Role of magnesium in the prevention of postoperative arrhythmias in neonates and infants undergoing arterial switch operation

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Abstract

The objectives of the study were to measure magnesium levels in neonates and infants undergoing arterial switch operation and to ascertain the role of magnesium supplementation in the prevention of postoperative arrhythmias. Group I (n = 25): magnesium was administered in the dose of 30 mg/kg over 10 minutes in normal saline (5 ml) immediately after cessation of cardiopulmonary bypass (CPB). Group II (n = 25): normal saline (5 ml) was administered over 10 minutes immediately after cessation of CPB. Samples of arterial blood were collected at four time points: 1) after induction of anaesthesia; 2) 10 minutes after initiation of CPB; 3) at rewarming during CPB; and 4) 4 hours after shifting the patient to the intensive care unit. Samples were measured for ionized magnesium (iMg), blood gases, haematocrit level, electrolytes, ionized calcium and glucose. Continuous ECG rhythm analysis and documentation of arrhythmias was performed for 24 hours after surgery. The mean preoperative iMg levels were below the normal level in both the groups. A significant increase in iMg levels (P = 0.00) was seen in both groups during rewarming. There is no statistically significant difference in the incidence of arrhythmias between the magnesium supplemented group (4%) and the control group (20%) in the postoperative period, a tendency towards reduction in arrhythmias was only observed in the magnesium supplemented group.

Keywords: Magnesium; Arrhythmia; Congenital heart surgery

1. Introduction

Magnesium has a major influence on myocardial tissues. It plays an essential role in the maintenance of resting membrane potential [1]. Magnesium inhibits outward flow of potassium, and at the same time, the influx of calcium, thus maintaining the electrochemical gradient. Magnesium deficiency can impair cardiac conduction, increase the risk for arrhythmias, predispose to coronary artery spasm, and contribute to neurological irritability [1, 2]. Magnesium also has been shown to reduce platelet aggregation, inhibit catecholamine release associated with stressful events, such as tracheal intubation, and reduce systemic and coronary vascular resistance [3, 4]. Magnesium appears to be important in arrhythmia prophylaxis after heart surgery in adults and may contribute to improved cardiac contractile indices after cardiopulmonary bypass (CPB) [5, 6]. The incidence of hypomagnesaemia during and after heart surgery has been well characterized in the adult population. Alterations in magnesium in paediatric patients during and after heart surgery have not been as well characterized. The role of magnesium in arrhythmia prevention and optimal magnesium dosage protocols in paediatric patients undergoing heart surgery remains unclear. Plasma depletion and total body magnesium depletion also occur in paedia-

2. Materials and methods

This randomized controlled clinical study was performed in 50 neonates and infants undergoing arterial switch operation for transposition of great arteries, after obtaining approval from the Hospital Ethics Committee and taking informed consent from the parents of the children. Exclusion criteria were: refusal to participate in the study, emergency surgery, age > 1 year, children on antiarrhythmic medications, congenital heart block or other arrhythmias. Anaesthetic management and surgical techniques were standardized for all the children. CPB was conducted at moderate hypothermia (28 °C) using a membrane oxygenator (Minimax, Meditronic, CA, USA). Systemic heparinization was achieved with heparin 400 IU/kg keeping kaolin activated clotting time (ACT) more than 480 s as per the Protocol of the Centre. The CPB circuit was primed with 600 ml of Ringer’s lactate. Mannitol 20%, 1 ml/kg,
sodium bicarbonate 1 ml/kg and packed red blood cells were added to the prime. The prime was haemofiltered before commencement of the CPB to achieve the haematocrit of around 30% by removing excess of prime through haemofiltration. Haemofiltration was performed during CPB so as to achieve a haematocrit of 35–40% before separation from CPB. Deep hypothermic circulatory arrest was not used in any case. Continuous ultrafiltration was performed in all the patients. Pump flows were maintained at 150 ml/kg at normothermia and 100 ml/kg during hypothermia. The children were rewarmed to a nasopharyngeal temperature of 35°C. Heparin was neutralized with protamine in the ratio of 1:3 and additional protamine was administered, if the ACT value was more than 140 seconds. The cardioplegic solution was made from a commercially available St. Thomas solution based concentrate (Plegiocard, Samarth Pharmaceuticals, Gujarat, India) one ampoule of 20 ml added to one bottle of Ringer lactate (500 ml) delivered as a 1:4 mixture of a cold blood cardioplegia. The ampoule of Plegiocard contains magnesium chloride 16 mEq/20 ml.

Neonates and infants were prospectively and randomly assigned to one of the two groups by a computer generated sheet. The consultant anaesthesiologist incharge of the case administered either magnesium or placebo. In group I (n=25), magnesium was administered in the dose of 30 mg/kg in normal saline (5 ml) over 10 min immediately after cessation of CPB. In group II (n=25), normal saline (5 ml) was administered over 10 min immediately after cessation of CPB. Samples of arterial blood were collected at four time points: after induction of anaesthesia, during CPB at 10 minutes, while rewarming during CPB, and 4 hours after shifting the patient to the Intensive Care Unit (ICU). Samples were measured for ionized magnesium (iMg), blood gases, haematocrit level, electrolytes, ionized calcium (Ca²⁺) and glucose in Phoxplus-M (Nova Biomedical analyzer, Waltham, MA, USA). Continuous ECG rhythm analysis and documentation of arrhythmias was performed for 24 hours after surgery by an independent observer blinded to the study group. Calcium and potassium were supplemented to normal levels if a deficiency existed.

3. Statistical analysis

The data were entered in Microsoft Excel format and analysed using SPSS15 software. An independent t-test was used to compare between groups for continuous variables. χ²-Test was applied for categorical variables. Repeated-measure ANOVA was used to see the linear trend.

4. Results

Demographic data and other variables were similar between the study groups as shown in Table 1. The surgery and anaesthesia were conducted by the same team in both the groups. The same type of surgery was performed in both the groups. The mean serum calcium, potassium and glucose levels were comparable in both the groups at all the measurement points.

The mean preoperative iMg levels in the magnesium group was 0.30±0.11 mmol/l and in group II it was 0.30±0.08 mmol/l with overall mean levels of 0.299±0.96 mmol/l. These levels were below normal levels for this age group and were comparable in both the groups as seen in Table 2.

Ten minutes after the institution of CPB, there was significant fall in iMg levels to 0.15 mmol/l in group I and 0.12 mmol/l in group II, as compared to pre-CPB values. A significant increase in iMg levels (P=0.00) was seen in both the groups during the rewarming period of CPB, with mean magnesium levels of 0.67±0.22 mmol/l in the magnesium group I and 0.61±0.19 mmol/l in group II.

Magnesium levels 4 hours postoperatively in the ICU were 0.74±0.25 mmol/l in group I which was magnesium supplemented and 0.40±0.06 mmol/l in the placebo group. iMg levels were increased in group I as compared to the levels at rewarming but were not statistically significant (P=0.20). However, a significant decrease in serum magnesium levels was observed in the placebo group postoperatively as compared to the levels during the rewarming phase of CPB (P=0.00) (Fig. 1).

Only one patient (4%) out of 25 in the magnesium supplemented group had junctional tachycardia in the first 24 postoperative hours. Whereas in the placebo group, one patient (4%) had supraventricular tachycardia and four

| Table 1. Demographic data and CPB characteristics |
|-----------------|-----------------|-----------------|
|                | Group I (n=25)  | Group II (n=25) | P-value |
| Age (days)     | 41.36±11.37    | 42.32±12.07     | 0.77    |
| Weight (kg)    | 3.02±0.35      | 3.07±0.25       | 0.56    |
| CPB duration (min) | 82.72±8.72 | 80.04±4.80      | 0.18    |
| Cross-clamp time (min) | 49.60±7.33 | 48.24±4.99      | 0.45    |
| Urine output (ml) | 40.40±6.44 | 38.12±9.64      | 0.33    |
| Haemofiltration (min) | 448.00±63.71 | 426.00±64.74 | 0.23    |

CPB, cardiopulmonary bypass.

| Table 2. Ionized magnesium levels across the perioperative period |
|-----------------|-----------------|-----------------|
|                | Group I         | Group II        | P-value |
| Preoperative (mmol/l) | 0.30±0.11 | 0.30±0.08 | 0.98    |
| Cooling CPB (mmol/l) | 0.15±0.08 | 0.12±0.04 | 0.16    |
| Rewarming CPB (mmol/l) | 0.67±0.22 | 0.61±0.19 | 0.29    |
| PostCPB (mmol/l) | 0.74±0.25 | 0.40±0.26 | 0.000   |

CPB, cardiopulmonary bypass.
(16%) had junctional tachycardia taking the overall incidence of arrhythmias to 20%. There was a reduced incidence of postoperative arrhythmia in the magnesium supplemented group, however, the difference in incidence of arrhythmias was not statistically significant as compared to the placebo group.

5. Discussion

Magnesium is an important determinant of the resting membrane potential of cardiac cell membranes. It regulates the sodium-potassium–adenosine triphosphate pump, thus affecting the intra-cellular/extra-cellular potassium ratio and the resting membrane potential of myocardial cells [7]. The iMg concentration varies with age with serum levels of 0.46 (0.43–0.49) mmol/l at the age of <1 month and 0.72 (0.67–0.74) mmol/l in the age group of one month to one year [8].

The various causes of hypomagnesaemia in paediatric patients undergoing heart surgery are the large volume of CPB prime solution compared to the circulating blood volume of infants, haemodilution, blood transfusion that causes chelation of magnesium, continuous haemofiltration and administration of large doses of calcium and diuretics [9].

There are very few studies regarding the role of magnesium in the prevention of arrhythmias in paediatric patients undergoing cardiac surgery. All these studies are heterogenous in terms of age group and types of surgeries performed [10]. We chose a uniform homogenous group of infants undergoing an arterial switch operation with the same surgical and anaesthesia teams.

In our study, preoperative iMg levels were low in both groups of children. This finding conforms with previous studies [8, 11, 12]. Low levels in both the groups may be due to malnutrition, infants receiving magnesium deficient diets and fluids along with medication like diuretics and digitalis which cause increased loss of magnesium in urine. During the rewarming period of CPB, there was enhancement of iMg levels in all the infants from the initial levels and levels at rewarming, However, in group II (placebo), magnesium levels at 4 hours postoperatively were lower than the levels seen during the rewarming period of CPB; this may be due to the infusion of magnesium free fluids and the use of diuretics, and haemofiltration.

In our study, the postoperative magnesium levels at 4 hours increased significantly in group I as compared to baseline levels and levels at rewarming, However, in group II (placebo), magnesium levels at 4 hours postoperatively were lower than the levels seen during the rewarming period of CPB; this may be due to the infusion of magnesium free fluids and the use of diuretics, and haemofiltration.

Dorman et al. [13] and Dittrich et al. [14] in their randomized clinical trials demonstrated the association between the supplementation with magnesium and the decrease in overall incidence of postoperative arrhythmias in children and adults after surgery for congenital heart disease.

Manrique et al. [9] performed a randomized, double-blind, controlled trial in 99 children. Magnesium sulphate or placebo was administered during the rewarming phase of CPB as follows: group I was given placebo (29 patients); group II was given 25 mg/kg MgSO4 (30 patients) and group III was given 50 mg/kg MgSO4 (40 patients). They observed a dose-related reduction in the incidence of junctional ectopic tachycardia in children supplemented with magnesium sulphate with 17.9% incidence of arrhythmia in placebo group as compared to 6.7% incidence in the group supplemented with 25 mg/kg MgSO4 and no arrhythmia in 50 mg/kg MgSO4 group. Manrique et al. [9] evaluated the incidence at the time of ICU admission, whereas we observed the incidence over a period of 24 hours; moreover, they used a dose of 50 mg/kg MgSO4 in one group which was high compared to our study (30 mg/kg). Also, magnesium was infused in the CPB circuit during rewarming by Manrique et al. [9], whereas we gave magnesium postCPB.

The incidence of postoperative arrhythmias in all the above studies was different due to heterogeneous composition of patient population and different natures of the operations performed. So, we chose a uniform homogenous group of infants undergoing an arterial switch operation with the same surgical and anaesthesia teams.

In our study, the incidence of postoperative arrhythmias in the magnesium supplemented group was not statistically significant as compared to group II (placebo). However, a lower incidence of arrhythmias was observed in the magnesium supplemented group. Only one patient (4%) had junctional tachycardia in the magnesium supplemented group I as compared to group II where interruption of sinus rhythm was observed in five patients (20%). Of these, four patients (16%) had junctional tachycardia and one patient (4%) had a supraventricular tachycardia.

5.1. Limitations of the study

Low incidence of arrhythmias limits the number of patients for analysis. A similar study with large number of patients may show a significant difference between the two groups.

6. Conclusion

Magnesium levels are low in infants and neonates with transposition of great arteries undergoing an arterial switch operation. There is no statistically significant difference in arrhythmias between the magnesium supplemented group and the control group in the postoperative period, however, only a tendency towards reduction in arrhythmias was observed in the group supplemented with magnesium in the dose of 30 mg/kg.

References


