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## SPECIFICS OF CORRECTIONAL METABOLIC THERAPY IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND DIABETES MELLITUS

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**Summary.** *There were examined 51 patients with acute myocardial infarction, including 26 with diabetes mellitus to determine the specifics of metabolic therapy with glucose-insulin-potassium in patients with acute myocardial infarction and type 2 diabetes mellitus. It was found that severity of acute heart failure by Killip and cardiogenic shock in patients with acute myocardial infarction were greater in patients with diabetes mellitus. The use of glucose-insulin-potassium in patients with acute myocardial infarction and type 2 diabetes mellitus is justified, particularly considering its antiarrhythmic effect. GIP infusion had no significant effect on blood glucose levels, which may indicate the safety of such ratios of glucose, insulin and potassium chloride.*

**Keywords:** *acute myocardial infarction, diabetes mellitus, glucose-insulin-potassium (GIP).*

Group of patients with acute myocardial infarction (AMI) and diabetes mellitus (DM) comprises one of the patient categories in modern cardiology, who have poor prognosis, despite considerable achievements of thrombolytic therapy. In such patients, compensatory ability of undamaged by infarction myocardium is decreased due to following mechanisms: initial congestive heart failure, caused by diabetic cardiomyopathy, severe coronary artery disease, decreased vasodilation reserve of epicardial and resistance arteries and myocardial metabolism disturbances [1, 3]. So, the influence on one of those segments by the glucose-insulin-potassium (GIP) is used for more than 50 years in practical cardiology.

**The goal** of study was to determine specifics of metabolic therapy with glucose-insulin-potassium in patients with acute myocardial infarction and type 2 diabetes mellitus.

### MATERIALS AND METHODS

51 patients with acute myocardial infarction were the object of study, 26 (51.0%) of them — with concomitant type 2 diabetes mellitus. The average age of studied patients was  $65.37 \pm 0.99$ ; 7.13 years (mean  $\pm$  error; standard deviation), maximum 79 years, minimum 45 years). 39 (76.5%) patients were diagnosed ST segment elevation myocardial infarction, and 12 (23.5%) — non-ST segment elevation myocardial infarction. 19 (37.3%) patients were diagnosed recurrent AMI. 18 (35.3%) patients were diagnosed acute heart failure of II and higher class by Killip. 13 (50%) patients with AMI and concomitant diabetes mellitus got GIP infusions additionally to standard treatment.

Patients were examined according to Ukrainian standards, this included detailed analysis and comparison of morphometrical atrial and ventricular parameters using echography and results of heart de- and repolarization study using electrocardiography, biochemical markers of AMI, coagulation and fibrinolytic status in addition to general clinical examinations. All patients underwent BP, HR, saturation (arterial blood hemoglobin saturation with oxygen), respiratory rate monitoring and ECG monitoring (using monitor UTAS UM 300). Diabetes mellitus was defined as type 2 DM according to National Diabetes Date Group criteria. Type 2 DM was defined in patients older 40 years, who were diagnosed diabetes mellitus and who did not require insulin injections for more than 2 years after beginning of antihyperglycemic therapy and were not prone to ketoacidosis development.

Statistic analysis included parametric and nonparametric methods. Normality of variation distribution was checked with the values of coefficient of skewness and kurtosis, results of unifactorial Kolmogorov-Smirnov test with correction by Lilliefors, W test Shapiro-Wilks (software SPSS for Windows Release 13.00, SPSS Inc., 1989–2004). If variabilities had abnormal distribution, in such case we used nonparametric statistic methods (software SPSS for Windows Release 13.00, SPSS Inc., 1989–2004), particularly Mann-Whitney U (MW). Divergence between groups was determined using nonparametric method – sign test (ST). To evaluate divergence of categorical variables we used Fisher's exact test (FET) (software Statistica for Windows Release 5.1, 1984–1998 by StatSoft, Inc.).

## RESULTS AND DISCUSSION

It was established, the survival rate after myocardial infarction is related to residual function of left ventricle and so, to weight of damaged myocardium [2]. However, incidence and severity of congestive heart failure and cardiogenic shock in case of diabetes mellitus are higher, than expected based on size of damaged area (table 1). Significance between acute heart failure class by Killip and presence of type 2 diabetes mellitus in patients with acute myocardial infarction, according to chi-square test is shown in table 2 (according to Pearson's chi-squared test, probability ratio, linear through linear association and Fisher's exact test).

To detect the influence of GIP infusion on mortality rate, cardiac arrest and cardiogenic shock development during acute STEMI, large randomized controlled trial CREATE-ECLA [5–8] was performed. Its results detected slight significant decrease of ischemia recurrence in group of GIP in the first day as well as during the 7-days and 30-days observation. During subgroups analysis it was not noted any effect of GIP use, which depended of symptoms duration before the time of randomization, severity class by Killip, presence of diabetes mellitus and reperfusion therapy and its type.

But it should be noted, that GIP was used in unusually high concentrations for our country: 25% glucose solution, 50 UI/L of regular insulin, 80 mEq/L of potassium. Infusion rate was 1.5 mL/kg/hour and it lasted for 24 hours [8]. Administration of such hypertonic glucose solution can lead to aggregation of red blood cells and platelets, that can trigger disturbances of microcirculation, perfusion ability and, as a result electric myocardial instability [3]. In our study polarizing solution consisted of 5% glucose solution and 0.5% potassium chloride solution, 100 ml of which contains potassium ion 67.06 mmol/L, chloride ion 67.06 mmol/L, with addition of 4 Units of insulin, infusion rate 20 gtt/min. Effect of such concentrations, according to our data had no influence on blood cells coagulation properties. Haemocoagulative parameters (prothrombin index, APPT, INR) had no significant difference ( $p > 0.05$ ).

Effect of GIP is based on conversion of damaged myocardium metabolism from free fatty acids oxidation towards glucose, which is energetically favorable in conditions of hypoxia, that could adequately maintain contractile function of stunned myocardium. Due to insulin, that is component of GIP, there is an inhibition of free fatty acids release out adipocytes, that potentiates energy production balance shift towards glucose metabolism. Potassium has crucial role in bioelectrical cell activity and maintaining of neuromuscular excitability and conductivity [3–4]. That is why, potassium chloride, as a part of GIP, in association with insulin contributes to intracellular potassium level restoring and balances levels of magnesium, sodium, calcium ions, that positively affect electrical stability of myocardium.

So, in group of patients with GIP infusion we did not note any episodes of ventricular and supraventricular arrhythmias comparing to patients without GIP infusion, where such disturbances were noted in 5 (19.23%) of 13 patients ( $P_{\text{efn}} = 0.039$ ).

Blood glucose level in patients with AMI and concomitant type 2 diabetes mellitus increased by 14% after infusion of GIP and in group of patients without diabetes mellitus increase of this parameter was 9.6%. This indicates the good enough tolerance of such infusions in patients with diabetes mellitus and their safety in use.

Table 1

**Relationship between acute heart failure class by Killip and presence of concomitant type 2 diabetes mellitus in patients with acute myocardial infarction**

Patients with AMI	Absolute number and percentage of patients with AHF by Killip		Total
	I class	II-IV class	
With concomitant type 2 diabetes mellitus	13 (25,5%)	13 (25,5%)	26 (51,0%)
Without diabetes mellitus	20 (39,2%)	5 (9,8%)	25 (49,0%)
Total	33 (64,7%)	18 (35,3%)	51 (100,0%)

Table 2

**Data about significance between acute heart failure class by Killip and presence of concomitant type 2 diabetes mellitus in patients with acute myocardial infarction, based on chi-square test**

	Value	df	Significance (two-tailed)	Significance (two-tailed)	Significance (one-sided)
Pearson's chi-squared test	5.023(b)	1	.025		
Probability ratio	5.160	1	.023		
Fisher's exact test				.040	.025
Linear through linear association	4.924	1	.026		

Of course it is impossible to replace prompt reperfusion therapy by infusion of GIP, but in condition of such therapy remoteness in specific population category and availability of GIP it is appropriate to implement this therapy to postpone unfavorable consequences of acute coronary syndrome.

### CONCLUSIONS

1. Severity of acute heart failure by Killip and cardiogenic shock in patients with acute myocardial infarction is higher in case of diabetes mellitus.
2. Use of glucose-insulin-potassium makes sense in patients with AMI and concomitant type 2 diabetes mellitus, especially considering its antiarrhythmic effect.
3. GIP infusions made no significant influence on blood glycemia level, that can indicate the safety of such ratios of glucose, insulin and potassium chloride.

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### ОСОБЕННОСТИ КОРРЕКЦИОННОЙ МЕТАБОЛИЧЕСКОЙ ТЕРАПИИ У БОЛЬНЫХ ОСТРЫМ ИНФАРКТОМ МИОКАРДА В СОЧЕТАНИИ С САХАРНЫМ ДИАБЕТОМ

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**Резюме.** С целью определения особенностей метаболической терапии глюкозо-инсулин-калиевой смесью у больных острым инфарктом миокарда в сочетании с сахарным диабетом 2 типа было обследовано 51 больной с острым инфарктом миокарда, из них 26 — в сочетании с сахарным диабетом. Установлено, что выраженность острой сердечной недостаточности по Killip и кардиогенного шока у больных острым инфарктом миокарда больше при сахарном диабете. Применение глюкозо-инсулино-калиевой смеси оправдано у больных ОИМ в сочетании с сахарным диабетом 2 типа, особенно учитывая ее противоваритмический эффект. Инфузии ГИК не имели существенного влияния на уровень гликемии крови, что может свидетельствовать о безопасности именно таких соотношений глюкозы, инсулина и калия хлорида.

**Ключевые слова:** острый инфаркт миокарда, сахарный диабет, глюкозо-инсулин-калиевая смесь.

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