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Research Article

The State of The Prostacyclin-Thromboxane System in Patients with Acute Circulatory Disorders in The Early Postoperative Period After Aorto-Coronary Bypass Surgery

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Abstract

In order to clarify the role of the prostacyclin-thromboxane system (PTS) in the development of acute circulatory disorders in the early postoperative period after coronary artery bypass surgery. Its condition was studied in 86 patients with coronary artery disease. In patients with the development of vascular insufficiency and shock, a decrease in the level of thromboxane in the blood was revealed, while in patients with arterial hypertension, elevated concentrations of thromboxane in the blood were determined in the absence of changes in the level of prostacyclin. There were no significant differences in the content of prostacyclin and thromboxane between groups of patients with uncomplicated postoperative course and with the development of such complications as heart failure and hypovolemia. It has been established that the factors influencing the state of PTS in patients after coronary artery bypass grafting (CABG) are: the duration of cardiopulmonary bypass, blood loss during surgery, the number of platelets in the blood, hypocapnia. The factors influencing the aggregation ability of platelets are: the duration of cardiopulmonary bypass, the number of platelets, the degree of “emptying” of platelet alpha granules of platelets, the functional state of PTS.

Keywords: prostacyclin-thromboxane system; hemostasis; platelet aggregation; heart failure; coronary artery bypass grafting

Introduction

Relevance of the study: The intensity of coagulation- fibrinolysis processes in the early postoperative period, the risk of developing thromboembolic complications, on the one hand, and bleeding, on the other, and, finally, the possibility of developing various degrees of circulatory disorders in operated patients dictates the need to study the systems that regulate these processes.

According to the literature, the prostacyclin - thromboxane system (PTS) is one of the leading systems of neurohumoral regulation, which determines both the state of central and peripheral hemodynamics and platelet -vascular hemostasis [2, 3, 4, 6, 9].

Prostacyclin has a powerful antiaggregatory and vasodilating effect [4, 5, 7, 9]. Thromboxane, in contrast, is a platelet aggregator and vasoconstrictor [3, 6, 7, 9]. A finely balanced normal ratio between prostacyclin and thromboxane provides optimal blood rheological properties, volumetric parameters of blood flow, general and regional hemodynamics [3, 7, 8, 9, 11, 12].

It is relevant to study the state of PTS in patients with coronary heart disease (CHD) who underwent coronary artery bypass grafting (CABG) under cardiopulmonary bypass (EC). Operations on the "open heart" among surgical interventions occupy a special place. As a result of the impact on the body of a complex of factors, such as extensive surgical trauma, hypothermia, hemodilution, the use of the EC method, "artificial hemophilia", multicomponent anesthesia, etc., patients after surgery experience complex disorders in the system of hemostasis and hemodynamic system, which requiring maximum tension of regulatory mechanisms for maintaining homeostasis.

Purpose of the Study: In order to elucidate the role of PTS in the development of acute circulatory disorders, we studied its condition in 86 patients with coronary artery disease after coronary artery bypass grafting in the early postoperative period.

Material and Research Methods

The work is based on examination data of 86 patients with coronary heart disease, exertional and rest angina pectoris, who were operated on in the Department of Cardiac Surgery of the Scientific Center for Surgery of the Russian Academy of Medical Sciences.

All examined patients were male. The age of patients is 30-65 years. The mean age is 50.64 ± 0.94 years. According to the severity of the disease, all patients were assigned to the III and IV functional class (FC) according to the New York classification of cardiologists.

All examined patients in the preoperative period received the main drug therapy with nitroglycerin preparations, tranquilizers, according to indications, antiarrhythmic drugs, cardiac glycosides, and potassium preparations were prescribed according to indications.

42 patients underwent coronary artery bypass grafting of 2-5 coronary arteries, 11 patients underwent coronary artery bypass grafting + mammary coronary artery bypass grafting, 3 patients underwent coronary artery bypass grafting in combination with resection of an aneurysm of the left ventricle. All surgeries were performed under conditions of cardiopulmonary bypass with a non- pulsating nature of blood flow using the standard technique of hypothermic perfusion with a decrease in temperature in the esophagus to 27 degrees and the creation of hemodilution with a decrease in hematocrit to 25-30%. All patients underwent multicomponent general anesthesia with the use of muscle relaxants.

A complex of methods was used to examine patients. It included: a study of the state of PTS, platelet hemostasis, central and peripheral hemodynamics, acid-base balance and blood gas composition.

Patients were examined on the eve of the operation - in the morning, on an empty stomach, at the end of the operation, 3 and 18 hours after the operation.

The state of PTS was assessed by the content in the venous blood plasma of stable metabolites of prostacyclin and thromboxane, 6-keto-PGF1a and TxB2, determined by radioimmunoassay using commercial kits from the Institute of Isotopes of the Hungarian Academy of Sciences. Blood samples were taken from the cubital vein into cooled polypropylene tubes containing a prostaglandin synthetase inhibitor indomethacin (20 µl / ml) and 6% EDTA (20 µl/ml blood). Plasma was separated by centrifugation at 3000 rpm and 4°C for 20 min. Plasma was kept at -20°C prior to radioimmunoassay.

Platelet hemostasis was studied by the aggregation properties of platelets and the reaction of platelet release by β-thromboglobulin, determined by radioimmunoassay using commercial kits from Amersham (England). The aggregation properties of platelets were determined according to the V.R. Born method using the ELVI-840 instrument.

To assess the state of central and peripheral hemodynamics and the clinical course of the early postoperative period, we analyzed in all patients indicators characterizing the activity of the cardiovascular system, acid-base balance and blood gas composition.

Depending on the clinical course of the early postoperative period, patients were identified with an uncomplicated course of the postoperative period and with the development of acute circulatory disorders.

In 44 patients in the early postoperative period, complications such as heart and vascular insufficiency, arterial hypertension, hypovolemia, shock and bleeding were noted at certain stages of observation. We analyzed the state of PTS in these most common complications after CABG at all three stages of observation in the early postoperative period.

Results and discussion

The indicators of the content of prostacyclin and thromboxane metabolites in the blood and the functional properties of platelets in patients with acute circulatory disorders in the early postoperative period are presented in Table 1.

Studied indicators	Clinical course of the postoperative period					
	Uncompl icated flow	Arterial hyperten sion	Vascular failure	Shock	Cardia c failure	Hypo volemia
6-keto-PGF1A	401.0 ±	317.1 ±	368.1 ±	493.2	405.7	417.8
(pg /ml)	31.1	32.6	1.6	± 59.1	± 77.7	± 49.8
TxB2	326.7 ±	494.5 ±	203.5 ±	160.6	318.4	380.4
(pg /ml)	20.5	58.3*	48.2	± 33.6*	± 34.0	± 49.4
6-keto-PGF1a /	1.05±0.	0.71 ±	1.9 ±	2.43±	1.26 ±	1.14
TxB2	07	0.12*	0.47 *	0.37*	0.27	± 0.12
6 keto-PGF1a /	3.08 ±	3.06±0.	4.1 ±	6.95 ±	4.2 ±	2.5 ±
Number of	0.41	43	1.48	0.71*	0.88	0.44
thrombi.Pg /						
thousand blood clots						
TxB2 /Number of	2.28 ±	3.89 ±	1.96 ±	2.57 ±	2.97 ±	3.06
thrombi.Pg/thousand	0.17	0.67*	0.59	0.33	0.37	± 0.63
blood clots						
Quantity platelets	153.1 ±	119.4 ±	133.5 ±	73.2 ±	123.4	170.6
(thousand /ml)	9.9	12.5*	19.1	5.77*	± 12.5	± 15.8
Speed aggregations	11.8±0.	8.0 ±	10.8 ±	7.0 ±	10.9 ±	12.18
Platelets (mm/min)	78	2.51	1.68	1.3*	2.49	±1.49
β- thromboglobulin	183.6 ±	180.4 ±	201.8 ±	222.0	161.7	164.8
(ng /ml)	11.7	17.3	33.8	± 23.3	± 23.04	±211

*- $p < 0.05$, ** - $p < 0.01$ - significant differences in comparison with the uncomplicated course of the postoperative period

Table 1: The content of 6- keto- PGF1 A and TXB2 in the blood and indicators of platelet hemostasis in patients after CABG with different variants of the course of the early postoperative period.

As can be seen from the data presented in the table, the most pronounced disturbances in the state of PTS due to changes in the thromboxane link of the system are observed in patients with such complications as shock, vascular insufficiency, and hypertension syndrome. Low concentrations of thromboxane, significantly different from similar indicators in patients with uncomplicated postoperative course, were determined in shock and vascular insufficiency. The content of thromboxane in blood plasma in shock by 50.8%, and in vascular insufficiency by 37.7% lower compared with the values obtained in patients with uncomplicated postoperative period. In hypertensive syndrome, high levels of thromboxane in blood plasma were

detected, significantly exceeding its content in patients with an uncomplicated postoperative period.

Thus, the content of thromboxane in the blood of patients with arterial hypertension and vascular insufficiency differ significantly from each other. These states, being opposite in nature, have diametrically opposite values of thromboxane in the blood.

The content of prostacyclin in blood plasma in patients with acute circulatory disorders did not have significant differences compared with the same indicator in patients with uncomplicated postoperative period.

Thus, we have established significant changes in the level of the thromboxane metabolite in patients with the development of such complications as shock, vascular insufficiency and hypertension syndrome, which caused an imbalance between the levels of prostacyclin and thromboxane. In shock and vascular insufficiency, the prostacyclin-thromboxane ratio significantly exceeded the values obtained in patients with uncomplicated postoperative course. In patients with arterial hypertension, a significant decrease in the prostacyclin-thromboxane ratio was noted. It should be noted the unidirectionality of changes in the state of PTS in such complications as vascular insufficiency and shock. With these complications, there was a decrease in the content of thromboxane in the blood plasma, which determined a unidirectional shift in the balance between prostacyclin and thromboxane towards the predominance of the prostacyclin metabolite.

The most pronounced changes in the state of PTS were observed in patients with shock. The level of TxB2 during the development of this complication was significantly lower than the values obtained in patients with an uncomplicated course of the postoperative period, which led to an imbalance between the studied hormones in the direction of the absolute predominance of prostacyclin. Our study found that low thromboxane levels in patients with shock are due to prolonged EC and significant blood loss during surgery, and also, probably, to the fact that platelets with a high thromboxane - synthesizing ability are selectively consumed during DIC, which is a constant attribute of shock of any etiology. High levels of prostacyclin relative to the number of platelets were noted in patients with shock, which, along with other factors, are likely to take an active part in the compensatory-adaptive reaction of the body in response to a stressful situation. By preventing platelet aggregation and disaggregating fresh platelet clots, prostacyclin may prevent the formation of microthrombi in the microcirculatory system in patients with shock.

There were no significant differences in the content of prostacyclin and thromboxane between groups of patients with uncomplicated postoperative course and with the development of such complications as heart failure and hypovolemia.

The correlation analysis in patients with arterial hypertension revealed a direct dependence of systolic blood pressure and total peripheral vascular resistance on the level of thromboxane (correlation coefficients 0.672 ($p<0.05$) and 0.673 ($p<0.05$), respectively) and an inverse relationship of systolic and mean arterial pressure on the level of prostacyclin, which confirms the pathogenetic role of these hormones in the development of arterial hypertension.

In patients with vascular insufficiency, a positive relationship was established between the magnitude of diastolic pressure and the level of thromboxane (correlation coefficient 0.638).

Thus, disturbances in the state of PTS in patients in the early postoperative period are accompanied by changes in vascular tone. Decreased thromboxane levels and a shift in the prostacyclin-thromboxane ratio towards the predominance of prostacyclinare accompanied by a decrease in vascular tone, while an increase in the level of thromboxane and a decrease in the ratio lead to arterial hypertension.

In our work, we analyzed the factors influencing the state of PTS and platelet hemostasis.

It has been established that the longer the IC, the lower the level of TxB2 and the lower the number of platelets in the blood, the more reduced the aggregation ability of platelets and the higher the level of β-thromboglobulin in the blood.

The levels of metabolites of prostacyclin and thromboxane were inversely related to the number of platelets in patients after CABG: the lower the number of platelets in the blood, the higher the level of the studied hormones relative to their content, and vice versa.

It was determined that the less platelets in the blood, the lower platelet aggregation and the higher the level of β - thromboglobulin in the blood. A negative correlation was established between the indicators of platelet aggregation and the level of β - thromboglobulin.

It has been established that blood loss during surgery, exceeding 1000 ml, leads to a decrease in the level of metabolites of prostacyclin and thromboxane in the blood.

The level of prostacyclin in the blood is significantly affected by violations of ventilation processes in the lungs. In our work, it was found that hyperventilation of the lungs, leading to hypocapnia, contributes to an increase in the level of prostacyclin in the blood. This is consistent with the data of a number of studies (10,11), where it was also found that hyperventilation of the lungs, leading to hypocapnia, promotes the synthesis of vasodilatory PGs, in particular prostacyclin.

Given that one of the main functions of PTS is the regulation of the functional state of platelets, a study was made of the relationship between the levels of prostacyclin, thromboxane and platelet aggregation. The established negative correlation (correlation coefficient 0.64) between the ratio of 6-keto-PG F 1a / platelet count and platelet aggregation ability suggests that the factor contributing to the decrease in platelet aggregation properties in patients after CABG is an increase in the level of prostacyclin relative to the number of platelets.

Thus, we found that the factors influencing the state of PTS in patients after CABG surgery are: the duration of cardiopulmonary bypass, blood loss during surgery, the number of platelets in the blood, hypocapnia.

The factors influencing the aggregation ability of platelets are: the duration of cardiopulmonary bypass, the number of platelets, the degree of “emptying” of platelet alpha granules, the functional state of PTS.

Thus, based on the foregoing, we can conclude that PTS makes a significant contribution to the establishment of an adaptive response of the body in response to surgical trauma. An increase in the level of prostacyclin and thromboxane relative to the number of platelets is an important compensatory-adaptive reaction of the body aimed at ensuring the adequate functioning of the hemostatic and hemodynamic system. Disturbances in the balance between the levels of prostacyclin and thromboxane in patients after CABG surgery are accompanied by disorders of vascular tone and hemostasis.

The study of the state of PTS in patients on the first day after CABG expands the understanding of the pathophysiology of the early postoperative period and allows developing tactics for the treatment of violations of the state of the platelet hemostasis and hemodynamics, based on the analysis of changes in the regulatory factors of the hemostasis and hemodynamics system.

Conclusions

1. In patients with IHD, coronary artery bypass grafting causes a significant increase in the level of prostacyclin and thromboxane relative to the number of platelets with a simultaneous decrease in the rate of platelet aggregation

and an increase in the level of β - thromboglobulin in the blood compared to preoperative levels.

2. In patients in the early postoperative period after CABG, with the development of vascular insufficiency and shock, a decrease in the level of thromboxane in the blood was revealed, while in patients with arterial hypertension, elevated concentrations of thromboxane in the blood were determined in the absence of changes in the level of prostacyclin.

3. There were no significant differences in the content of prostacyclin and thromboxane between groups of patients with uncomplicated postoperative course and with the development of such complications as heart failure and hypovolemia.

4. It has been established that the factors influencing the state of PTS in patients after CABG are: the duration of cardiopulmonary bypass, blood loss during surgery, the number of platelets in the blood, hypocapnia. The factors influencing the aggregation ability of platelets are: the duration of cardiopulmonary bypass, the number of platelets, the degree of "emptying" of platelet alpha granules, the functional state of PTS.

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