Original Article

Status of Prostacycline-Thromboxane System and Platelet Functional Activities in Patients with Acute Myocardial Infarction Depending on Stages of Heart Failure

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Abstract

Among possible pathogenic and adaptive mechanism of acute myocardial infarction and development of its complications, the system of prostanoids, particularly prostacycline-thromboxane system is of prime importance. But many questions relating the role of prostacycline-thromboxane system in pathogenesis of myocardial infarction associated with heart failure have studied insufficiently. The objective of this work is to study the ststus of prostacycline-thromboxane system in patients of acute myocardial infarction associated with heart failure and its correlation with the platelet functions depending on stages of heart failure.

This study was performed in the department of Internal Medicine in Kharkov State Medical Institute, Ukraine in 1985-89. 120 patients with acute myocardial infarction leading to heart failure were studied. The status of prostacycline-thromboxane was considered by the level of stable metabolites of prostacycline and thromboxane - A2 as 6-keto-PGF and TXB2 respectively in venous plasma. 6-Keto-PGF-1α and TXB2 levels were determined by Radio-immunological method with the help of kits manufactured by the English Firm "New England Nuclear". To determine the platelet aggregation properties, the instrument "Bian-120" transmitter was used. It was established clinically that prostacycline- thromboxane activation depends on clinical features of myocardial infarction, i.e. its localization, depth, extension or affected size of MI, first attack or re-infarction. Maximum changes of prostacycline thromboxane system took place in extensive myocardial infarction which was expressed in increased level of TXB2 and significant change of prostanoid imbalance ratio. Parameters of platelet aggregation function and prostacycline thromboxane system were interrelated during heart failure, which were expressed by their changes in aggregation diagram.

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Introduction

Myocardial infarction is the most widespread disease causing high percentage of invalidity and mortality.[1]. Among all cardiovascular diseases, it is the most dangerous as it causes more sick rate, disability and mortality. Prognosis and severity of myocardial infarction to a considerable extent are related to the after effects of illness, which appear during the first days of the disease[2], and result in death. Fifty percent cases may occur due to complication of heart failure[3,4].

Despite considerable achievements in the field of pathogenesis of heart failure, not all the pathogenic mechanisms have been studied till now and for that reason there is a little progress in its treatment. Among possible pathogenic and adaptive mechanism of acute myocardial infarction and development of its complications, the system of prostanoids, particularly prostacycline-thromboxane system is of prime importance[5]. Discovery of prostacycline-thromboxane system permits to study the pathogenesis of coronary atherosclerosis, ischemic heart disease and myocardial infarction and to propose some ideas concerning the participation of this system in the pathogenesis of heart failure as well[6,7].

It has been shown previously that among the causes of the development of heart failure associated with acute myocardial infarction, the main role belongs to the clinical specification of the disease i.e. depth and extension and the localization of the infarction, the nature of infarction i,e, primary or repeated attacks of the disease[4]. However, many questions relating the role of prostacycline-thromboxane system in pathogenesis of myocardial infarction associated with heart failure have studied insufficiently, though it is known that the value of prostacycline-thromboxane effect is determined by their quantitative ratio.

The later is caused by intensity of their byosynthesis and metabolism in lungs, vessels, platelets and other tissues[8,9].

Prostacycline and thromboxane-B2 are metabolites of 20 poly-unsaturated carbon fatty acids- the main regulators of vascular platelet interaction[10]. M S Muller et al made an attempt to characterize platelet function at acute myocardial infarction as well as local and systemic factors that may influence on their status under such conditions[11]. Action of powerful anti-platelet factor of prostacycline on platelet during acute myocardial infarction has been studied as well. The prostaglandin bears particular interest, because it is the most powerful anti-aggregating substance and has powerful endogenous protective action against micro-thrombus formation during acute myocardial infarction[12].

The main objective of this work is to study the ststus of prostacycline-thromboxane system in patients of acute myocardial infarction associated with heart failure and its correlation with the platelet functions depending on stages of heart failure.

Methods and Materials

This study was performed as a part of the dissertation in the department of Internal Medicine, Hospital no. 27 in Kharkov State Medical Institute, Ukraine in 1987-89. In the coronary care unit and in intensive care unit, 120 patients with acute myocardial infarction were studied.

The status of prostacycline-thromboxane was considered by the level of stable metabolites of prostacycline and thromboxane -A2 as 6-keto-PGF and TXB2 respectively in venous plasma. 6-Keto-PGF-1α and TXB2 levels were determined by Radio-immunological method with the help of kits manufactured by the English Firm "New England Nuclear". The blood samples were drawn from subclavian or cubital veins into the cooled silico-glass or propylene test tubes which contained EDTA anticoagulant for determination of prostanoids in the serum according to Morris's recommendations.

To determine the platelet aggregation, the instrument "Bian-120" transmitter (GVRBorn's method[13]) was used. The blood was taken from the subclavian or cubital veins into the plastic tubes with 3.8% solution of sodium citrate at the rate of 9:1. Aggregation action of platelet was determined by "Bian-120" transmitter and measurer permitting to graphically dropping of optical density in the aggregation process.

Results

Among the selected patients, only 6 were women. Their age and sex distribution are shown in the table 1. TheMaximum 51 (42.5%) patients were of age between 50-59 years.

TABLE 1. Distribution of respondents according to their age and sex.

Age	No of pts (%)	Men (%)	Women (%)
	-	-	-
20-29	1 (0.8)	1 (0.9)	-
30-39	11 (9.2)	11 (9,6)	-
40-49	36 (30)	36 (31.6)	-
50-59	51 (42.5)	46 (40.3)	5 (83.4)
60-69	17 (14.2)	16 (14.0)	1 (16.6)
<70	4 (3.3)	4 (3.5)	-
T0TAL	120 (100)	114 (95.0)	6 (5.0)

According to the classification of acute heart failure by M J Wolk, S Scheidt, Killip[14], all studied patients were divided into four stages of heart failure (Table II). Among them 23 (19.1%) without symptoms of heart failure were referred to the stage I; 47 (39.2%) patients having signs of marked heart failure and crept or rales as less than 50% surface of both lungs were included into the stage II. Stage III contained 39 (32.5%) patients with cardiac asthma in 20 (16.7%) patients and with pulmonary edema in 19 (15.8%) patients. Stage IV contained 11 (9.2%) patients with cardiogenic shock.

TABLE 2.Classification of acute heart failure by M J Wolk, S Scheidt, Killip & Distribution of the respondent.according to localization of MI .

Localization of MI	Stage I	Stage II	Stage III		Stage IV
	No. of Pts n=23 (19.1%)	No. of Pts n=47 (39.2%)	Card. asthma n=20 (16.7%)	Pulm. edema n=19 (15.8%)	No. of Pts n=11 (9.2%)
Anterior n=53(44.2%)	6 (5.0)	22 (18.3)	11 (9.1)	9 (7.5)	5 (4.2)
Antero-lateral n=32(26.7%)	9 (7.5)	15 (12.5)	5 (4.2)	2 (1.6)	1 (0.9)
Antero-septal n=21(17.5%)	8 (6.6)	6 (5.0)	3 (2.5)	4 (3.3)	-
Ant-inferior n=5(4.2%)	-	1 (0-9)	-	2 (1.6)	2 (1.6)
Inferior n=6(5%)	-	3 (2.5)	-	1 (0-9)	2 (1.6)
Circulatory 3(2.5%)	-	-	1 (0-9)	1 (0-9)	1 (0.9)

The respondents were distributed according to the localization of their MI. Of them anterior infarction was 53 (44.2%), antero-lateral was 32(26.7%), antero-septal was 21(17.5%), antero-inferior was 5 (4.2%), and inferior was 6 (5.0%), Their distribution was shown according to their stages. (Table 1I)

Table III showed that prostacycline level was highest when symptoms of heart failure was absent at 1st stage and lowest at the 4th stage. Thromboxane (TXB2) level was higher in 3rd and 4th stages than in stages I and II. The more prominent is imbalance ratio, the severe is the acute heart failure; i.e. predominance of thromboxane link in the system. The degree of imbalance was lineally increased up to the III stage but reduced somewhat at 4th stage, what supports the role of the system in the pathogenesis of pulmonary edema.

Microcirculation status was evaluated according to platelet aggregation (Table IV). Platelet aggregation rate was somewhat higher in II stage but lowest in cardiac asthma where in pulmonary oedema, this parameter did not differ from I& II stages. Clear dependence was found in analyzing platelet index values which was decreasing as heart failure becoming more and more severe. Platelet refraction index was directly proportional to the stages of acute heart failure.

Dynamics of parameters of prostacycline -thromboxane system were analyzed on the 1-2, 3-4, 5-7 and 10-12 days in patients with Acute MI according to the stages of heart failure (table V). During I stage, 6-ketoPGF-1α level from 1st to 4th days was actually unchanged. Up to 7th day, these values significantly increased and then decreased to the initial level to the end of 12th day. TXB2 level had found reverse tendency. In 2nd stge, 6-ketoPGF-1α level had behaved same as Ist stage but increasing TXB2 level was found initially and then decreasing at the 12th day. Balance of TXβ2/6-ketoPG-1α was raised on the 1st day and after that found decreased only a little bit.

During III stage of heart failure with cardiac asthma, 6-ketoPGF-1α level was lowest on 3-4 days and then found increased. TXB2 level was found same as 6-ketoPGF-1α and their ratio was high initially and then somewhat decreased up to 10-12 days. At the 3rd stage of heart failure with pulmonary edema, TXB2 level was found highest during 1-2 days and both parameters were sharply reduced up to the 10th - 12th days where TXB2 reduced mre than 6-ketoPGF-1α. In this process their ratio level reached equal to one.

Together with the dynamic change of prostacycline-thromboxane system, there was an analysis study about the change of functional platelet activity during the period of MI depending on the progression of heart failure (Table VI). At the stage I of heart failure, platelet aggregation rate level was the highest during up to 3-4 days. It was reduced by 1/3 and up to 5-7 days, it returned to original state. But at 10-12 days, this value sharply reduced and equals 2 times lower than original level. Platelet aggregation index and its corresponding refraction index remained same up to 4th day, after that aggregation index increased in 5-7 days but refraction index increased, which occurred on the basis of increasing level of aggregation rate. Up to 10-12 days, aggregation index significantly reduced and refraction index increased.

The 2nd stage of heart failure was characterized by more significant delaying in dynamics and by stabilizing of platelet aggregation index. Aggregation rate was only somewhat reduced with little variations up to 12th day. At the same time aggregation rate and aggregation index did not change during this period. At the 3rd stage, during cardiac asthma aggregation rate reduced at 5-7 days then increased up to 10-12 days but refraction index had reduced tendency while refraction index increasing. At the 3rd stage with pulmonary edema, aggregation rate was somewhat stable and aggregation index had a tendency to reduction but refraction index to increase.

TABLE III Status of prostacycline-thromboxin (M±m) system in patients with acute myocardial infarction depending on the stages of heart failure.

Prostanoid parameter	Total No n=120	Stage I Pts n=23	Stage II Pts n=47	Stage III		Stage IV No. of Pts n=11
				Card. asthma n=20	Pulmonary edema n=19	
6-ketoPGF-1 (pg/ml)	81.6± 1.8	86.6± 1.8	83.3± 2.4	84.4± 5.4	72.0± 7.3	72.1± 4.1
$TX^2{}_2$(pg/ml)	102.6± 3.1	78.5± 5,5	98.2± 4.6	107.1± 8.3	138.9± 8.8	120.6± 7.2
$TX^2{}_2$/6-keto-PGF-1± ratio	1.4± 0.1	1.0± 0.1	1.2± 0.1	1.4± 0.1	2.5± 0.4	1.8± 0.3

TABLE V. Dynamics in Prostacycline -Thromboxane system (M±m) in patients with Acute MI according to the stages of heart failure.

Stages of heart failure	Days of the disease	Prostanoid parameter		
		6-ketoPGF-1 (pg/ml)	TX² 2 (pg/ml)	TX² 2/6-ketoPGF-1±
I	1-2	76.8 ± 1.9	81.8 ± 13.3	1.0 ± 0.1
	3-4	80.0±8.5	85.9±8.1	1.2±0.2
	5-7	111.8±13.2	77.6±14.2	0.7±0.2
	10-12	85.5±3.6	70.3±7.5	0.8±0.1
II	1-2	76.9±4.9	102.3±9.6	1.4±0.1
	3-4	82.5±6.4	95.0±9.8	1.3±0.2
	5-7	90.9±3.8	103.9±8.4	1.2±0.1
	10-12	81.3±3.6	91.8±8.7	1.2±0.1
III Cardiac asthma	1-2	74.5±8.7	103.6±19.6	1.6±0.3
	3-4	70.1±3.7	92.7±14.7	1.5±0.2
	5-7	85.6±9.6	107.4±11.5	1.3±0.1
	10-12	108.0±11.3	111.2±9.4	1.1±0.2
III Pulmonary edema	1-2	56.9±7.1	147.2±7.1	3.3±0.7
	3-4	93.9±15.0	119.7±19.1	1.3±0.2
	5-7	82.2±14.3	161.6±10.5	2.4±0.6
	10-12	46.0±5.9	47.0±6.0	1.0±0.2

TABLE VI. Dynamics of Pleteletagreegation parameters (M±m) in patients with Acute MI according to the stages of heart failure.

Stages of heart failure	Days of the disease	Platelet aggregation parameter		
		Aggregation rate (C^{-1})	Aggregation index (%)	Platelet refraction index (%)
I	1-2	36.7 ± 8.1	65.8 ± 2.7	34.2 ± 2.7
	3-4	23.2 ±3.7	64.4 ±3.7	35.7 ±3.7
	5-7	39.4±3.5	88.8±6.2	11.2 ±6.2
	10-12	19.0 ±2.5	51.0± 5.6	49.1± 5.6
II	1-2	30.4 ±3.7	58.0 ±4.6	42.0±4.6
	3-4	34.8 ± 4.1	58.7 ±4.8	41.3 ±4.8
	5-7	25.0 ±2.4	59.2 ±2.9	41.2 ±2.8
	10-12	24.7 ±5.7	56.0 ±3.5	44.7 ±3.4
III Cardiac asthma	1-2	21.0 ±2.2	67.7 ±1.1	32.7 ±1.1
	3-4	11.9 ±0.7	52.3 ±14.0	51.0 ±13.2
	5-7	5.8 ±2.1	35.4 ±3.8	64.8 ±2.8
	10-12	24.9 ±2.2	42.9 ±11.4	61.1 ±8.5
III Pulmonary edema	1-2	29.5 ±5.7	76.3 ±6.5	29.0 ±5.1
	3-4	20.5 ±5.4	44.3 ±12.2	55.7 ±12.2
	5-7	29.0 ±5.9	36.3 ±14.2	48.7 ±3.7
	10-12	-	29.0±3.6	71.0±6.9

Discussion

Prostacycline level was inversely proportional to the stages of heart failure but thromboxane level and their imbalance ratio were directly proportional (Table III). Their levels were higher in pulmonary edema than that in cardiogenic shock. Such evidences support the role of thromboxane in the pathogenesis of pulmonary edema.

Microcirculation status was evaluated according to platelet aggregation parameters. Because of little quantity of patients having acute myocardial infarction with 4th stage of cardiogenic shock, parameters of these group of patients were not performed (Table IV). Functional platelet properties showed that they influence on those parameters like aggregation and refraction but not on aggregation rate.

Dynamics in prostacycline and thromboxane found increased day by day but decreased at 10-12 days in I and II stages but in 3rd stage with cardiac asthma, they increased up to10-12 days. Balance ratio obtained to the maximum on the 1st days of disease and after that found decreased only in every stages (Table V). But in pulmonary edema it increased at 5-7days and deceased at 10-12 days which might be related to the exhausted compensatory potential of the system during acute period of the disease.

Analyzing indices of platelet aggregation potential in patients having acute MI, table VI showed that the severe the heart failure, higher was the refraction index. Character of aggregation index variations had been of particular importance. If during the 1st and 2nd stages it varied about definite mean value, during 3rd stage with pulmonary edema it gradually reduced. Less informative was aggregation rate. The severe was the heart failure; less was aggregation rate.

Comparing parameters of prostacycline-thromboxane system and platelet aggregation ability in case of acute heart failure seemed the fact that higher is the thromboxane level and imbalance ratio, higher is the platelet refraction index and lower is the aggregation index.

Results of this study worked out close interconnection between dynamic changes of prostacycline-thromboxane system and the platelet aggregation potential in patients with acute myocardial infarction depending on the stages of heart failure.

Acute myocardial infarction complicated with acute heart failure is characterized by activation of prostacycline thromboxane system which is expressed in progressive reduction of prostacycline level and increase of thromboxane level in venous blood as heart failure becomes more severe. Imbalance ratio of prostacycline-thromboxane system is formed by progressive deterioration of heart failure.

Parameters of platelet aggregation function and prostacycline thromboxane system were interrelated during the stages of heart failure. It was observed that there was an increase of platelet refraction index, where as aggregation rate did not change, but aggregation index was increased in patients with acute myocardial infarction without complication of heart failure i.e. at first stage.

During managing of patients with acute myocardial infarction, it seems to be expedient to investigate the parameters of prostacycline thromboxane system and platelet aggregation in different stages of heart failure to follow up the prognosis of acute heart failure and to select the proper therapy.

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