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The influence of polarizing GIK mixture on the indicators of myocardial necrosis

For many years attempts have been undertaken in order to diminish the area of necrosis in myocardial infarction. Cardiosurgical methods and invasive vascular procedures such as angioplasty have proven efficacy but restricted availability. As far as pharmacological methods are concerned, GIK mixture is frequently mentioned, but is still waiting for clinical approval (1,6,7). Enzymes activity in blood serum, such as CPK, CK-MB, AspAT and AlAT are helpful in estimating the area of necrosis and the course of myocardial infarction (2).

The purpose of the study was to estimate the influence of GIK mixture on dynamic changes in markers of myocardial infarction in its acute phase.

MATERIAL AND METHODS

The study was carried out in a group of patients with acute transmural myocardial infarction hospitalised in Cardiology Intensive Care Unit in the Department of Internal Diseases, Medical University of Lublin within the period of one year. The following criteria for entering this group were established: recognised acute myocardial infarcion of inferior or anterior wall, based on clinical signs – e.g. retrosternal pain, lasting longer than 30 min and ECG criteria: elevation of ST segment >= 1mm in at least 2 leads of a routine ECG record; starting with fibrinolytic treatment. Patients were randomly divided into 2 groups. The first group (GIK) consisted of patients who, exept for typical treatment in myocardial infraction, were given during the first 24 hours two infusions of GIK (500 ml of 10% glucose, 10 units of maxirapid insulin and 3.0 g of KCl), each infusion lasting for 12 hours. The second group (placebo) consisted of patients who, exept for typical treatment in myocardial infarction, were given during the first 24 hours 2 infusions of 500 ml of 0.9% NaCl each. During this research 112 patients with symptoms of infarction were admitted to the hospital. In 88 patients typical sings of anterior myocardial infarction were present in ECG records. In 24 patients infarction of lateral wall or subendocardial infarct was recognised. The group of 88 patients excluded those who experienced pain for more than 12 hours and those who had severe complications while being admitted to the hospital. These complications were: ulmonary haemostasis (grade III according to Killip), cardiogenic shock, resuscitation caused by circulatory arrest, disorders of conduction requiring endocavitar stimulation, diabetes, renal failure, bronchitis. Finally, 52 patientes entered the trial group and then they were given GIK mixture or a NaCl solution (0.9%). In 8 patients (15%) infusion was stopped during the first 24 hours. It was caused by acute complications of myocardial infarction (circulatory arrest, disorders of conduction requiring stimulation, shock, pulmonary oedema, embolism, haemostatic complications). The

examined group consisted of 44 patients: 19 with anterior myocardial infarct and 25 with inferior infarct. Both groups are discussed in Table 1.

Table 1. General characteristics of patients with acute myocardial infarction treated with GIK or placebo (NS – nonsignificant)

	GIK (n=27)		Placebo (n=17)		p
Sex	female	male	female	male	
	6	21	6	11	NS
Age (years)	60.3 ± 12.2		64.8 ± 6.9		NS
Weight (kg)	73.1 ± 13.1		65.6 ± 3.6		NS
Height (cm)	169 ± 10		163 ± 10		NS
BMI (kg/m2)	25.6 ± 3.5		24.6 ± 3.4		NS
Site of infarction	anterior	inferior	anterior	inferior	
	12	15	7	10	NS
Chest pain before (hours)	7.9 ± 5.6		5.3 ± 3.4		NS
History of arterial hypertension	No	Yes	No	Yes	
	17	10	6	11	P= 0.07
History of myocardial infraction	No	Yes	No	Yes	
	22	4	16	1	NS

The patients were randomised into 2 groups: placebo and GIK. There were 27 patients in GIK group and 17 patients in placebo group. Every patient included into a study group had the following parameters checked directly before and after 24 hours of treatment with GIK or placebo: concentration in blood serum of CPK, CK-MB, GOT, GTP. The total activity of CPK was measured by a kinetic method with 340 nm using Hoffman-La Roche lab equipment. Isoenzyme CK-MB was measured by immunochistochemic method with the use of specific antibodies. Enzyme activity was measured in 37°C. The activity of AspAT and AlAT was measured by kinetic method with 340 nm with the use of Cormay lab equipment.

RESULTS

In the examined group of patients with myocardial infarction a statistically significant increase in CPK activity was observed after 24 hours. On initial examination, CPK activity, was 372 ± 490 U/j, after 24 hours 852 ± 762 U/j, p=0.012. In patients receiving GIK the increase of CPK activity was smaller (mean CPK activity increased from 446 ± 560 U/j to 718 ± 673 U/j) and was observed randomly. In placebo group initial CPK activity was 266 ± 358 U/j, and after 24 hours 1045 ± 861 U/j; the increase was statistically significant. In placebo group CPK activity increased independently of the site of infarction. In the group treated with GIK the increase was not statistically significant, both in case of inferior wall myocardial infarction and in case of anterior wall. Changes of CPK activity are presented in Table 2.

In a group of patients with myocardial infarction, after 24 hours the increase of CK-MB in blood serum was noted – from 85.1 ± 56.7 U/j to 141 ± 110 U/j, although it was not statistically significant p=0.09). In a group receiving GIK the increase of CK-MB was very moderate (from 105.2 ± 55 to 121 ± 91 U/j) and randomly observed. In placebo group CK-MB activity was initially 59 ± 51 U/j and after 24 hours 167 ± 134 U/j; the increase was at the borderline of statistical significance (p=0.09). Considering the infarction site, a statistically significant increase in CK-MB activity was proven in patients with anterior wall infarction in placebo group. Results of CK-MB activity in groups, after taking into consideration the site of infarction, are presented in Table 3.

Table 2. CPK activity in blood serum during GIK and placebo treatment in patients with myocardial infraction

				GIK anterior wall infarction	
				exam 1	exam 2
				560±663	797±831
				NS	
		GIK		GIK inferior wall infarction	
		exam 1	exam 2	exam 1	exam 2
Whole group		446±560	718±673	323±418	632±471
exam 1	exam 2	NS		NS	
372±490	852±762	Placebo		Placebo anterior wall infarction	
p=0.0012		exam 1	exam 2	exam 1	exam 2
		266±358	1045±861	486±536	1226±720
		p=0.0013		p=0.02	
				Placebo inferior wall infarction	
				exam 1	exam 2
				135±64	937±956
				p=0.024	

Table 3. CKMB activity in blood serum during GIK and placebo treatment in patients with myocardial infarction

				GIK anterior wall infraction	
				exam 1	exam 2
				121±58	131±101
				NS	
		GIK		GIK inferior wall infraction	
		exam 1	exam 2	exam 1	exam2
Whole group		105.2±55	121±91	114±66	85±41
Exam 1	exam 2	NS		NS	
85.1±56.7	141±110	Placebo		Placebo anterior wall infraction	
NS (p=0.09)		exam 1	exam 2	exam 1	exam 2
		59±51	167±134	86±62	164±64
		NS (p=0.09)		p=0.01	
				Placebo inferior wall infraction	
				exam 1	exam 2
				48±49	168±161
				NS	

On examination, after 24 hours of treatment, a highly significant increase of AspAT activity in blood serum was noted, independently of the site of infarction. In a group treated with GIK, AspAT activity increased from 48.4 ± 46.5 U/j to 111.7 ± 94.1 U/j (p= 0.0014). In placebo group the increase was from 32.3 ± 17.4 U/j to 94.2 ± 72.7 U/j (p= 0.0046). Results of AspAT activity in blood serum regarding the site of infarction are presented in Table 4.

Table 4. ASPAT activity in blood serum during GIK and placebo treatment in patients with myocardial infraction

				GIK anterior wall infraction	
				exam 1	exam 2
				58.5±55.2	152.6±115
				p=0.014	
		GIK		GIK inferior wall infraction	
		exam 1	exam 2	exam 1	exam 2
Whole group		48.4±46.5	111.7±94.1	38.3±35.7	70.7±40.2
exam 1	exam 2	p=0.0014		p=0.0013	
41.9±38	104.6±85.4	Placebo		Placebo anterior wall infraction	
NS		exam 1	exam 2	exam 1	exam 2
		32.3±17.4	94.2±72.7	46.8±26.1	107.8±96.5
		p=0.0046		NS	
				Placebo inferior wall infraction	
				exam 1	exam 2
				25.1±7.8	87.4±62.6
				p=0.01	

In GIK group the activity of AlAT was initially 21.5 ± 15.1 U/j and after 24 hours 47.6 ± 73.2 U/j. In placebo group AlAT the activity in blood serum was respectively 20.5 ± 13.3 U/j and 54.7 ± 86.5 U/j. The observed increase of AlAT in blood serum was not, however, statistically significant because of wide standard deviation. In analysis regarding the site of infarction only changes in enzyme activity in case of inferior wall infarction in placebo group

Table 5. ALAT activity in blood serum during GIK and placebo treatment in patients with myocardial infraction

				GIK anterior wall infraction	
				exam 1	exam 2
				27.9±20.1	73.5±102.8
				NS	
		GIK		GIK inferior wall infraction	
		exam 1	exam 2	exam 1	exam 2
Whole group		21.7±15.1	47.6±73.2	16.2±5.6	24.5±14.7
exam 1	exam 2	NS		NS	
21.2±14.2	50.4±77.2	Placebo		Placebo anterior wall infraction	
NS		exam 1	exam 2	exam 1	exam 2
		20.5±13.3	54.7±86.5	22±11.3	34.1±19.2
		NS		NS	
				Placebo inferior wall infraction	
				exam 1	exam 2
				19.9±14.6	62.4±101.6
				p=0.01	

were statistically significant. Results of AlAT activity in blood serum regarding the site of infarction are presented in Table 5.

DISCUSSION

Greater excretion of some myocardial cells enzymes from the site of infarction produces the increase of their concentration in blood serum (4, 5). It is known from experimental studies that slower increase of CPK in blood serum may be connected with smaller damage of myocardial cells (8). In the examined group of patients with acute myocardial infarction statistically significant increase of CPK and AspAT in blood serum was observed, after comparing the initial examination with results after 24 hours of treatment. Increase of CK-MB activity was at the borderline of statistical significance; ALAT activity also increased, but was not statistically significant. In a group receiving GIK the increase of CPK was not so big and randomly observed, comparing to the placebo group, where values were significant and high, not connected with site of infarction. Similar results were observed for CK-MB. The increase in GIK group was insignificant and in placebo group high, at the borderline of significance.

AspAT activity in blood serum after 24 hours had a tendency to increase, independently of treatment and site of infarction. Except for a group of patients with inferior wall infarction, receiving placebo, no significant increase of ALAT was observed. In the examined group, lower activity of indicative enzymes was noted in case of inferior wall infarction, comparing to patients with anterior wall infarction. It is applicable especially to CPK level.

Lower, profitable level of CPK and CK-MB in patients treated with GIK is highly suggestive of the positive effect of treatment with insulin, glucose and kalium. It can depend on the restriction of the infarction area. These observations correlate with clinical observations of Dłużniewski (2), who noted a significantly smaller increase of enzyme activity in a group treated with GIK, comparing to the control group. Similar conclusions were presented by Eberli et al. (3). The authors, on the basis of observations concerning dynamic increase of CPK and AlAT noted that in patients treated with glucose and insulin the damage of myocardial cells during acute infarction and reperfusion stage was not so much evident and advanced comparing to patients in placebo group. Discussions, lasting for 30 years, concerning the usefulness of GIK mixture in acute myocardial infarction cannot be solved in one prospective study, although noted changes in biochemical parameters during GIK treatment may speak in favour of this method.

CONCLUSIONS

In the above presented study it was stated that a profitable profile of CPK and CK-MB in patients treated with GIK speak in favour of preventive influence of GIK on ischemic myocardium.

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SUMMARY

For the estimation of the role of GIK in diminishing post-infarction necrosis, the influence of GIK mixture on indicative enzymes (such as: CPK, CK-MB, ASPAT and ALAT) was checked. In a group of patients treated with GIK the increase of CPK and CK-MB activity after 24 hours was less pronounced, comparing to placebo group and differences between groups were at the borderline of statistical significance. Other parameters in both groups did not change in statistically significant way. A noted profitable change in CPK and CK-MB activity speaks in favour of GIK mixture and it is role in diminishing myocardial necrosis.

Wpływ mieszanki polaryzującej KIG na wskaźniki martwicy mięśnia serca

W celu oceny skuteczności KIG w ograniczaniu martwicy zawałowej zbadano wpływ mieszanki polaryzującej na poziom wskaźników martwicy mięśnia serca, takich jak: kinaza fosfokreatynowa (CPK), izoenzym (CK-MB), aminotransferaza asparaginowa (ASPAT) i alaninowa (ALAT). W grupie pacjentów otrzymujących KIG wzrost aktywności CPK i CK-MB po 24 godzinach był mniejszy niż w grupie placebo, a różnice między grupami były na granicy istotności statystycznej. Pozostałe badane parametry w obu grupach nie zmieniły się w sposób statystycznie istotny. Stwierdzenie korzystnych zmian stężeń CPK i CK-MB przemawia za skutecznością mieszanki polaryzującej KIG w ograniczeniu martwicy mięśnia sercowego.