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The influence of glucose-insulin-kalium mixture (GIK) on the selected parameters of acid-base balance in acute myocardial infarction

In the fifties, Laborit introduced a new method of treatment in myocardial infarction with the use of polarising mixture, consisting of kalium, insulin and glucose (2, 3). This method was afterwards widely accepted and introduced into clinical practice mainly because of publications of Sodi-Pallares and co-workers (7, 8). Metabolic concept of preserving myocardium is based upon the fact that anaerobic metabolism of glucose may be the energetic source for myocardial cells and insulin introduced at the same time facilitates glucose intake by these cells. Metabolic acidosis, appearing as a result of necrosis, leads to kalium loss and potentially is responsible for a higher level of kalium in extracellular fluid. Insulin and kalium administration may correct these disturbances influencing concentration of hydrogen ion, intra- and extracellularly, which can influence indicators of acid-base equilibrium.

OBJECTIVE

The aim of the study was to estimate the influence of GIK mixture on the selected parameters of acid-base equilibrium in patients with acute myocardial infarction.

MATERIAL AND METHODS

The study was carried out in a group of patients with acute transmural infarction, hospitalised in Cardiology Intensive Care Unit in the 1st 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 infarction 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 >= 1 mm 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, except for typical treatment in myocardial infarction, were given during 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 lasted for 12 hours. The second group (placebo) consisted of patients, who, except for typical treatment in

myocardial infarction, were given during 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 signs of anterior myocardial infarction were present in ECG records. In 24 patients infarction of lateral wall or subendocardial infarct was recognised.

In a group of 88 patients there were excluded those who experienced pain for more than 12 hours and those who had severe complications while admitted to the hospital. These complications were: pulmonary 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 patients 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 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 – non-significant)

	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±13.6		NS
Height (cm)	169 ± 10		163 ± 10		NS
BMI (kg/m^2)	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	**No**	**Yes**	**No**	**Yes**	
hypertension	17	10	6	11	p = 0.07
History of myocardial	**No**	**Yes**	**No**	**Yes**	
infarction	22	4	16	1	NS

Patients were randomised into 2 groups: placebo and GIK. There were 27 patients in GIK group and in placebo group – 17 patients. Every patient had arterial blood samples taken (from digital pulp) in order to check pH, concentration of bicarbonates $AHCO_3$ (mEq/l), partial pressure of oxygen – pO_2 (mmHg) and carbon dioxide – pCO_2 (mmHg). Parameters of acid-base equilibrium were checked with the use of a CORNING 238 analyser. This assay was based on direct measure of pH, pCO_2, pO_2 with appropriate electrodes. Other factors were deducted from Henderson – Hasselbach equation.

In statistical analysis t-test was applied for random and combined variables and one-way ANOVA analysis. Statistical significance was accepted for $p< 0.05$.

RESULTS

On patient examination during admittance, no statistically significant differences were observed in pH between GIK and placebo group. In a GIK group mean pH value was 7.39 ± 0.04 and in placebo group 7.38 ± 0.05. On examination after 24 hours, pH increased significantly in both groups. In GIK group after 24 hour infusion it was 7.42 ± 0,03 ($p = 0.02$) and in placebo 7.42 ± 0.05 ($p = 0.03$). 24 hours later no statistically significant differences were observed between these two groups.

In a group of patients with anterior myocardial infarction receiving GIK, blood pH increased significantly (from 7.38 ± 0.03 to 7.43 ± 0.02; $p = 0.02$). Blood pH also increased in placebo group with inferior myocardial infarction (from 7.38 ± 0.05 to 7.42 ± 0.02; $p = 0.02$). There was no significant difference in analysis between groups in initial and next (after 24 hours) examination, as far as the site of infarction is concerned. No significant differences in pCO_2 were observed between GIK and placebo group on examination before the treatment. In GIK group pCO_2 was 35.3 ± 6.4 mmHg, in placebo group 37 ± 6.3 mmHg. In the examined group with myocardial infarction after 24 hours of hospitalisation, significant decrease of pCO_2 was observed. (from 35.9 ± 6.3 mmHg to 33.8 ± 4.8 mmHg $p = 0.029$). In GIK group the observed changes were within the boundaries of statistical significance (pCO_2 lowered from 35.3 ± 6.4 mmHg to 32.9 ± 5.4 mmHg $p = 0.052$). In placebo group pCO_2 decreased randomly from 37 ± 6.3 mmHg to 35.1 ± 3.6 mmHg. On examination after 24 hours no significant differences were observed between GIK and placebo group. On initial examination there was no significant difference between the groups in analysis as far as the site of infarction is concerned. On examination after 24 hours of treatment, differences between the groups were within the boundaries of significance, because in patients receiving GIK, with inferior myocardial infarction, it decreased to 31.3 ± 5.8 mmHg and was lower comparing to the other groups, considering the site of infarction. No significant difference in $AHCO_3$ was observed between GIK and placebo groups in the initial examination. (21.3 ± 3.7 mEq/l versus 21.7 ± 2.2 mEq/l) also in analysis considering the site of infarction. The observed increase of $AHCO_3$ after 24 hours of hospitalisation occurred randomly in both groups. In GIK group $AHCO_3$ increased to 21.4 ± 3.2 mEq/l and in placebo group to 22.9 ± 3.2 mEq/l. In patients with inferior myocardial infarction treated with GIK on examination after 24 hours $AHCO_3$ was 20.3 ± 3.1 mEq/l and this level was significantly lower comparing to the group of placebo patients with the same site of infarction. (23.6 ± 2.1 mEq/l; $p = 0.02$). Bicarbonate concentration in the group of patients with inferior myocardial infarction treated with GIK, on examination after infusion, decreased comparing to patients with anterior myocardial infarction also treated with GIK (20.3 ± 3.1 mEq/l versus 23.5 ± 2.3 mEq/l; $p = 0.018$). In the group of patients receiving GIK, pO_2 on initial examination was 88.8 ± 40.6 mmHg, and in placebo group 88.9 ± 35.6 mmHg; differences between groups occurred randomly. On admittance to the hospital, pO_2 was lower in patients with anterior myocardial infarction comparing to patients with inferior myocardial infarction (75.8 ± 28.7 mmHg versus 97.5 ± 41.7 mmHg) and differences between the groups were

within the boundaries of significance ($p = 0.07$). No significant changes in pO_2 were observed after 24 hours of treatment, both in GIK and placebo group, also comparing the site of infarction. In GIK group pO_2 increased to 98.6 ± 34.2 mmHg, and in placebo group to 90.2 ± 49 mmHg.

DISCUSSION

Numerous publications indicate that in an early stage of myocardial infarction metabolic acidosis influences the circulatory system, causing severe disturbances (5, 9, 10). It was proved that in patients with complicated myocardial infarction changes in the acid-base equilibrium, such as decrease in pH and bicarbonates, occurred more frequently than in patients with myocardial infarction, but without complications (4).

In the examined group of patients with myocardial infarction, pH values on the initial examination and after 24 hours were within the boundaries, but during the first day of clinical observation a significant increase of pH was noticed. This increase was similar in GIK and placebo groups. Changes in pH, heading towards alkalosis, observed during first 24 hours of acute myocardial infarction, may potentially coexist with hypokaliemia (1), which seems to substantiate GIK administration.

In the whole examined group of patients the partial pressure of carbon dioxide in the arterial blood decreased. On the initial examination mean values of the carbon dioxide were within the low normal range. On examination after 24 hours they were below the low normal range (32-34 mmHg). The observed low partial pressure of carbon dioxide is consistent with other authors' reports, who are trying to explain this phenomenon in hyperventilation mechanism. In most patients it was enough to maintain pH in the normal range (6). Changes in bicarbonate concentration in blood serum were observed randomly.

It was stated that obtaining even a small increase of pO_2 in patients with myocardial infarction is a very important aim in therapy and to some extent it prevents complications connected with acidosis in myocardial infarction (5).

In the examined group of patients the partial pressure of oxygen in the arterial blood on the initial examination was standard, but pO_2 values were significantly higher in patients with inferior myocardial infarction comparing to patients with anterior myocardial infarction; this difference was close to statistical significance. After 24 hours of treatment the partial pressure of oxygen in the arterial blood changed for better, increasing both in placebo and in GIK group. This increase was bigger in GIK group, although not statistically significant.

Long lasting arguments concerning usefulness of GIK mixture in the treatment of acute myocardial infarction cannot be settled during a single clinical research, but the observed changes in parameters of acid-base equilibrium during GIK treatment may speak in favour of this method.

CONCLUSIONS

Administration of GIK mixture does not significantly influence parameters of acid-base equilibrium in patients with acute necrosis of myocardium.

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SUMMARY

The aim of the paper was assessing the influence of polarising GIK mixture on the selected indicators of acid-base equilibrium in patients with acute myocardial infarction treated fibrinolytically. The patients had arterial blood taken in order to check pH, partial pressure of oxygen and carbon dioxide, and the content of bicarbonates. Changes in the examined parameters in the group obtaining GIK and in the one obtaining placebo were subject to critical analysis. Changes in gasometric parameters taking place under the influence of GIK administered to patients were also analysed according to the site of infarction. It was observed that after 24 hours from the beginning of infusion pH increased and pCO_2 decreased in comparison to the initial examination. These changes did not depend on the kind of applied infusion (GIK or physiological saline infusion), no significant changes in bicarbonates being observed. However, after applying GIK infusion, an increase in oxygen pressure in comparison with the control group was observed, and differences between the groups were within the boundaries

of significance. Neither was there observed any influence of infarction site on changes in the assessed parameters of acid-base equilibrium in the group treated with GIK nor in the one receiving placebo.

Wpływ mieszanki polaryzującej KIG na wybrane parametry równowagi kwasowo-zasadowej w świeżym zawale mięśnia serca

Celem pracy była ocena wpływu mieszanki polaryzującej KIG na wybrane wskaźniki równowagi kwasowo-zasadowej u chorych z pełnościennym zawałem mięśnia serca, leczonych fibrynolitycznie. We krwi tętniczej oznaczano: pH, ciśnienie parcjalne tlenu i dwutlenku węgla, zawartość wodorowęglanów. Analizie statystycznej poddano zmiany badanych parametrów w grupie otrzymującej KIG albo placebo. Analizowano także zmiany parametrów gazometrycznych pod wpływem podawania KIG w zależności od lokalizacji zawału. Po 24 godzinach od rozpoczęcia wlewu obserwowano wzrost pH i spadek pCO_2 w porównaniu z badaniem wyjściowym. Zmiany te były niezależne od rodzaju stosowanego wlewu (KIG lub wlew soli fizjologicznej), bez istotnych zmian stężenia wodorowęglanów. Jednak po podaniu wlewu KIG obserwowano wzrost prężności tlenu w porównaniu z grupą kontrolną, a różnica była na granicy istotności statystycznej. Nie obserwowano wpływu lokalizacji zawału na zmiany ocenianych parametrów równowagi kwasowo-zasadowej zarówno w grupie leczonej KIG, jak i otrzymującej placebo.