ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN – POLONIA
VOL. LX, N 2, 122 SECTIO D 2005

Department of General Chemistry
Department of Anaesthesiology Intensive Care
Medical University of Lublin

JOLANTA WROŃSKA, WOJCIECH DĄBROWSKI, JADWIGA BIERNACKA, JÓZEF DOBIJA, ZIEMOWIT RZECKI, MARIA SZPETNAR, KAZIMIERZ PASTERNAK

The effect of normovolemic haemodilution on blood magnesium concentrations in patients nundergoing extracorporeal circulation

It is widely known that magnesium(Mg) is of great importance to the physiology of humans and its deficiency may cause many disorders which often require intensive treatment. Mg is the second intracellular cation in terms of quantity; its extremely high levels are found in the skeletal muscles, liver and myocardium. Its physiological level in blood serum ranges from 0.8 to 1.2mmol/l – 24% combined with proteins, 10% in complexes and 65% in the ionized form. It is worth stressing that even the smallest changes in Mg concentration in blood serum are reflected in its intracellular level, which, in turn, affects the cell function (7). Moreover, even temporary or secondary deficiency of this element is likely to lead to significant clinical dysfunctions of various organs and aggravate or alter the clinical picture of an underlying disease. Therefore, many researchers underline the role of normomagnesemia in blood, especially in patients with myocardial pathology (1, 8). Dysfunctions of the myocardium are mostly associated with abnormal irritability and conductivity of the stimulus-transmitting system, which on ECG initially manifests itself as longer P-R and Q-T waves, while at higher deficiency – as tachycardia, atrial fibrillation, pre-term ventricular beats and in extreme cases – ventricular fibrillation.

This problem is particularly relevant in patients subjected to cardiosurgical procedures with extracorporeal circulation (ECC) (10). A complex nature of such procedures, especially intraoperative normovolemic haemodilution (NH) may alter blood Mg levels, which is likely to result in dysfunctions of various organs, particularly postoperatively stunned myocardium.

The aim of the study was to analyze the changes in blood magnesium levels in patients undergoing coronary artery bypass procedures with ECC and normovolemic haemodilution.

MATERIAL AND METHODS

The study was approved by the Bioethical Committee of the Medical University of Lublin (No KE-0254/244/2000) and included the 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 – oral lorazepam (Lorafen, Polfa, PL) – 2mg and i.m. Promethiazine (Dophergan, Polfa, Pl) – 50mg. One hour before anaesthesia all the patients received oral lorazepam – 3mg and i.m. morphine (Morphicum hydrochloricum, Polfa, Pl) – 0.1mg/kg body wt. The patients underwent general anaesthesia with

fentanyl (Fentanyl, Polfa, Pl) in the dose of 0.01–0.02mg/kg body wt., midazolam (Dormicum, Roche) – 0.05–0.1mg/kg body wt. and etomidat (Hypnomidat, Janssen, G) – 0.1–0.5mg/kg. Muscle relaxation was obtained by injecting a single dose (0.08–0.1mg/kg body wt.) of pancuronium (Pavulon, Organon-Teknica, F). Anaesthesia was maintained throughout the procedure using midazolam-fentanyl infusion and inhalatory fractionated doses of foran (Izofluran, Abbot, USA). During the implantation of aorto-coronary by-passes the circulation and ventilation were maintained by the heart-lung machine S III (Stockert). The following substances were used for priming: Ringer«s solution (Ringer, Freseniús-Kabi, G) – 1000ml, 6% solution of hydroxyethylated starch (HAES, Fresenius-Kabi, G) – 500ml, 20% mannitol (Mannitol, Fresenius-Kabi, G) – 250ml, sodium hydroxycarbonate (Natrium bicarbonatum, Polfarma Pl) – 20ml and heparin – 75ml. The same priming was used for all patients. Cardioplegia was prepared using 0.9% salt solution supplemented with 3g of potassium chloride (Kalium chloratum, Polfa, Pl) and 20ml of sodium hydroxycarbonate. The degree of NH induced by constant volume of priming (1800ml) was determined on the basis of haematocrit measurements and body weight. The patients received supplementation of potassium chloride during surgery.

Depending on NH, the patients were divided into 2 groups: A – those weighing < 75kg and group B – those weighing > 75kg. All the patients consumed their last meals 12 hours before surgery; immediately after the procedure they were transported to the Postoperative Intensive Care Unit (PICU), where they received a short-term infusion of 5% glucose solution with insulin and 3 or 6 g of potassium chloride. Nobody received Mg infusion during surgery and postoperative period.

Determinations were performed in 7 stages: 1) just before anesthesia after the radial artery cannulation, 2) during NH and ECC, 3/ immediately after surgery, 4) in the evening of the zero's postoperative day (about 6 hours after surgery), 5) in the morning of the 1st postoperative day, 6) in the evening of 1st postoperative day, 7) in the morning of the 2nd postoperative day. Blood samples were collected from the radial artery and immediately centrifuged (25000r/min., temp. 0°C); the obtained serum was frozen at – 20°C. The magnesium blood concentrations were determined by spectrofotometric methods.

The results were statistically analysed using the Wilcoxon and Mann-Whitney tests in interstage and intergrup relations.

RESULTS

The examinations were conducted in 20 men aged 53–70 (61 ± 6.9). Sixteen patients had had myocardial infarction during the past 3 years and 18 were treated due to concomitant arterial hypertension (I° or II° according to WHO classification). None of the patients was treated for endocrinological, neurological and other systemic diseases or was resuscitated because of circulatory arrest. The mean duration of the procedure was 205 min ± 35 and of anaesthesia 235min ± 30. In all the patients the aorta was typically clamped and the mean closure time was 45.1min ± 15.5. The aorto-coronary anastomosis was performed in shallow hypothermia which value was 34.5°C ± 0.4. In all the cases the heart-lung machine disconnection was uneventful and there was no need of intra-aortic counterpulsation. The haemodilution initiation of cardiopulmonary bypass caused a decrease in haematocrite in both groups; however, lower values were observed in group A. There were significant differences between group A and B in the 2nd ($p < 0.001$) and 3th ($p < 0.05$) stages.

Tab.1 Haematocrite changes in both groups

		Blood magnesium concentrations in each groups						
stages		1	2	3	4	5	6	7
group A	median	40.7	20.6**	28.8**	35.9**	37.3*	37	38,1
	quartile 1	37.3	20	28.2	34.5	36	36.2	37.7
	quartile 3	42.7	21.4	29.7	36.5	38.6	37.5	39.5
group B	median	40.2	28*	30.1*	34.5*	36.6	39	39.6
	quartile 1	39.2	27.4	29.7	32.6	35.4	38.2	38.4
	quartile 3	42.1	28.6	31.2	35.6	37.6	39.3	40.1
Intergroup relationships								
A:B		-	p<0.001	p<0.05	-	-	-	-

* p<0.05; ** p<0.01; *** p<0.001 comparison with first stage

The observation of blood magnesium concentrations showed decrease in 2 (p<0.001) and 3 (p<0.05) stage in all patients (Fig 1.). Similar changes were also observed in the same stages in the group with body mass lower than 75 kg (2/ p<0.01; 3/ p<0.05). However, the patients with body mass higher than 75 kg showed a decrease blood mangesium concentrations only in stage 2 (P<0.01). Fig. 2, 3. There were no statistical differences between these both groups.

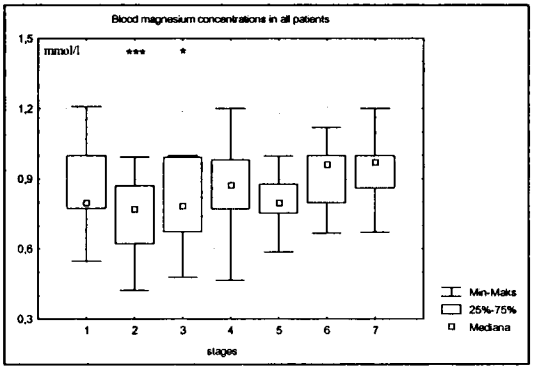

Fig. 1. Blood magnesium concentrations in all patients during several stages

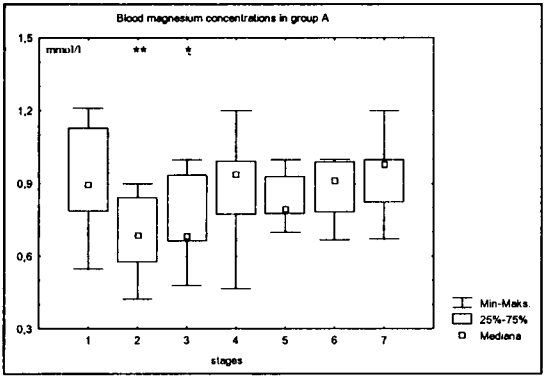

Fig. 2. Blood magnesium concentrations in patients with body mass lower then 75 kg

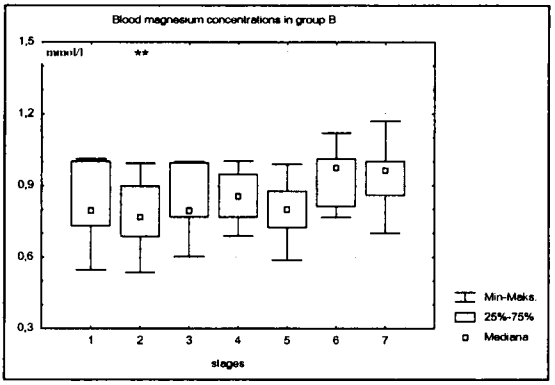

Fig. 3. Blood magnesium concentrations in patients with body mass higher than 75 kg

DISCUSSION

Changes in blood Mg concentrations during ECC are not explicitly defined; recent reports stress the importance of normomagnesemia maintenance, particularly in patients with stunned myocardium. (4, 9, 12). Low Mg levels are likely to favour intra- and postoperative arrhythmias which, in turn, may lead to cardiogenic shock. Hypomagnesemia may also be a diagnostic factor allowing to predict many life-threatening arrhythmias (4, 14, 15). The observations by Zaman et al. (15), which concerned the changes in P wave and serum magnesium and potassium levels in patients after myocardial revascularization, seem to confirm this. According to them, hypomagnesemia observed on the first postoperative day is a relevant symptom preceding atrial fibrillation. Many authors stress the fact that Mg supplementation used early prevents such a severe complication (4, 14). Moreover, Parra et al.(9) point to a significant relation between hypomagnesemia and arrhythmia as well as low stroke volume. According to them, prolonged low Mg levels in serum exert direct effects on perioperative mortality among patients subjected to coronary artery bypass graft (CABG). Interestingly, clinically significant hypomagnesemia was mainly observed in patients treated with β-blockers. Could drugs of this group really favour decreased levels of this important electrolyte in blood?

Our studies showed that patients undergoing surgical myocardial revascularization with extracorporeal circulation are at high risk of decreased serum magnesium concentrations. Polderman and Girbes (10) suggest that the mechanism responsible for this may be a combination of increased urinary excretion and intracellular shift, induced by a multi-stage character of ECC procedures. A decrease in body temperature during surgery and high urinary magnesium excretion play the main role in this pathology. Probably the the kidney's tubular dysfunction results in urinary magnesium excretion (10) but the effects of ECC on the kidney function are difficult to assess. Furthermore, hypomagnesemia during CABG is attributed to haemodilution (13). Examining the changes in blood magnesium concentrations in cardiosurgical patients, Satur et al. (13) observed that initiation of NH caused a 17.3% decrease in serum Mg levels, which persisted until the first postoperative day. They concluded that the main reasons for magnesium depletion are: the most important – NH and the second one – intraoperative and postoperative cellular depletions. Likewise, similar changes of blood Mg concentrations were observed in our examinations, particularly in patients with body weight mass lower than 75 kg. Interestingly, a decrease in the electrolyte discussed was lower in patients with body mass higher than 75 kg. These data suggest that the degree of NH may be a significant factor indicating the level of hypomagnesiemia.

Analyzing the changes in blood magnesium concentrations in patients operated on with ECC, the intraoperative catecholaminemia described by many authors is also worth stressing (5, 6). It is well known that stress leads to magnesium deficiency. On the other hand, high magnesium levels in blood limit stress-related reactions increasing the cells resistance to stress markers circulating in blood. Therefore, it may be supposed that intraoperative catecholaminemia significantly decreases Mg levels in blood (5, 10). This fact may also explain lower Mg concentrations observed in our group of patients with lower body mass. Dąbrowski et al. (6) in their study examining the effects of normovolemic haemodilution on catecholamine levels demonstrated significantly higher levels of adrenaline and noradrenaline in patients with higher blood dilution. Although the study performed does not allow to determine explicitly to what degree the observed hypomagnesemia depended on the intensification of adrenergic reaction of the organism, it may be supposed that Mg level changes in ECC are strongly related to serum catecholamine concentrations.

To sum up, it should be stressed that magnesium exerts protective effects on the nervous tissue, particularly on the central nervous system (3). According to Polderman et al. (11), high Mg levels in blood prevent the contractions of cerebral vessels, which significantly reduces ischaemic damage to the brain. This seems particularly important in patients undergoing procedures with ECC (2) as it is well known that 30% of such operations are complicated with neuropsychological changes associated with intraoperative disorders of cerebral circulation. It is difficult to determine accurately in what degree hypomagnesemia observed in our study affected CNS homeostasis; however, it is true that rapid and uncontrolled drops in blood Mg levels are health- and life-threatening and its supplementation should be used in each patient requiring ECC surgery.

CONCLUSIONS

1. Operative procedures with ECC result in decreased magnesium levels in blood.
2. A decrease in Mg concentration depends on the extent of normovolemic haemodilution.

REFERENCES

1. Agus Z. S.: Hypomagnesemia. J. Am. Soc. Nephrol., 10, 1616, 1999.
2. Arrowsmith J. et al.: Central nervous system complications of cardiac surgery. Br. J. Anaesth., 84, 378, 2000.
3. Bareye F. M. et al.: Postinjury treatment with magnesium chloride attenuates cortical damage after traumatic brain injury in rats. J. Neurotrauma, 17, 1029, 2000.
4. Booth J. V. et al.: Low serum magnesium level predicts major adverse cardiac events after coronary artery bypass graft surgery. Am. Heart. J. 145, 1108, 2003.
5. Casthley P. A. et al.: Magnesium and arrythmias after coronary artery bypass surgery. J. Cardiothorac. Vasc. Anaesth., 8, 188, 1994.
6. Dąbrowski W. et al.: Wpływ śródoperacyjnej hemodilucji na stężenia endogennych amin katecholowych podczas rewaskularyzacji krążenia wieńcowego. Anest. Int. Ter., 36, 18, 2004.
7. Haigney M. C. P. et al.: Noninvasive measurement of tissue magnesium and correlation with cardiac levels. Circulation, 92, 2190, 1995.
8. Nair R. R., Nair P.: Alteration of myocardial mechanics in marginal magnesium deficiency. Magnes. Res., 15, 287, 2002.

9. Parra L. et al.: Plasma magnesium in patients submitted to cardiac surgery: its influence on perioperative morbidity. J. Cardiovasc. Surg., 42, 37, 2001.
10. Polderman K. H., Girbes A. R. J.: Severe electrolyte disorders following cardiac surgery: a prospective controlled observational study. Crit. Care, 8, R459, 2004.
11. Polderman K. H., van Zanten A..R., Girbes A. R. J.: The importance of magnesium in critically ill patients: a role in mitigating neurological injury and the prevention of vasospasm. Intensive Care Med., 29, 1202, 2003.
12. Ralston M. A. et al.: Serum and tissue magnesium concentrations in patients with failure and serious ventricular arrhytmias. Ann. Intern. Med., 113, 841, 1990.
13. Satur C. M. et al.: Magnesium flux caused by coronary artery bypass operation: three patterns of deficiency. Ann. Thorac. Surg., 58, 1674, 1994.
14. Shiga T. et al.: Magnesium prophylaxis for arrhythmias after cardiac surgery; meta-analysis of randomized controlled trials. Am. J. Med., 117, 325, 2004.
15. Zaman A. G. et al.: The role of signal averaged P wave duration and serum magnesium as a combined predictor of atrial fibrillation after elective coronary artery bypass surgery. Heart, 77, 527, 1997.

SUMMARY

Magnesium is the second most relevant intracellular element in terms of quantity, whose deficiency may cause severe dysfunctions of various organs. Its blood changes seem particularly important in haemodynamically unstable patients, among them undoubtedly those subjected to operations with extracorporeal circulation. The aim of the study was to analyse the changes in blood magnesium levels in patients undergoing coronary artery bypass procedures with extracorporeal circulation and normovolemic haemodilution. The study, approved by the Bioethical Committee encompassed 20 patients, aged 53–70 years operated on due to I° and II° degree coronary disease (according to CCS). Coronary bypass grafts were conducted using ECC and normovolemic haemodilution. All the patients were administered the same priming. The examinations were carried out in 7 stages: 1) before the induction of anaesthesia; 2) during normovolemic haemodilution; 3) after surgery; 4) in the evening of the zero postoperative day; 5) in the morning of the first postoperative day; 6) in the evening of the first postoperative day; 7) in the morning of the second postoperative day. The patients were divided into 2 groups: A – with body mass< 75kg, B – with body mass > 75kg. The degree of haemodilution was defined as the ratio of blood dilution using constant priming to the patient's body mass. The results showed decreased magnesium levels in all the patients at stages 2 and 3; lower values were found in group A. Operative procedures with extracorporeal circulation cause a decrease in blood magnesium levels; this decrease depends on the degree of normovolemic haemodilution.

Wpływ normowolemicznej hemodilucji na stężenie magnezu we krwi pacjentów poddanych operacjom z zastosowaniem krążenia pozaustrojowego

Magnez jest drugim co do ilości ważnym wewnątrzkomórkowym pierwiastkiem, którego niedobory mogą być przyczyną poważnych zaburzeń w funkcjonowaniu wielu narządów. Szczególnie istotne wydają się przy tym jego wahania we krwi pacjentów niestabilnych hemodynamicznie, do których bez wątpienia zaliczyć można pacjentów operowanych z zastosowaniem krążenia pozaustrojowego. Celem pracy była analiza zmian stężeń magnezu we krwi pacjentów poddanych zabiegom pomostowania naczyń wieńcowych w warunkach krążenia pozaustrojowego i normowolemicznej hemodilucji. Po

uzyskaniu zgody Komisji do Spraw Etyki do badań zakwalifikowano 20 pacjentów w wieku od 53 do 70 lat,operowanych z powodu stabilnej choroby wieńcowej określanej według skali CCS na I lub II stopień. Pomostowanie naczyń wieńcowych przeprowadzono z zastosowaniem krążenia pozaustrojowego i normowolemicznej hemodilucji. U wszystkich badanych zastosowano stałą objętość wypełnienia aparatu płuco-serca (*priming*). Badania przeprowadzono w siedmiu etapach:1) przed indukcją znieczulenia; 2) odczas normowolemicznej hemodilucji; 3) po zakończonej operacji; 4) wieczorem w zerowej dobie pooperacyjnej; 5) rano w pierwszej dobie pooperacyjnej; 6) wieczorem w pierwszej dobie pooperacyjnej; 7) rano w drugiej dobie pooperacyjnej. Pacjentów podzielono na dwie grupy: A – o masie ciała < 75kg, B – o masie ciała > 75kg. Stopień hemodilucji określono jako stosunek rozcieńczenia krwi stałym primingiem a masą ciała pacjentów. Przeprowadzone badania wykazały spadek stężenia magnezu u wszystkich badanych w 2 i 3 etapie, przy czym niższe jego wartości obserwowano w grupie A. Wnioski: operacje z zastosowaniem krążenia pozaustrojowego powodują spadek stężenia magnezu we krwi; spadek stężenia magnezu zależy od stopnia normowolemicznej hemodilucji.