the cross-clamping time. Patients suffer from systemic oxidative stress with an increase of oxidative stress markers and a decrease in antioxidant reserves and this is leading to increase postoperative morbidity mortality Some studies shows that perioperative metabolic therapy or antioxidant therapy improves the outcomes in cardiac surgery patients [18-19]. We studied levels of two well-known oxidative stress markers in patients undergoing elective on-pump valve surgery with CPB. We found an early increase of 8-isoprostane and MDA in systemic blood. Levels initially peaked after CPB, and then had a progressive decrease. Our data and results are in correlations with the founding's from others studies. Our data showed that formation of ROS occurs in the myocardium early at the first 5 minutes of reperfusion. We found that at the T1 and T2 time there is a positive correlation between aortic cross-clamp duration and blood plasma levels of 8-isoprostane and MDA, and this indicates that depending on the severity of the ischemic period, oxidative injury occurs during reperfusion, and it is related with a delay postoperative recovery and cardiac dysfunction. We divided the patients into two groups based on the aortic cross clamp duration (less or more then 50 min.) and we found a significant increase in the two ROS biomarkers at all time points compared to T0 for both groups, especially at T1 and T2. Our data show that oxidative damage occurs within a short time frame (<50 minutes), although at lower levels than the damage that occurs over

longer time frames (>50 minutes). These results indicate that it is important to shorten the time of ischemia to prevent the oxidative injury.

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