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Mechanism of Reperfusion Syndrome and Prevention of Oxidative Stress

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Abstract **Original Research Article**

Coronary artery bypass grafting (CABG) leads to reperfusion syndrome, driven by oxidative stress and lipid peroxidation (LPO). This study investigated the relationship between intraoperative hemolysis (IOH) and oxidative stress in CABG patients. Based on free hemoglobin (Hbfree) levels, 123 patients were categorized into three groups: no IOH (Hbfree $\leq$ 0.1 g/L, n=43), low IOH (0.1–0.5 g/L, n=42), and high IOH ($\geq$0.5 g/L, n=38). LPO markers (diene conjugates [DC], malondialdehyde [MDA]) and antioxidant defense factors (α-tocopherol, retinol) were analyzed. Postoperatively, LPO product levels increased significantly in all groups, with the highest levels in the high IOH group ($p<0.001$). Antioxidant levels were lowest in this group, indicating oxidative stress activation. Findings suggest that reducing intraoperative hemolysis could mitigate oxidative stress and related complications. Perioperative strategies should focus on enhancing antioxidant defenses and minimizing oxidative damage in CABG patients.

Keywords: Coronary Artery Bypass Grafting, Hemolysis, Arrhythmias

INTRODUCTION

After coronary artery bypass grafting (CABG), reperfusion syndrome develops due to the resumption of blood flow in the heart. To initiate LPO processes after prolonged myocardial ischemia, a smaller amount of oxygen is sufficient than for an intact organ [1,2]. The pathogenetic mechanism of reperfusion syndrome is oxidative stress. Active oxygen species, acting in concentrations significantly exceeding physiological ones, initiate processes of lipid peroxidation (LPO) of cardiomyocyte cell membranes, cause irreversible oxidative modification of proteins and their proteolytic degradation, damage the structure of nucleic acids and high-molecular carbohydrates, inactivate antioxidant enzymes and deplete antioxidant non-enzymatic systems. This is due to the fact that during ischemia, the ability of the energy-producing systems of mitochondria to consume oxygen decreases, which creates its excess in the cell, facilitating conditions for the initiation of LPO processes and the activity of enzymatic and non-enzymatic antioxidant systems decreases, the number of initiator metabolites increases and systems producing ROS are activated. Numerous literature data show the participation of oxidative stress in reperfusion damage to the heart. However, there is no information on its activity from the degree of intraoperative hemolysis. Clarification of the relationship between the degree of hemolysis, the activity of oxidative processes and the development of complications in patients with coronary artery disease in the early period of coronary artery bypass grafting is an important scientific and practical task [3,4].

PURPOSE THE STUDY

To study changes in the prooxidant-antioxidant state in patients after CABG with varying degrees of intraoperative hemolysis (IOH).

MATERIAL AND METHODS

The degree of IOH was assessed by the level of free hemoglobin (Hbfree) using the HemoCue Plasma/Low Hb analyzer, Sweden [Svenmarker S., 2000]. In accordance with [Hbfree] in blood plasma, patients with CABG were divided into 3 groups: 1 - without IOH (Hbfree ≤ 0.1 g / l), n = 43, 2 - with low IOH (nIOH) - with [Hbfree]. >0.1 g/L and <0.5 g/L, n=42, 3 – with high IOG (hIOG) corresponded to [free Hb] ≥0.5 g/L, n=38 [Omar H.R. et al., 2015, Pan KC, 2016]. Patients underwent determination of lipid peroxidation (LPO: diene conjugates – DC and malondialdehyde – MDA) and antioxidant defense factors, AOP (*-tocopherol – *-T and retinol) in blood plasma. The concentration of [DC] in blood plasma was estimated using an SF-46 spectrophotometer (Russia). The content of [MDA] in blood plasma was determined using a Solar PV1251C spectrophotometer at a wavelength of 540 nm. The concentration of retinol and *-tocopherol (*-T) was determined by the spectrofluorimetric method.

RESULTS OF THE RESEARCH

At the end of the CABG, compared with the initial value, an increase in the content of LPO products was noted. In the group with viOG, [DK] was higher than in the 1st (p<0.001) and 2nd groups (p<0.001), as well as in the comparison (p<0.001) and control (p<0.001) groups. Similar changes at the beginning of CABG concerned [MDA], namely, an increase in the indicator was noted in the group without IOG by 74.3 (40.0; 108.6)% (z=-5.647; p<0.001), in the group with nIOG – by 175.7 (95.4; 271.4)% (z=-56647; p<0.001) and in the group with iIOG – by 281.1 (194.7; 541.5)% (z=-5.339, p<0.001), amounting to 1.8 (1.43; 2.6) μmol/l; 4.2 (3.20; 5.40) μmol/l and 5.8 (3.65; 9.60) μmol/l in groups 1, 2 and 3, respectively (p<0.001).

At the same time, the content of AOP indicators at the end of the operation in the group with vibro-angiotensin II was minimal, amounting to 0.74 (0.44; 1.26) μmol/l for retinol and 13.7 (11.3; 15.3) μmol/l for α-tocopherol, differing from their concentrations in other groups (p<0.001).

CONCLUSIONS

Prevention of oxidative stress should be aimed at reducing intraoperative hemolysis. Hemolysis in the circuits of the CPB apparatus during surgery in patients with coronary artery disease leads to the activation of oxidative stress, which is manifested by an increase in peroxidation products and a decrease in antioxidant protection in the blood plasma.

Taking into account the pathogenetic role of the prooxidant-antioxidant state in the development of complications of CABG surgery, it is advisable to develop a set of perioperative preventive measures aimed at reducing the activity of oxidative processes, as well as increasing antioxidant protection in the preoperative period.

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