

Magnesium supplementation during cardiopulmonary bypass to prevent junctional ectopic tachycardia after pediatric TOF surgery – A randomized controlled study

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Abstract

Objective: The occurrence of postoperative junctional ectopic tachycardia (JET) is more frequent in certain types of congenital heart surgery. Magnesium decreases the incidence of junctional ectopic tachycardia after surgery. Therefore we prospectively examined the effect of magnesium treatment on the incidence of postoperative JET in pediatric patients undergoing surgical repair of congenital heart defects.

Methods and results: We performed a randomized, double-blind, controlled study in 90 pediatric patients. Magnesium sulphate (MgSO₄) or placebo was administered during the rewarming phase of cardiopulmonary bypass: group 1, placebo group (30 patients); group 2, 25 mg/kg of MgSO₄ (30 patients); and group 3, 50mg/kg of MgSO₄ (30 patients). The overall incidence of JET was 11.1%. Group 1 patients had higher proportion of JET 6 (20%), than group 2 and group 3 (10 %, 3.3%).

Conclusions: Supplementation with MgSO₄ during cardiopulmonary bypass seems to reduce the incidence of hypomagnesaemia and junctional ectopic tachycardia at admission to the cardiac intensive care unit. This effect seems to be dose related.

Keywords: Junctional Ectopic Tachycardia, Cardio Pulmonary Bypass, Tetralogy of Fallot

1.Introduction

Junctional Ectopic Tachycardia (JET) or His-bundle tachycardia is a narrow complex tachycardia that might be present as a primary idiopathic arrhythmia during infancy (so called congenital JET); however it commonly occurs in the postoperative period after congenital cardiac surgery [1]. JET is associated with hemodynamic instability, longer mechanical ventilation time, and longer stays in the cardiac intensive care unit (CICU) [2]. It is one of the most important factors which may increase the morbidity and mortality after congenital heart surgery. Mortality rates related with this incidence have been reported to vary from 3 to 13.5% [3,4]. In the majority of cases, JET occurred immediately after surgery or during the first post-operative day [3]. The exact cause of JET is unknown, but several association and predictors of JET have been studied and identified. Early attention to these factors makes it possible to

avoid them when possible and to create preventive strategies.

While acute electrolyte imbalances definitely increase the incidence of arrhythmias, hypomagnesaemia seems to be the most essential factor in pathogenesis of JET [5]. Hypomagnesaemia causes an intracellular potassium deficiency and augmented intracellular calcium concentration, leading to an increase in myocardial excitability [6]. The incidence of hypomagnesaemia during and after cardiac surgery has been well reported in the adult population. Alterations in serum magnesium in pediatric patients during and after cardiac surgery have not been as well-characterized. The role of magnesium in arrhythmia prevention and optimal magnesium dosage protocols in pediatric patient's remains unclear, and their administrations in pediatric cardiac patients have not been demonstrated nor have dosage guidelines been established.

In pediatric cardiac surgeries, tetralogy of fallot (TOF) repair surgeries have relatively higher incidence of JET due to resection near Atrioventricular node and proximal conduction system. Therefore we aimed to determine the incidence of hypomagnesaemia and JET in pediatric patients undergoing tetralogy of fallot repair surgery who requires cardiopulmonary bypass (CPB), and to evaluate the effect of prophylactic administration of magnesium sulphate (MgSO₄) on the occurrence of post-operative arrhythmias.

2. Material Method

Study was approved by our institutional ethics committee (UNMICRC/ANAES/2014/19) and informed and written consent had been obtained from parents of all the patients who were participated. Study was done in the period of November 2014 to June 2015 at U.N. Mehta institute of cardiology and research centre, Ahmedabad. We performed a randomized, controlled study in 90 children who underwent only TOF surgery. Our exclusion criteria for participation in the study were age >18 years, emergent surgery, or refusal to participate in the study, patients with any chronic arrhythmia other than sinus tachycardia or taking any medication prescribed for control of a chronic arrhythmia. Patients were randomly divided into three groups, Group A: Patients receiving Placebo Group B: Patients receiving MgSO₄ 25 mg/kg Group C: Patients receiving MgSO₄ 50 mg/kg Preoperative variables including demographics, previous medical history, and previous abnormal electrocardiogram were collected. The classification of the surgery was assessed by the Aristotle level of complexity. Intraoperative variables CPB time and cross clamp time were recorded of all

patients. Serum magnesium levels were checked at four time points: 1) Before CPB; 2) 10 minutes after initiation of CPB; 3) 10 min after drug addition during rewarming and 4) On arrival at intensive care unit. Post-operative complications - hypotension/bradycardia, presence of renal failure, and presence of cardiac failure were checked. The incidence of JET after CPB /after shifting/within 6 hr. of shifting in CTRR were also noted. JET was defined as (1) a heart rate of 170 beats/min or more with a QRS complex morphology similar to the baseline normal sinus or atrial rhythm; (2) an atrioventricular dissociation with a ventricular rate higher than or equal to the atrial rate; (3) a ventricular/atrial association with a retrograde 1:1 or Wenckebach conduction. Mechanical ventilation, length of ICU stay, hospital length of stay was also noted.

2.1 Statistical analysis

The statistical analysis was performed using SPSS v20.0. The values were expressed as mean±SD. To compare the continuous data between three groups Analysis of Variance (ANOVA) was used, whereas for comparison of categorical variable chi-square test was used. 'P' <0.05 was considered statistically significant.

3. Result

Total 90 patients were included in the study. Thirty patients were randomly assigned to group 1 (placebo group), 30 patients to group 2 (receiving 25 mg/kg of MgSO₄), and 30 patients to group 3 (receiving 50 mg/kg of MgSO₄). There's no significant (p>0.05) difference found in demographics such as age, gender, weight and BSA and intraoperative variables namely CPB time, cross clamp time and ICU stay of the population (Table 1).

Table 1: Baseline demographic, intraoperative and postoperative data among the three groups

	Group 1 Placebo	Group 2 MgSO ₄ (25 mg/kg)	Group 3 MgSO ₄ (50 mg/kg)	P value
Age (days)	46.56 ± 19.41	46.2 ± 25.55	51.56 ± 20.97	0.550
Sex	M = 17 F = 13	M = 15 F = 15	M = 22 F = 8	-----
Weight (kg)	13.83 ± 3.34	13.25 ± 3.51	14.23 ± 3.43	0.610
BSA (m ²)	0.597 ± 0.108	0.586 ± 0.088	0.608 ± 0.085	0.662
CPB time (min)	88.36 ± 18.25	99.100 ± 25.043	93.633 ± 19.343	0.149
Cross clamp time (min)	71.533 ± 15.146	82.300 ± 22.741	78.933 ± 19.080	0.092
ICU stay (days)	4.16 ± 1.34	3.83 ± 1.116	3.616 ± 1.349	0.247

CPB: Cardio Pulmonary bypass, ICU: Intensive care unit

The average serum Mg level at each time point was compared among the three study groups. The ionized magnesium level in the study group at each time point is presented in table 2. The levels of Mg at time 1 and time 2 were not statistically different between the groups (p= 0.054 and p=0.113). In the study group 3, serum Mg level significantly increased

at time 3 (2.316 ± 0.242) (10 minutes after the drug administration) and decreased again at time 4 (2.140 ± 0.189) (on arrival at ICU). At time 3, the average of serum Mg level in group 3 (50 mg/kg of MgSO₄) was significantly greater than the levels in groups 1 and 2 (group 3, 2.31 ± 0.24; group 2, 2.17 ± 0.185; group 1, 2.03 ± 0.28; P<0.001) (Table 2).

Table 2: Ionized magnesium level at each time point by study groups

Time points	Group 1 Placebo	Group 2 MgSO ₄ 25 mg/kg	Group 3 MgSO ₄ 50 mg/kg	P value
Serum mg level before CPB (t1)	2.301 ± 0.302	2.148 ± 0.212	2.170 ± 0.267	0.054
Serum mg level 10min after CPB (t2)	2.104 ± 0.327	1.963 ± 0.206	2.012 ± 0.236	0.114
Serum mg level 10 min after drug addition CPB (t3)	2.033 ± 0.280	2.167 ± 0.185	2.316 ± 0.242	<0.001
Serum mg level on arrival at ICU (t4)	1.946 ± 0.221	2.006 ± 0.241	2.140 ± 0.189	0.003

CPB: Cardio Pulmonary bypass, ICU: Intensive care unit

Intraoperative data were comparable in all three groups. The overall incidence of JET was 11.1%. Group 1 (20%) patients had higher proportion of JET than group 2 (10%) and group 3 (3.3%). Similarly greater frequency of hypotension and renal

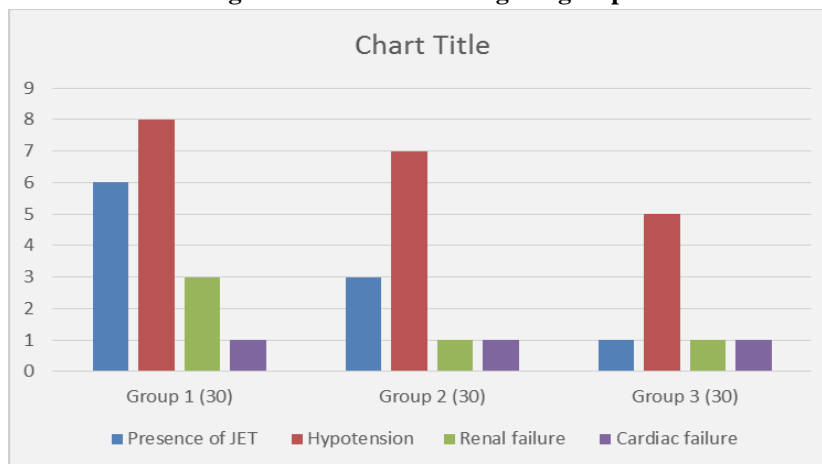
failure was observed in group 1 (26.6 and 10%) patients as compared to group 2 (23.3% and 3.3%) and 3 (16.6% and 3.3%) patients. However the incidences of cardiac failure were same in all three groups (3.3%) (Table 3) (Figure 1).

Table 3: Frequency of incidence among the group

	Group 1 Placebo	Group 2 MgSO ₄ (25 mg/kg)	Group 3 MgSO ₄ (50 mg/kg)	P value
Presence of JET	6 (20%)	3 (10%)	1 (3.3%)	0.1179
Hypotension	8 (26.6%)	7(23.3%)	5(16.6%)	0.6376
Renal failure	3 (10%)	1 (3.3%)	1(3.3%)	0.4287
Cardiac failure	1 (3.3%)	1(3.3%)	1(3.3%)	1.0000

JET: Junctional ectopic tachycardia

Figure 1: Incidence among the groups



4. Discussion

Postoperative JET, the congenital variant, presents as a transient phenomenon immediately after surgery in congenital heart disease [7-10]. It usually begins after 6 - 72 hours following cardiopulmonary bypass surgery for repair of congenital heart lesions [11]. It occurs in 15 to 25% of infants following repair of TOF, in up to 12% of infants following repair of ventricular septal defect in 10% of infants following repair of atrioventricular septal defect, and in 30% of infants following repair of Anomalous pulmonary venous connection [7].

During the surgery, patients are exposed to hemodilution, blood loss, blood transfusions, and an increase of catecholamines that may lead to chelation of magnesium. All these factors contribute to the reduction in plasma magnesium levels. In addition,

during surgery, continuous hemofiltration, modified ultrafiltration, and administration of large doses of calcium and diuretics cause the depletion of magnesium. Other factors causing hypomagnesaemia include the intracellular elimination shifts induced by the extracorporeal circulation and the decrease in body temperature during surgery [12-18].

In our study we found that incidence of JET in tetralogy of fallot surgery can be reduced by administration of MgSO₄ during CPB. This decrease in Incidence is also dose dependent. Incidence of JET in placebo group is 20% while it is 10% and 3% in group receiving 25mg/kg and 50mg/kg of magnesium during CPB respectively. The overall incidence in our study population was 11.1%, which is comparable with the previously reported studies. Our finding suggests that supplementation of magnesium during

CPB reverses hypomagnesaemia and reduces the frequency of JET as detected on arrival in the CICU.

4.1 Level of serum magnesium

Some previous studies have taken ionized magnesium for consideration but in our institute there is no facility to measure ionized magnesium. So we observed serum magnesium in our study as some studies suggested strong correlation between total and ionized magnesium serum concentration [19].

As in previous studies, [20] our data at the time of the CICU admission showed that the frequency of hypomagnesaemia was marginally higher between placebo and magnesium groups. We speculate that this difference may be clinically insignificant. This little difference may be explained by multiple factors that occur after CPB and influence whole blood magnesium levels, such as ultra-filtration, intravenous fluids, blood transfusions, and drugs [21-23].

4.2 JET and antiarrhythmic effect of magnesium:

JET is associated with longer ventilation time, longer intensive care unit stay and higher mortality after pediatric cardiac surgery. Incidence of JET is higher after TOF repair surgery compared to other pediatric cardiac surgery. The antiarrhythmic effects of magnesium in polymorphic ventricular tachyarrhythmia have been attributed to a decrease in inward calcium current via L-type calcium channels and to the stabilization of membrane potential by facilitation of potassium entry into the cells. Therefore magnesium increases the negative membrane resting potential reducing myocardial excitability. It increases the relative refractory period and decreases the vulnerable period, reducing the risk for re-entry. Dittrich and associates [24] in their randomized clinical trial in 131 patients demonstrated the association between the supplementation with magnesium and a decrease in the overall incidence of post-operative arrhythmias in children and adults after surgery for congenital heart disease. Our study has also demonstrated supplementation of magnesium is associated with lower incidence of JET during perioperative period which is dose dependent.

5. Limitations of the Study

Baseline characteristics and surgical complexity were equal in our study groups; population does not represent all the pediatric cardiac surgical patients who may be at risk for postoperative JET. For example, patients requiring emergency surgery and patients who were critically ill (preoperatively) were excluded from our study. In addition, our study was not designed to evaluate the incidence of JET after CICU admission. Thus the incidence of JET and/or other arrhythmias over a

prolonged postoperative period was not evaluated. Another limitation of this study is the lack of available tools to measure intracellular activity of the magnesium. Intracellular magnesium may be more of an indicator of hypomagnesaemia and arrhythmias. The low incidence of JET limits the number of patients for analysis. Studies with a large number of patients will be needed to validate our results.

6. Conclusion

JET is the most frequent arrhythmia during and after congenital cardiac surgery. Therefore, it is important for everybody involved in the perioperative care of congenital heart surgery patients to recognise and treat JET early. Our study suggests that supplementation of MgSO₄ during CPB reduces the incidence of hypomagnesaemia and reduces the overall incidence of JET. In addition, this effect seems to be dose related.

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