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Changes in the Iron Pool in Patients with Coronary Bypass Surgery

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Abstract **Original Research Article**

The development of complications after coronary artery bypass grafting (CABG) is caused by reperfusion syndrome due to the restoration of blood flow in the ischemic zone, the main pathogenetic mechanism of which is oxidative stress. The study of changes in iron levels was carried out based on the determination of serum iron (Fe), transferrin (Tr), total serum iron binding capacity (OGCC), latent blood iron binding capacity, LVCC, ferritin (F) in blood plasma. There were no restrictions on the total concentration of nitrites and nitrates – NOx in the blood. According to the degree of intraoperative hemolysis (IOH), determined by the level of free hemoglobin, Hbsp., patients with coronary artery bypass surgery (CABG) were divided into 3 groups: group 1 – without IOH (Hbsp <0.1 g/l), h =43, group 2 – with low IOH (nIOH) with Hbs. >0.1 g/l and <0.5 g/l, n=42, group 3 with high IOG (vIOG) – Hbs.≥0.5 g/l, N=38. In patients with a high risk of changes in bi-lo indicators, the maximum was an increase of 91.9%, p <0.001, [F] – by 165.9% (p<0.001), a decrease of 22.0%, p <0.001, and LVH - by 45.0%, p <0.001. In the group without IOG change. The studied indicators of the iron pool were not revealed. At the end of CABG, compared with the baseline value, there was a decrease in [Nox] in blood plasma and its increase within 5-7 days after surgery, to the greatest extent in the group with vIOG. The revealed changes in the iron pool in patients with coronary bypass surgery indicate the influence of iron on the activity of oxidative processes, predisposing to the development of complications. This is confirmed by the nature of changes in the concentration of nitrites and nitrates, which depended on the severity of intraoperative hemolysis, indicating the effect of hemolysis products, including iron, on the formation and utilization of nitric oxide.

Keywords: Coronary Artery Bypass Grafting, Hemolysis, Arrhythmias

INTRODUCTION

As is known, the development of complications after coronary artery bypass grafting (CABG) is caused by reperfusion syndrome due to the restoration of blood flow in the ischemic zone, the main pathogenetic mechanism of which is oxidative stress [1, 2, 3]. Among the initiator molecules of oxidative stress, along with reactive oxygen species, nitric oxide (no) is released - the active form of oxygen and nitrogen), capable of initiating nitrosative stress. Nitric oxide is one of the key signaling molecules in vascular homeostasis. In small concentrations, due to its basal production, it has the ability to inhibit platelet aggregation, smooth muscle cell proliferation, and migration, reduce the expression of cell adhesion molecules by the endothelium, and inhibit the migration of activated leukocytes into the intima of the arteries [4, 6]. The pleiotropic nature of the effects does not prove the importance of its adequate production for the prevention of the development of cardiovascular complications of CABG surgery.

Deficiency is not the cause of endothelial dysfunction, manifested by excessive vasoconstriction, proadhesive b and proaggregative effects on platelets and leukocytes, contributes to the development of oxidative stress, activation of inflammation and proapoptotic effects. The transformation of positive effects into negative ones is facilitated by a significant increase in the production of reactive oxygen species, which do not transform into highly toxic peroxynitrite (ONOO-) [6].

Considering the possibility of complications after coronary artery bypass surgery in conditions of artificial blood circulation (IC), many of which have a systemic origin (myocardial infarction, arrhythmias, heart failure, acute cerebrovascular accident), it is obvious that their development may be associated with a change in blood balance, the consequence of which may be There may be activation of a number of pathogenetic mechanisms (oxidative stress, inflammation, thrombosis, etc.).

The use of artificial blood circulation (IC) during CABG surgery makes it possible to create optimal conditions for performing surgery on a "dry" heart, maintaining blood circulation in organs and tissues. However, due to the influence of a number of intraoperative factors: turbulence of blood flow, pronounced shear stress, the effect of positive and negative pressure, hydrodynamic forces and surface tension, IR promotes hemolysis [7]. A major role in the occurrence of hemolysis belongs to such patient-dependent factors as smoking, alcohol intake, etc. [8].

In turn, the use of an IR device, in the contours of which conditions for hemolysis are created, indicates a possible change in the pool of iron released from heme by free hemoglobin [9]. As is known, an increase in free hemoglobin, heme, and iron in the blood serum is a risk factor for cardiovascular diseases [10, 11]. At the same time, the level of free hemoglobin and iron, a component of heme, can affect the metabolism of nitric oxide and the level of its metabolites. The inflammatory process initiated by fragments of erythrocyte cell membranes can also contribute to a change in the level of non due to the activation of inducible net synthase [13,14].

There is insufficient information in the literature about changes in iron and nitric oxide in patients with coronary heart disease and CABG surgery. There is a clear need to study disorders of iron and nitric oxide homeostasis, the marker of which is the blood content of its stable metabolites, nitrites and nitrates (Nox), in patients undergoing CABG surgery in IC conditions.

THE PURPOSE OF THE STUDY

To study changes in iron and nitric oxide in patients with coronary artery disease after coronary bypass surgery in conditions of artificial circulation, depending on the degree of intraoperative hemolysis.

MATERIALS AND METHODS OF RESEARCH

Sources published by readers after surgery K: 123 people with unusual speed (groups 1-3). The study corresponded to the principles of the Helsinki Declaration of the World Medical Association "Ethical principles of conducting scientific medical research with human participation" and was approved by the ethical committees of the Educational Institution "GrSMU" and healthcare institutions.

City District Clinical Center [http://www.med - pravo.ru/Archives/Helsinki.txt], the information consent is fully from all participants.

The participants of the entire group were confident in growth (63.0 (58; 67) years, p> 0.05) and improvement in quality of life (81.3%, p> 0.05), i.e. 1. In cooperation with [Hbsv.] within the group of partners divided into three groups: group 1 - without IOG (Hbsv. < 0.1 g/l), n=43, group 2 – with a low content of and (nIOG) – with [Hbsv.]. >0.1 g/l and <0.5 g/l, n = 42, group 3 – with a high content of and (vIOG) - with [Hbsv.] ≥0.5g/l, n = 38 [15, 16]. The degree of IOH was assessed by the level of free hemoglobin (Hbs) using a Hemocue plasma analyzer/low hemoglobin, Sweden [17].

The groups did not differ in height, apparently, in the number of myocardial infarctions in the anamnesis (p> 0.05), the frequency of chemical cardiomyopathy (p> 0.05) and frequent irregular heart rhythm (p> 0.05).

Blood was taken from the IC apparatus at the beginning, before the coronary bypass was applied, and at the end of the IC, after its application, iron parameters (serum iron, total iron binding capacity of blood serum, OHSS, transferrin, ferritin) were determined using an automatic biochemical analyzer Mindray he BS-200 using reagents ("Diasens", RB). The concentration of iron in blood serum was determined spectrophotometrically at a wavelength of 560 nm using ferrosine, which forms a colored complex with Fe2+ C, which is determined after its reduction [18]. The total iron-binding capacity of blood serum represents the largest amount of iron that can bind transferrin until it is completely saturated [19]. The determination of changes in transferrin content in blood serum is based on measuring changes in the optical density of the test sample due to agglutination of latex reagent particles coated with antibodies to transferrin at a wavelength of 340 nm. Determination of ferritin content in blood serum is based on photometric determination of changes in the optical density of the test sample due to agglutination of latex particles coated with antibodies to ferritin [20]. A concentration study was conducted stable metabolites of nitric oxide are nitrites and nitrates [NOx] according to the generally accepted method using cadmium and Griss reagent by spectrophotometry [21]. This is due to the rapid conversion of NO into nitrite and nitrate ions (stable metabolites) - NOx due to its high reactivity. Statistical processing of the obtained data was carried out using the STATISTICA 10.0 software package. using descriptive statistics methods for quantitative (the Kraskell-Wallis method), the method of comparing dependent variables using the Wilcoxon criterion. Descriptive statistics data are presented in the form of Me (Q25; Q75), where Me is the median of the variable, Q25 is the value of the lower quartile, and Q75 is the value of the upper quartile. The differences were considered significant at $p < 0.05$.

RESEARCH RESULTS

At the beginning of the KSH, there are differences between the value of [Hb].] was not observed in the studied groups, $p > 0.05$. After CABG, there was an increase in [Hcv.] in the 2nd (with nIOG) and 3rd (vIOG) groups. At the same time, in the group with nIOG [Hbsb.] increased by 3.3 (2.5; 5) times ($p < 0.001$), in the group with vIOG – by 12 (7; 15) times ($p < 0.001$). In the 1st group of changes [Hb.] was not observed in blood plasma, indicating the absence of IOG ($p > 0.05$).

The study of iron parameters in patients with CABG surgery revealed the presence of the following changes.

In the group of patients without IOG, compared with the baseline level, no changes in iron levels were found at the end of CABG ($p > 0.05$), but there was a change in indicators in patients with IOG. Changes in the parameters, compared with their initial values, were more significant in patients with vIOG - an increase in [Fe^{2+}] in blood plasma by 91.9 (4.8; 117.5)%, $p < 0.001$, ferritin – by 165.9 (135.1; 212.6)%, $p < 0.001$, and a decrease in transferrin levels – by 22.0 (19.7; 30.2)%, $p < 0.001$, and LVEF – by 45.0 (31.3;68.7)%, $p < 0.001$. In patients with nIOH, the changes were less pronounced: an increase in [Fr.] in blood plasma by 22.9 (14.58; 35.48)% ($p < 0.001$), ferritin – by 37.5 (25.06; 45.9)% ($p < 0.001$), as well as a decrease in transferrin levels – by 8.1 (3.8;13.8)%, $p < 0.05$ and LVEF – by 9.7 (4.4;24.9) %, $p < 0.001$.

A decrease in the content of the transferrin transport protein in patients with vIOG may be due to its binding to free iron. Excessive saturation of transferrin with iron leads to its rapid elimination from the vascular bed. In turn, increased transferrin saturation, as a result of an increase in free iron in blood plasma in patients with vIOG, is indicated by a decrease in LVEF. The increase in ferritin is consistent with the literature data on the nature of changes in iron-depositing protein in patients with sickle cell anemia. Compared with baseline, the most significant decrease in [NOx] was observed in patients in the vIOG group - by 43.0 (19.4; 58.9)%, $p < 0.001$. The decrease in IOG and nIOG was less pronounced (by 12.2 (7.63; 17.3), $p < 0.001$ and by 13.8 (9.04; 19.1)%, $p < 0.001$, respectively. A week after CABG, compared with [NOx] at the end of surgery, there was an increase in [NOx] in patients of the first group by 1.39 (1.18; 1.66), $p < 0.001$ times, in the nIOG group by 1.69 (1.36; 2.23) times, $p < 0.001$, in the vIOG group by 3.71 (1.56; 5.50) times, $p < 0.001$. The greatest increase in the level of nitrites and nitrates was observed in patients with vIOG, $p < 0.001$. The reason for the increase in [NOx] in the postoperative period may be due to the activity of the inducible isoform of NOS, for which appropriate conditions arose in the 3rd group with vIOG.

DISCUSSION OF THE RESULTS

Thus, an increase in serum iron levels, a decrease in transferrin and LVEF, and an increase in ferritin levels in patients with a high degree of IOG indicate an increase in free iron levels in blood plasma, contributing to the development of complications in patients with coronary artery disease after CABG surgery due to activation of oxidative and inflammatory reactions [4, 9]. Studies have shown a decrease in [NOx] in blood plasma in patients at the end of CABG and its increase within 5-7 days after surgery. The severity of the observed changes depended on the degree of IOG. The decrease in [NOx], which was most noted in the group with vIOG, may be the result of excessive NO consumption in reactions of interaction with reactive oxygen species as initiators of oxidative stress, in particular, in the reaction of interaction with superoxidanion and its conversion to peroxynitrite (ONOO-), as well as the interaction of NO is associated with the oxy- and deoxy-forms of hemoglobin to form methemoglobin and nitrosylhemoglobin, respectively [22]. Excessive NO intake in patients with vIOG may contribute to a decrease in the anti-adhesive, antiaggregational and anti-inflammatory properties of the vascular wall, which predisposes to the development of complications caused by thrombosis. It is important to note that free hemoglobin circulating in the blood, effectively consuming NO, reduces its level in blood plasma, contributing to the processes of NO-dependent vasoconstriction and to the development of endothelial dysfunction. An increase in nitrites and nitrates in blood plasma 5-7 days after CABG surgery reflects increased activity of inducible NO synthase (iNOS) in groups with IOG. The daily production of NO with the participation of iNOS contributes to the formation of large amounts of peroxynitrite, which has a nitrosylating effect on proteins, which leads to damage to cell membranes, cytotoxic damage to vascular endothelial cells, myocardium, and the development of a systemic inflammatory response, predisposing to thrombosis and the development of complications and adverse outcomes after CABG surgery.

CONCLUSIONS

1. The destruction of red blood cells in the circuits of the artificial blood circulation system during surgery in patients with coronary heart disease leads to a change in the level of iron in the blood plasma, which indicates an increase in its free fraction.
2. Performing CABG surgery under conditions of artificial circulation in patients with coronary heart disease causes ambiguous changes in the level of nitrites and nitrate compounds [NOx] in blood plasma: a decrease immediately before the completion of surgery and an increase 5-7 days after it.
3. A direct proportional relationship has been established between changes in the level of free iron and the concentration of nitrites and nitrates on the degree of intraoperative hemolysis.
4. It is obvious that changes in iron and NO levels caused by hemolysis can contribute to the development of complications of coronary bypass surgery.

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