Changes of blood magnesium concentration in patients undergoing surgical myocardial revascularisation

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Abstract. Background. Magnesium (Mg) is the second most relevant intracellular element, which plays an important role in many physiological processes. Magnesium disorders are particularly important in haemodynamically unstable patients, such as patients after extracorporeal circulation. The aim of this study was to analyze the changes in blood Mg levels in patients undergoing coronary artery bypass procedures with extracorporeal circulation. Patients and Methods. Twenty male patients, aged 50-69, undergoing CABG with ECC under general anaesthesia, were included in the study. All of them were operated on due to I and IIo degree coronary disease (according to CCS). The blood concentrations of Mg were examined in five stages: 1) before the induction of anaesthesia; 2) during extracorporeal circulation; 3) after surgery; 4) in the morning of the first postoperative day; 5) in the morning of the second postoperative day. The blood Mg concentrations were determined by spectrophotometric methods. Results. The blood concentration of Mg decreased during extracorporeal circulation and immediately after surgery and increased in the morning of the first and second postoperative days. Conclusion. The CABG with extracorporeal circulation resulted in a significant decrease in blood Mg concentration.

Keywords: magnesium, extracorporeal circulation, CABG

Magnesium (Mg) is the second most abundant intracellular cation essential for many vital functions. Its physiological concentration in the blood ranges from 0.8 to 1.2 mmol/L with 65 % of Mg occurring in its ionized form. One of the factors affecting the blood magnesium concentration is stress. Increased hormone concentrations in the adrenal cortex and medulla result in renal hypersecretion of this element. On the other hand, decreased Mg concentration in blood induces stress and is likely to cause cardiac arrhythmias. Thus, “a magnesium vicious circle” is observed, which may lead to severe complications. Therefore, many authors emphasize the significant role of blood normomagnesaemia in patients with cardiovascular diseases [1-3]. As is widely known, hypomagnesaemia in the above-mentioned
cases is likely to cause cardiac arrhythmias (especially supraventricular), atrial fibrillation, lengthened P-R and Q-T segments, or even ventricular fibrillation. Therefore this problem is very important in patients undergoing coronary artery bypass graft (CABG) surgery with extracorporeal circulation [4, 5]. The complexity of such procedures and the intra- and postoperative treatment administered disturb hormonal balance, which results in increased blood hormone levels, mainly catecholamines. It should be stressed that these changes result not only from surgical stress, but also from intraoperative normovolemic haemodilution [6, 7].

The aim of this study was to analyze the changes in blood Mg levels in patients undergoing coronary artery bypass procedures with extracorporeal circulation.

**Patients and methods**

The study was approved by the Bioethical Committee of the Medical University of Lublin (No KE-0254/244/2000) and included patients who underwent operations due to I° and II° coronary disease (according to CCS).

In the evening preceding the operation the patients were administered premedication – lorazepam (Lorafen, Polfa, PL) 2 mg orally and promethazine (Diphergan, Polfa, PL) – 50 mg i.m. One hour before anaesthesia all the patients received 3 mg of lorazepam orally and promethazine (Diphergan, Polfa, PL) at the dose of 0.01-0.02 mg/kg body wt., midazolam (Dormicum, Roche) – 0.05-0.1 mg/kg body wt. and etomidate (Hypnomidat, Janssen, G) – 0.1-0.5 mg/kg. Muscle relaxation was obtained by injecting a single dose (0.08-0.1 mg/kg body wt.) of pancuronium (Pavulon, Organon-Teknica, F). The anaesthesia was maintained throughout the procedure using midazolam-fentanyl infusion and inhalatory doses of isoflurane (Forane, Abbot, USA). During the implantation of aortocoronary bypasses circulation and ventilation were maintained by the heart-lung machine S III (Stockert). The following substances were used for priming: Ringer’s solution (Ringer, Fresenius-Kabi, G) – 1000 mL, 6% solution of hydroxyethylated starch (HAES, Fresenius-Kabi, G) – 500 mL, 29% mannitol (Mannitol, Fresenius-Kabi, G) – 250 mL, sodium hydroxycarbonate (Natrium bicarbonatum, Polfarma Pl) – 20 mL and heparin – 75 mg. The same priming was used for all patients. Cardioplegia was prepared using 0.9% saline solutions supplemented with 3 g of potassium chloride (Kalium chloratum, Polfa, PI) and 20 mL of sodium hydroxycarbonate. During all surgery and early postoperative period (for all zero postoperative day) the patients received supplementation of a mixture: potassium chloride 250 mg/h and magnesium sulfate 200 mg/h.

All the patients had their last meal 12 hours before surgery; immediately after the procedure they were transferred to the Postoperative Intensive Care Unit (PICU) where they received a short-term infusion of 5% glucose solution with insulin.

The determinations of blood Mg concentration were performed in 5 stages: 1) just before anaesthesia after the radial artery cannulation, 2) during ECC, 3) immediately after surgery, 4) in the morning of the 1st postoperative day, 5) in the morning of the 2nd postoperative day.

The blood samples were collected from the radial artery and immediately centrifuged (25000 rpm., temp. 0°C); the obtained serum was frozen at -20°C. The blood Mg concentrations were determined by spectrophotometric methods.

The results were analyzed statistically using the Wilcoxon and Mann Whitney U tests for interstage and intergroup differences.

**Results**

The study encompassed 20 male patients aged 50-69 years (table 1). In all of them the course of the operation and anaesthesia was uneventful and there was no need for intra-aortic contrapulsation. The mean duration of procedures was 189.2 min ± 32 and of anaesthesia – 205 min ± 45. In all the patients the aorta was clamped in a routine way and the time of its closure was 37.21 min ± 13.5. During the work of the heart-lung machine mild hypothermia was applied with mean temperature of 35.2 °C ± 0.42. In 16 patients weaning from the heart-lung machine required continuous dopamine or dobutamine infusions in the doses dependant on the clinical state (8.3 μg/kg/min ± 2.2 and 6.3 μg/kg/min ± 3.3, respectively); 4 patients did not require pharmacological support of haemodynamic balance in this period. Postoperative atrial fibrillation was noted in 9 patients. In these cases amiodarone infusion was administrated with good results.

The mean serum concentration of Mg in the first stage was 0.75 mmol/L. The extracorporeal circulation procedure resulted in a decrease in its level in the second stage (p < 0.001) and a slow increase in the third (p < 0.05), the fourth (p < 0.001) and the
fifth stage (p < 0.01) (figure 1, table 1). There was no relationship between frequency of atrial fibrillation and low Mg blood concentrations.

Discussion

Changes in Mg levels in serum and erythrocytes during extracorporeal circulation procedures are not explicitly described. The latest reports stress the importance of postoperative maintenance of normomagnesemia [4, 5, 8], as low Mg levels are likely to contribute to intra- and postoperative arrhythmias, which may lead to cardiogenic shock. This results from the stabilizing effects of Mg ions on the myocyte membrane as well as decreased reactivity of adrenal glands and reduced secretion of neurotransmitters from the nerve endings. Moreover, a significant correlation between the serum Mg concentration and myocardial insufficiency is emphasized [9, 10]. This fact is confirmed by Samejima et al. [9], who analyzed relationships between Mg and norepinephrine blood concentrations in patients with circulatory insufficiency and demonstrated reverse correlation of the parameters examined, with norepi-

Table 1. Mg blood concentrations in each stage.

<table>
<thead>
<tr>
<th>Blood magnesium concentrations in each stage</th>
<th>stages:</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>maximum</td>
<td>0.897</td>
<td>0.996</td>
<td>0.977</td>
<td>1.113</td>
<td>1.2</td>
<td></td>
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<tr>
<td>quartile 3</td>
<td>0.788</td>
<td>0.6802</td>
<td>0.7561</td>
<td>0.99217</td>
<td>0.9667</td>
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<tr>
<td>median</td>
<td>0.7807</td>
<td>0.59</td>
<td>0.6938</td>
<td>0.904</td>
<td>0.9335</td>
<td></td>
</tr>
<tr>
<td>quartile 1</td>
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<td>0.4839</td>
<td>0.6445</td>
<td>0.7964</td>
<td>0.7302</td>
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</tr>
<tr>
<td>minimum</td>
<td>0.6929</td>
<td>0.3843</td>
<td>0.547</td>
<td>0.6672</td>
<td>0.475</td>
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</table>

<table>
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<tr>
<th>Changes of blood magnesium concentrations – comparison with stage first</th>
<th>Wilcoxon test</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
</tr>
<tr>
<td>01:02 20 13 3.434606 0.00059</td>
<td></td>
</tr>
<tr>
<td>01:03 20 44 2.277293 0.02277</td>
<td></td>
</tr>
<tr>
<td>01:04 20 8 3.621269 0.000294</td>
<td></td>
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<tr>
<td>01:05 20 33 2.687952 0.007193</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Changes of blood Mg concentrations during each stage – comparison with 1st stage.
nephrine levels significantly correlated with the severity of myocardial function impairment. According to Banfi et al. [11], the development of myocardial insufficiency is strictly related to the activity of the neuro-hormonal system, particularly to the production and secretion of intra-cardiac norepinephrine. In their opinion, reduced haemodynamic function of the myocardium leads to increased metalloprotein 2 concentrations and accumulation of the mentioned substances in the fibroblasts, which markedly impairs the diastolic function of the myocardium. Therefore many researchers believe that the blood concentrations of Mg and norepinephrine are relevant diagnostic factors of myocardial insufficiency [12, 13]. The “inotropically positive” effects of Mg on the myocardium should also be stressed. The increased index of the left ventricle during Mg substitution [14] may result from inhibitory effects of Mg on the secretion of intracardiac norepinephrine [13] as well as from inhibition of type N calcium receptors [15]. Moreover, anti-arrhythmogenic effects of Mg seem important. As mentioned before, a decrease in Mg concentration is likely to result in haemodynamically severe arrhythmias and therefore many authors consider hypomagnesaemia an important diagnostic symptom [4, 16]. This is confirmed by Zaman et al. [16], who observed changes in the P wave as well as blood magnesium and potassium concentrations in patients undergoing myocardial revascularization. They demonstrated that hypomagnesaemia developing on the first postoperative day was significantly correlated with the frequency of atrial fibrillation and was a relevant prodromal symptom. Likewise, Parra et al. [5] in their analysis of changes in Mg levels during extracorporeal circulation procedures observed a relevant correlation between hypomagnesaemia and arrhythmias as well as low cardiac output. According to them, persistent low concentrations of Mg in serum directly affect perioperative mortality amongst patients undergoing surgical revascularization of the myocardium with extracorporeal circulation. Furthermore, it is worth stressing that clinically significant hypomagnesaemia was observed in cardio-surgical patients who were treated preoperatively with β-blockers. Further studies should be conducted to describe the effects of the above mentioned parameters accurately.

Moreover, while analyzing the effects of Mg on the perioperative arrhythmias, it is worth stressing, that its decrease in the blood contributes to a decrease in the dose of epinephrine inducing this pathology, which, according to Crawford et al. [17], is particularly important in anaesthesia with halogenated anaesthetics. Decreased minimal anaesthetic concentrations of these agents in normo- and hypermagnesaemia, in particular, may also be of importance [18, 19]. According to Thompson et al. [19], there is a strict correlation between minimal anaesthetic concentrations of halogenated anaesthetics and serum Mg levels.

The haemodynamics of the coronary circulation is also of importance for the proper function of the myocardium. According to Guo et al. [20] (who analyzed the relationship between Mg deficiency and the frequency of variant anginal attacks in women), intracellular Mg disorders significantly correlate with the degree of arterial tone and coronary pains. They believe that high Mg levels decrease reactivity of vessels thus improving the blood flow through the coronary vessels. Likewise, Vigorito et al. [21] noted that Mg reduced coronary vascular resistance in patients with normal coronary arteries undergoing a diagnostic catheterization. Most likely this “protective” effect of Mg results from inhibitory action of Mg on the secretion of the neurotransmitter – in the heart and vascular muscles – norepinephrine [15]. Recent reports stress the importance of the therapeutic effects of Mg in acute heart ischaemia, too [22-24]. Redwood et al. [24] in their study of the changes in the bioelectric activity of the heart in patients with unstable coronary disease, supplemented Mg concentration with intravenous infusions. They demonstrated a significant reduction in ischaemic lesions observed in ECG. Likewise, Ravn et al. [23] reported, that intravenous administration of Mg resulted in at least 50 % reduction in infarct size. Moreover, direct effects of Mg on the muscular cells of the vessels and myocardium are also worth stressing. According to Moens et al. [25], such effects result from the beneficial action of Mg on the intracellular ATP concentration and sodium-potassium pump in the cells. They expressed the view that Mg limits the myocyte oedema by reducing cellular metabolism and activity of the sodium-potassium pump, thus decreasing the production of oxygen reactive species that are likely to initiate myocyte apoptosis, that in turn results in post-reperfusion myocardial insufficiency [26]. Therefore, it may seem that both intra- and postoperative supplementation of Mg should be considered as a routine management in patients undergoing CABG.

Furthermore, the “analgesic” effects of Mg are interesting. Analyzing the influence of high Mg doses on the severity of postoperative pain and required doses of remifentanil Shutz-Stuber et al. [27] noted, that continuous Mg substitution following the induction of anaesthesia significantly reduced the amount
of remifentanil administered. Similar conclusions were drawn by Zarauza et al. [28] and Wilder-Smith et al. [29]; however the analgesic effect of Mg has not been fully explained and remains the subject of many clinical observations.

The protective effects of Mg on the nervous tissue, particularly on the central nervous system, should be emphasized [30]. According to Polderman et al. [31], high Mg levels prevent constriction of cerebral vessels and markedly reduce ischaemic brain damage. This fact seems particularly relevant for patients operated on with extracorporeal circulation, since 30% of such operations are complicated by neuropsychological changes connected to intraoperative disorders of the cerebral circulation [32]. It is difficult, however, to determine to what degree hypomagnesaemia observed in our study affected homeostasis of the CNS. It seems that rapid and uncontrollable drops in blood Mg concentrations are hazardous for the health and life of patients and supplementation should be used in every patient undergoing extracorporeal circulation.

This study demonstrated that procedures with extracorporeal circulation contribute to hypomagnesaemia. According to Polderman and Girbes [33], a decrease in Mg concentration results from procedure-induced intracellular disorders, as well as increased loss of this element in the urine. They attribute the cause of this pathology to the damage of renal tubules due to intraoperative hypothermia. Likewise, Samejima et al. [9] report that such disorders are mainly the result of cellular Mg loss and increased urine Mg concentration. It should be stressed that determinations of urine Mg levels also enable us to determine the route by which this element is lost [34]. Moreover, intraoperative hypocholesterolemia, described by many researchers, is of importance [9, 15]. Stress leads to depletion of Mg, while a high concentration of Mg reduces stress-related reactions and “immunizes” cells against stress markers circulating in the blood (feedback). Further studies are needed to determine precisely the relations between Mg concentrations and catecholamines in extracorporeal circulation.

Another important factor affecting the blood Mg concentration in patients undergoing procedures with extracorporeal circulation is intraoperative normovolemic haemodilution [6, 7, 35, 36]. In their study on changes in Mg concentration during extracorporeal circulation procedures, Ichikawa [35] and Satur et al. [37] demonstrated a 17% decrease in Mg levels induced by normovolemic haemodilution, which was also observed in the immediate postoperative period. Likewise, Inoue et al. [7] state that intraoperative haemodilution is the main factor contributing to the decrease of blood Mg concentration. Wrotiska et al. [36] underline that hypomagnesaemia is dependent on the degree of normovolemic haemodilution during ECC. This fact seems to explain the decreased Mg levels observed in our study following weaning from the heart-lung machine and immediately after the surgery. Therefore it may be supposed that the degree of normovolemic haemodilution significantly affects the blood Mg concentration. However, this relation requires further studies.

Conclusion

Myocardial revascularization procedures with extracorporeal circulation cause a significant decrease in blood magnesium concentration.

References

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