Lower risk of postoperative arrhythmias in congenital heart surgery following intraoperative administration of magnesium

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ABSTRACT

Objectives: Postoperative arrhythmias are common in children undergoing congenital heart surgery. We evaluated whether intraoperative administration of magnesium was associated with a reduced occurrence of specific postoperative arrhythmias, as has been described previously, or had a broader effect on multiple arrhythmia types, and whether there existed a dose–effect of intraoperative magnesium.

Methods: We used a historical prospective observational cohort study. Propensity score matching using logistic regression was applied to establish similar populations of treatment groups balanced on 5 important covariates.

Results: Based on propensity score–matched groups, magnesium 50 mg/kg administration was associated with a reduced odds of occurrence of postoperative arrhythmias: any arrhythmia (odds ratio [OR] = 0.50, $P < .001$), junctional ectopic tachycardia (OR = 0.56, $P = .004$), accelerated junctional rhythm (OR = 0.56, $P = .089$), atrial tachycardia (OR = 0.48, $P = .005$), ventricular tachycardia (OR = 0.52, $P = .04$), and atrioventricular block (OR = 0.47, $P = .03$). The effect of magnesium on reducing the odds of occurrence of postoperative arrhythmias did not differ between 25 mg/kg versus 50 mg/kg.

Conclusions: As many as one third of our patients undergoing congenital heart surgery had postoperative arrhythmias. Use of intraoperative magnesium was associated with a reduction in the odds of occurrence of all postoperative arrhythmias. Our results do not provide evidence that a greater dose of magnesium is associated with greater arrhythmia risk reduction. Despite the intraoperative use of magnesium, there continued to be a high residual incidence of postoperative arrhythmias, raising the question for studying new or additional agents. (J Thorac Cardiovasc Surg 2018;156:763-70)

Odds ratios for postoperative arrhythmias. *Significant effect in reducing arrhythmia occurrence.

Central Message

Postoperative arrhythmias are common after congenital heart surgery. Intraoperative magnesium administration is associated with reduced occurrence of multiple arrhythmia types.

Perspective

Postoperative arrhythmias are common after congenital heart surgery. Intraoperative magnesium administration was associated with a reduced occurrence of all arrhythmias types and no differences were observed between the 2 doses studied. Despite the use of magnesium, there continued to be a high residual incidence of postoperative arrhythmias (18%), raising the need for studying new or additional agents.

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Postoperative arrhythmias such as junctional ectopic tachycardia (JET) are common in children undergoing congenital heart surgery (CHS) and are reported in 5% to 38% of patients.¹⁻⁶ JET delays postoperative recovery, prolongs

cardiac intensive care unit (CICU) and hospital stays, and increases postoperative morbidity and mortality. Attention has been predominantly focused on postoperative JET, although evidence is lacking regarding an association between magnesium (Mg) use and dose and the reduction in the occurrence of other postoperative arrhythmias after CHS.

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Abbreviations and Acronyms

25-Mg	= 25 mg/kg
50-Mg	= 50 mg/kg
AJR	= accelerated junctional rhythm
AT	= atrial tachycardia
AV	= atrioventricular
BSA	= body surface area
CPB	= cardiopulmonary bypass
CHS	= congenital heart surgery
CICU	= cardiac intensive care unit
HB	= atrioventricular block
JET	= junctional ectopic tachycardia
Mg	= magnesium
No-Mg	= control group
OR	= odds ratio
PSM	= propensity score matching
VT	= ventricular tachycardia

Mg has been the most widely studied agent used to lessen postoperative arrhythmias. The heterogeneous nature of these studies makes it difficult to ascertain the effect of Mg on postoperative arrhythmias other than postoperative JET and if Mg dose matters. Lee and colleagues performed a meta-analysis of 5 studies reporting on the use of Mg during or after CHS; 3 reports studied intraoperative and 2 postoperative Mg administration.⁷⁻¹² The study populations were small and varied in size from 26 to 99 patients. The dose of administered Mg varied between 25 and 50 mg/kg intraoperatively. The method of Mg administration varied as either a single bolus (30 mg/kg) or a continuous infusion (4 mg/kg/hour). Evidence of arrhythmia suppression varied, and specific types of CHS assessed were limited in these studies.¹⁰ A recent meta-analysis of 35 studies in adult subjects undergoing cardiac surgery confirmed that Mg can reduce the occurrence of postoperative atrial fibrillation, but there was limited evidence to support Mg administration for prevention of other postoperative arrhythmias.¹³

We previously reported that intraoperative administration of Mg was associated with a lower risk for postoperative JET.¹⁴ Not defined in the medical literature and in an attempt to further expand our research, we wanted to study the impact of intraoperative Mg administration on postoperative arrhythmias other than postoperative JET and assess whether there existed a Mg dose-dependent effect. We reviewed our data on a large cohort of diverse patients with CHS who received either no Mg or 1 of 2 alternative doses (25 mg/kg vs 50 mg/kg) at the time of aortic crossclamp release. The purpose of this study was to evaluate (1) whether Mg administration was associated with a reduction in the occurrence of postoperative JET

and other arrhythmia types and (2) whether there was evidence of a dose-effect of intraoperative Mg on the occurrence of postoperative arrhythmias.

PATIENTS AND METHODS**Patient Population**

In total, 1871 patients who had undergone CHS with cardiopulmonary bypass (CPB) at our institute from 2005 to 2013 were selected and their medical records reviewed with approval from Children's National Health System Institutional Review Board (date and number of Institutional Review Board approval: October 1, 2013, Protocol 4188). Patients were excluded if they had (1) a history of preoperative arrhythmia, (2) incomplete or absent medical records, or (3) unclear description or no electrocardiographic evidence to assess postoperative arrhythmia. The electronic medical record, electrocardiograms, and telemetry records were reviewed from the time of entering the CICU until hospital discharge. The following clinical data were collected: date of surgery, sex, ethnicity, height, weight, body surface area (BSA), congenital heart disease type, congenital heart surgical procedure performed, dose of intraoperative Mg administered, occurrence of postoperative arrhythmic events, total surgical time, aortic crossclamp time, and CPB time.

Intraoperative Mg Administration

Patients with CHS were divided into 3 groups based on the dose of Mg administered intraoperatively: control group (no-Mg administration), 25-Mg (25 mg/kg), and 50-Mg (50 mg/kg). Mg dosage varied by era of surgery. In the no-Mg group, there were 750 cases randomly selected for study inclusion from a pool of 909 eligible cases out of a total of 1009 reviewed between 2005 and 2008. In the 25-Mg group, all 338 eligible cases were included from a total of 369 reviewed from May 2009 to July 2010. In the 50-Mg group, all 783 eligible cases were included from a total of 810 reviewed from August 2010 to July 2013. Patients in either the 25-Mg and 50-Mg group received a single bolus of Mg sulfate (25 or 50 mg/kg) into the CPB circuit at the beginning of rewarming. The cardioplegic solution (Plegisol, Baxter, Deerfield, Ill), which contains 0.325% of Mg chloride, was given to all of the patients, according to our standard CPB protocol.

Postoperative Arrhythmias

Arrhythmias were classified into 5 categories as follows. (1) JET was defined as a supraventricular arrhythmia (wide or narrow QRS complex—same morphology as in sinus rhythm) with no preceding P-wave at a rate that exceeded the normal junctional escape rate for age. The ventricular rate had to be more than 120 bpm. (2) If the ventricular rate was between 90 and 119 bpm, it was defined as accelerated junctional rhythm (AJR). (3) Atrial tachycardia (AT) was defined as a regular atrial rhythm that exceeded the underlying sinus rate and exhibited a sudden acceleration or rapid warm-up of rate with the P-wave morphology different from sinus rhythm/sinus tachycardia. (4) Ventricular tachycardia (VT) was defined as a sequence of 3 or more consecutive ventricular beats with a rate greater than 120 bpm and included nonsustained and sustained VT. (5) Atrioventricular block (HB) was defined as atrioventricular (AV) conduction block that included second-degree and third-degree AV block. First-degree AV block was excluded. Some patients had multiple arrhythmia types and were included in each respective arrhythmia category. The duration of the arrhythmia had to be frequent and long enough to be documented on either cardiac telemetry or on an electrocardiogram. Other than for nonsustained periods of VT, all arrhythmias were only included if lasted for >1 minute or recurred frequently. All children were on telemetry for the full length of their hospitalization.

Surgical Procedure Types

Because of the diverse composition of the study group, we divided surgical procedure types into 5 groups: (1) conotruncal/ventricular septal

defects, (2) single-ventricle anatomy, (3) atrial septal defect/pulmonary venous anomalies, (4) outflow obstruction defects, and (5) primary valvular heart defects or miscellaneous.

Statistical Analysis

Propensity score matching (PSM) was performed to balance covariates between treatment (Mg) and control (no-Mg) groups using multivariable logistic regression to derive the propensity scores and nearest neighbor matching based on a caliper width equal to 0.2 of the pooled standard deviation of the logit using 1 to 1 matching without replacement.^{15,16} This was done for low-dose (25-Mg) as well as high-dose (50-Mg) Mg to match controls to each of these Mg treatment groups. Five covariates previously shown to be associated with the occurrence of postoperative arrhythmias were used: age, weight, Aristotle score, cardiac diagnosis, and surgical time. The absolute standardized mean difference (d) was assessed to evaluate the quality of the matching in balancing the treatment and control groups.^{15,16} Conditional logistic regression was applied to compare the effects of each dose of Mg with the matched controls with respect to the incidence of any postoperative arrhythmia with each of the 5 specific arrhythmia types analyzed. Low- and high-dose Mg groups were also compared with the Mann-Whitney *U* test for medians and the Fisher exact test for independent proportions.

Odds ratios (ORs) were computed to estimate the treatment effect with 95% confidence intervals with no-Mg controls as the reference group, and significance was determined with the Wald test in conditional logistic regression to account for the matched sets. Forest plots were constructed to illustrate effects of Mg in reducing risk of postoperative arrhythmia events compared with control, with a dashed vertical line at an OR of 1.00 denoting no difference. Statistical power was greater than 85% for detecting an OR of 0.50 in reducing postoperative arrhythmias for each Mg dose compared with control using logistic regression with an alpha level of 0.05 (nQuery Advisor version 7.0; Statistical Solutions, Cork,

Ireland). Statistical analysis was conducted with the Stata software package with *PSMATCH2* module for matching (Stata Release 13, StataCorp, College Station, Tex). Two-tailed values of $P < .05$ were considered statistically significant. Overall arrhythmia incidence was the primary end point, and the individual rhythms were the secondary endpoints of the analysis.

RESULTS

Patient Population

The study population consisted of 1871 patients (no-Mg group, $n = 750$; 25-Mg, $n = 338$; and 50-Mg, $n = 783$) from a total cohort of 2188 patients undergoing cardiac surgery during the study period (Figure 1 and Table E1). Patients were selected by using the criteria described in the Methods section. Of these, 307 paired patients were selected for PSM comparing no-Mg versus 25-Mg and 540 paired subjects were selected comparing no-Mg versus 50-Mg. PSM resulted in a well-balanced study population with the absolute standardized mean differences between study groups ≤ 0.10 on all matched covariates (Tables 1 and 2). Six hundred four of the 750 control patients were used for matching. Two hundred forty-three were matched with both the 25-Mg and 50-Mg groups.

No-Mg Versus 25-Mg

No differences were noted in the baseline demographics between the 2 study groups specifically for age, weight, BSA, sex, race, type of cardiac defect, Aristotle score, aortic crossclamp time, CPB time, and total surgical time (Table 1).

FIGURE 1. Study population. The study population consisted of 1871 patients (no-Mg group, $n = 750$; 25-Mg, $n = 338$; and 50-Mg, $n = 783$). Three hundred seven paired patients were selected for propensity-score matching comparing no-Mg versus 25-Mg, and 540 paired patients were selected comparing no-Mg versus 50-Mg. Some control patients were used for matching in both the 25-Mg and 50-Mg group comparisons. 25-Mg, 25 mg/kg; 50-Mg, 50 mg/kg.

TABLE 1. Baseline characteristics for propensity score–matched controls and low-dose magnesium treatment

Variable	No-Mg control group (n = 307)	25-Mg (n = 307)	P value	d statistic
Age, mo	7 (4-26)	6 (2-22)	.18	0.10
Weight, kg	6.6 (4.3-11.7)	6.0 (3.9-10.3)	.15	0.10
BSA, m ²	0.35 (0.26-0.52)	0.32 (0.24-0.48)	.11	0.09
Male sex, n (%)	177 (58)	160 (52)	.20	0.11
Race, n (%)			.84	
White	135 (44)	130 (42)		0.03
African American	81 (26)	93 (30)		0.09
Hispanic	46 (15)	43 (14)		0.03
Asian	13 (4)	10 (3)		0.05
Other	32 (10)	31 (10)		0.02
Cardiac defect, n (%)			.53	
Conotruncal/VSD	125 (41)	139 (45)		0.09
Single ventricle	107 (35)	107 (35)		0.01
Atrial septal defect	20 (7)	20 (7)		0.01
Outflow obstruction	29 (9)	19 (6)		0.10
Miscellaneous/valve	26 (8)	22 (7)		0.05
Aristotle score, n (%)			.57	0.05
1 or 2	186 (61)	178 (58)		
3 or 4	121 (39)	129 (42)		
Crossclamp time, min	39 (26-50)	36 (21-49)	.17	0.10
CPB time, min	82 (65-105)	82 (64-106)	.99	0.02
Surgical time, min	200 (174-240)	205 (170-240)	.98	0.03

Continuous data are represented by the median (interquartile range). *No-Mg*, No magnesium given; *25-Mg*, 25 mg/kg; *d*, standardized mean difference; *BSA*, body surface area; *VSD*, ventricular septal defect; *CPB*, cardiopulmonary bypass.

25-Mg significantly reduced the odds of any postoperative arrhythmia (OR = 0.40, $P < .001$), postoperative JET (OR = 0.45, $P = .003$), postoperative AJR (OR = 0.40, $P = .037$), and postoperative AT (OR = 0.32, $P = .003$) (Table 3 and Figure 2). The effect of 25-Mg on postoperative VT (OR = 0.81, $P = .655$) and HB (OR = 0.76, $P = .492$) was not significant (Table 3 and Figure 2, A).

No-Mg Versus 50-Mg

No differences were noted in the baseline demographics between the 2 study groups specifically for age, weight, BSA, sex, race, type of cardiac defect, Aristotle score, aortic crossclamp time, CPB time, and total surgical time (Table 2). 50-Mg significantly decreased the occurrence of any postoperative arrhythmia (OR = 0.50, $P < .001$), postoperative JET (OR = 0.56, $P = .004$), postoperative AJR (OR = 0.56, $P = .089$), postoperative AT (OR = 0.48, $P = .005$), postoperative VT (OR = 0.52, $P = .040$), and HB (OR = 0.47, $P = .03$) (Table 4 and Figure 2, B).

25-Mg Versus 50-Mg

No differences were noted in the OR of effect between 25-Mg and 50-Mg on any postoperative arrhythmia (OR = 1.23, $P = .285$), postoperative JET (OR = 1.08,

$P = .792$), postoperative AJR (OR = 1.22, $P = .662$), postoperative AT (OR = 1.27, $P = .551$), postoperative VT (OR = 0.95, $P = .897$), and HB (OR = 0.73, $P = .466$) (Table 5).

Baseline characteristics of the 25-Mg and 50-Mg treatment propensity-matched groups were compared with the Pearson χ^2 analysis and Mann-Whitney U tests. No statistical differences were noted in 9 of 10 analyzed variables: age, weight, BSA, aortic crossclamp time, CPB time, surgical time, sex, race, and Aristotle score. Overall distribution of specific cardiac defects showed some variation. For example, the composition of single-ventricle patients to the total 25-Mg group versus the 50-Mg group was 35% versus 24%. In contrast, the composition of conotruncal/VSD subjects to the 25-Mg versus 50-Mg groups was similar, 45% versus 49%.

Residual Arrhythmia Risk

Despite the benefit of intraoperative administration of Mg, there continued to be a fairly high occurrence of postoperative arrhythmias (total [18%], postoperative JET [8%], AJR [3%], AT [4%], VT [3%], and HB [3%]) (Table 5).

Some patients had multiple arrhythmias and were counted in each of the arrhythmia groups. Among all unique No-Mg patients ($n = 604$ controls), the incidence of

TABLE 2. Baseline characteristics for propensity score–matched controls and high-dose magnesium treatment

Variable	No-Mg control group (n = 540)	50-Mg (n = 540)	P value	d statistic
Age, mo	6 (2-25)	5 (2-24)	.80	0.01
Weight, kg	6.1 (4.0-10.9)	5.7 (4.0-11.4)	.95	0.01
BSA, m ²	0.33 (0.24-0.50)	0.31 (0.25-0.51)	.97	0.01
Male sex, n (%)	287 (53)	278 (52)	.63	0.03
Race, n (%)			.12	
White	223 (41)	232 (43)		0.05
African American	161 (30)	163 (30)		0.01
Hispanic	76 (14)	52 (10)		0.10
Asian	21 (4)	17 (3)		0.04
Other	59 (11)	76 (14)		0.09
Cardiac defect, n (%)			.80	
Conotruncal/VSD	274 (51)	263 (49)		0.04
Single ventricle	112 (21)	129 (24)		0.08
Atrial septal defect	59 (11)	55 (10)		0.02
Outflow obstruction	45 (9)	42 (8)		0.02
Miscellaneous/valve	50 (9)	51 (9)		0.01
Aristotle score, n (%)			.76	0.02
1 or 2	319 (59)	313 (58)		
3 or 4	221 (41)	227 (42)		
Crossclamp time, min	40 (28-54)	38 (22-55)	.10	0.10
CPB time, min	82 (65-105)	80 (64-110)	.85	0.05
Surgical time, min	208 (187-242)	210 (180-240)	.84	0.01

Continuous data are represented by the median (interquartile range). *No-Mg*, No magnesium given; *50-Mg*, 50 mg/kg; *d*, standardized mean difference; *BSA*, body surface area; *VSD*, ventricular septal defect; *CPB*, cardiopulmonary bypass.

multiple arrhythmias was 31 of 604 (5.1%), which was significantly greater compared with 19 of 847 (2.2%) 25-Mg or 50-Mg patients ($P = .003$).

DISCUSSION

Postoperative arrhythmias impact the recovery of patients from congenital cardiac surgery, increase duration of intubation and CICU stay, and prolong total time in the hospital. Postoperative JET is the most common arrhythmia seen in children after open-heart surgery, with an average incidence of 14.3%.⁶ The frequency of other postoperative arrhythmias has not been as well documented and appears to vary among different surgical centers. In the current study, we observed in our control group that AT was the

second most common postoperative arrhythmia (8.3%), followed by AJR (4.8%), VT (5%), and HB (4.5%). Dittrich and colleagues⁹ reported a similar occurrence rate of JET (10.6%), AT (10.6%), and HB (3%). In the postoperative series published by Delaney and colleagues,¹⁷ the rate of postoperative JET was 8.5%, complete HB was 3.7%, and VT was 2.1%. Talwar and colleagues¹⁸ observed a lower occurrence rate for postoperative JET (3.5%) and supraventricular tachycardia (2.5%).

The potential benefit of Mg in reducing the occurrence of postoperative arrhythmias depends on the underlying mechanism responsible for their individual occurrence.¹⁹ The risk factor profile for occurrence of postoperative JET seems best associated with measures of myocardial

TABLE 3. Incidence of postoperative arrhythmias for controls and low-dose magnesium treatment

Event, n (%)	Total (n = 614)	Control group (n = 307)	25-Mg (n = 307)	Odds ratio*	95% CI	P value
Any arrhythmia	147 (24)	98 (32)	49 (16)	0.40	0.28-0.60	<.001†
JET	72 (12)	48 (16)	24 (8)	0.45	0.27-0.76	.003†
AJR	24 (4)	17 (6)	7 (2)	0.40	0.17-0.93	.037†
AT	39 (6)	29 (9)	10 (3)	0.32	0.15-0.68	.003†
VT	20 (3)	11 (4)	9 (3)	0.81	0.33-1.95	.655
HB	23 (4)	13 (4)	10 (3)	0.76	0.35-1.67	.492

25-Mg, 25 mg/kg; *CI*, confidence interval; *JET*, junctional ectopic tachycardia; *AJR*, accelerated junctional rhythm; *AT*, atrial tachycardia; *VT*, ventricular tachycardia; *HB*, atrioventricular block. *Reference group = control group. †Statistically significant treatment effect in reducing odds of arrhythmia occurrence.

FIGURE 2. A, Forest plots depicting the odds ratios for postoperative arrhythmias, no-Mg versus 25-Mg. 25-Mg significantly reduced the odds of occurrence of any postoperative arrhythmia (OR = 0.40, $P < .001$), postoperative JET (OR = 0.45, $P = .003$), postoperative AJR (OR = 0.40, $P = .037$), and postoperative AT (OR = 0.32, $P = .003$). The effect on postoperative VT (OR = 0.81, $P = .655$) and HB (OR = 0.76, $P = .492$) was not significant. *Statistically significant treatment effect in reducing arrhythmia. B, Forest plots depicting the odds ratios for postoperative arrhythmias, no-Mg versus 50-Mg. 50-Mg significantly decreased the occurrence of any postoperative arrhythmia (OR = 0.50, $P < .001$), postoperative JET (OR = 0.56, $P = .004$), postoperative AJR (OR = 0.56, $P = .089$), postoperative AT (OR = 0.48, $P = .005$), postoperative VT (OR = 0.52, $P = .04$), and HB (OR = 0.47, $P = .03$). *Statistically significant treatment effect in reducing arrhythmia. OR, Odds ratio; JET, junctional ectopic tachycardia; AJR, accelerated junctional rhythm; AT, atrial tachycardia; VT, ventricular tachycardia; HB, atrioventricular block; 25-Mg, 25 mg/kg; 50-Mg, 50 mg/kg.

ischemic/reperfusion injury incurred during the operative period. The underlying substrate for postoperative AT seems more related to atrial inflammation. Colchicine, an anti-inflammatory agent, has been demonstrated to decrease the odds of occurrence of postoperative atrial fibrillation by 52% in adult patients undergoing heart surgery.²⁰ The etiology of postoperative HB may be multifactorial— ischemic/reperfusion injury of the conduction system and mechanical trauma to the AV node–His bundle conduction axis.

Mg has been used in cardiac surgery to reduce postoperative arrhythmias for many years.^{21,22} Despite this, few data have been published on the key questions of (1) whether there is a dose-dependent relationship between Mg administration and postoperative arrhythmia occurrence and (2) whether the effect of Mg is arrhythmia-specific. Studies have reported using varying doses of Mg, assessing its effect mostly on postoperative JET and ventricular fibrillation, and in limited congenital

heart disease subsets. In the present study, we assessed the relationship between alternative doses of Mg (25 and 50 mg/kg) administered at the time of aortic crossclamp release and 5 postoperative arrhythmia subtypes in a diverse population of congenital heart diseases undergoing varying complexity levels of surgical repair.

Our data provide evidence that use of Mg is associated with a lower occurrence of all types of postoperative arrhythmias, with a statistically significantly lower risk of postoperative JET, AJR, and AT and borderline lower risks of postoperative VT and postoperative HB. There was little evidence of a dose–response effect.

It has been documented in clinical trials that Mg can reduce the occurrence of postoperative JET.^{8,9,14} A previously reported study of 99 patients by Manrique and colleagues⁸ suggested a dose-dependent effect of Mg administration with the effect greater at 50-Mg rather than 25-Mg. These investigators reported that following a dose of 50-Mg, the incidence of postoperative JET was zero.

TABLE 4. Incidence of postoperative arrhythmias for controls and high-dose magnesium treatment

Event, n (%)	Total (n = 1080)	Control group (n = 540)	50-Mg (n = 540)	Odds ratio*	95% CI	P value
Any arrhythmia	274 (25)	172 (32)	102 (19)	0.50	0.38-0.65	<.001†
JET	120 (11)	75 (14)	45 (8)	0.56	0.38-0.83	.004†
AJR	41 (4)	26 (5)	15 (3)	0.56	0.29-1.09	.089
AT	66 (6)	44 (8)	22 (4)	0.48	0.29-0.80	.005†
VT	43 (4)	28 (5)	15 (3)	0.52	0.28-0.94	.04†
HB	40 (4)	27 (5)	13 (2)	0.47	0.24-0.93	.03†

50-Mg, 50 mg/kg; CI, confidence interval; JET, junctional ectopic tachycardia; AJR, accelerated junctional rhythm; AT, atrial tachycardia; VT, ventricular tachycardia; HB, atrioventricular block. *Reference group = control group. †Statistically significant treatment effect in reducing odds of arrhythmia occurrence.

TABLE 5. Incidence of postoperative arrhythmias for low-dose and high-dose magnesium treatment

Event, n (%)	Total (n = 847)	25-Mg (n = 307)	50-Mg (n = 540)	Odds ratio*	95% CI	P value†
Any arrhythmia	151 (18)	49 (16)	102 (19)	1.23	0.85-1.78	.285
JET	69 (8)	24 (8)	45 (8)	1.08	0.64-1.79	.792
AJR	22 (3)	7 (2)	15 (3)	1.22	0.49-3.03	.662
AT	32 (4)	10 (3)	22 (4)	1.27	0.59-2.70	.551
VT	24 (3)	9 (3)	15 (3)	0.95	0.41-2.17	.897
HB	23 (3)	10 (3)	13 (2)	0.73	0.32-1.69	.466

25-Mg, 25 mg/kg; 50-Mg, 50 mg/kg; CI, confidence interval; JET, junctional ectopic tachycardia; AJR, accelerated junctional rhythm; AT, atrial tachycardia; VT, ventricular tachycardia; HB, atrioventricular block. *Reference group = 25-Mg. †No statistically significant differences between high dose and low dose in the incidence of arrhythmias.

Dorman and colleagues¹¹ reported in a series of 28 patients that the intraoperative administration of 30-Mg resulted in no postoperative JET. Our study, based on hundreds of patients with PSM at 2 different doses of Mg to minimize any selection bias and with a much broader diversity of congenital heart diseases, was not able to confirm these early observations. Postoperative JET still occurred despite the intraoperative administration of 50-Mg (8% incidence, 45 of 540 patients).

It has been controversial whether Mg can be used for prevention of postoperative AT or atrial fibrillation. All studies addressing this issue have focused on the adult cardiac surgical population.²³⁻²⁶ One study demonstrated a dose–effect of Mg in postoperative atrial fibrillation reduction (60-100 mg/kg), and others no effect of Mg in reducing the occurrence of postoperative atrial fibrillation.^{27,28} Our current data suggest that Mg use is associated with a ~50% reduction in the odds of postoperative AT. This finding surprised us, given that the underlying electrophysiological substrate may differ from postoperative JET.

Aortic crossclamp time is an important risk factor in the development of postoperative arrhythmia, especially for JET, HB, and VT. Ischemia and reperfusion injury plays a critical role in this process.²⁹ During CHS, the ischemic and reperfusion injury associated with aortic crossclamp can have detrimental effects on the sinus node, AV node, and conduction system, facilitating postoperative arrhythmia, especially in the neonate and infant because of immature and unstable recovery mechanisms.^{29,30}

Despite the intraoperative administration of Mg, there continues to be a high incidence of postoperative arrhythmias. Our findings beg the question for studying new or additional agents administered as a sole medication or combined with Mg to further reduce the occurrence of postoperative arrhythmias. For example, Amrousy and colleagues³¹ found that intravenous amiodarone administered at the time of induction of anesthesia for CHS lowered the incidence of postoperative JET from 28.9% to 9.2%. Mahmoud and colleagues³² noted the incidence of postoperative JET was decreased after the preoperative administration of propranolol from 38% to 21%. Kadam and colleagues³³ found that the perioperative

use of dexmedetomidine lowered the incidence of postoperative JET from 23% to 9%.

Summary

As many as one third of patients experience postoperative arrhythmias, of which JET and AT account for more than two thirds of the arrhythmias after CHS. Use of intraoperative Mg is associated with a reduction in the occurrence rate of multiple postoperative arrhythmias, especially JET and AT. Our results do not provide evidence that a greater dose (25 vs 50 mg/kg) of Mg is associated with greater arrhythmia risk reduction. Despite the use of Mg, there continued to be a high residual incidence of postoperative arrhythmias (Video 1).

Study Limitations

Our study is not based on a randomized trial design that potentially controls for the influence of confounding variables but rather a PSM cohort aimed at balancing measured baseline covariates that could influence the likelihood of postoperative arrhythmias. It represents an historical prospective review of one of the largest cohorts of children undergoing open-heart surgery for a diverse set of congenital heart defects and surgical procedure types. Small absolute standardized mean differences between the control and Mg populations indicated excellent quality of the propensity matching in balancing treatment groups and thus allowed objective comparisons of postoperative arrhythmias. Nevertheless, our observational (nonrandomized) study design limits the ability to draw firm causal inferences from these results.

Other limitations include the possibility of undetected arrhythmias, as this may have falsely decreased the frequency of arrhythmia events. The possibility exists that some wide complex arrhythmias may be atrial in origin

Jeffrey P. Moak, MD

Lower Risk of Postoperative Arrhythmias in Congenital Heart Surgery Following Intraoperative Administration of Magnesium

VIDEO 1. Text and verbal summary of the manuscript “Lower Risk of Postoperative Arrhythmias in Congenital Heart Surgery Following Intraoperative Administration of Magnesium.” Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)31027-4/fulltext](https://www.jtcvs.org/article/S0022-5223(18)31027-4/fulltext).

with bundle branch block or aberrancy and not necessarily ventricular in origin. There may be an era effect of CICU management that played a role in the development of postoperative arrhythmias. Over this period of time, differing approaches to the use of inotropes such as milrinone, dopamine, and epinephrine, which are known to facilitate the development of postoperative arrhythmias, may have contributed to changes in arrhythmia frequency and our results. However, the results of this study are useful in formulating hypotheses that can be tested in future prospective randomized clinical trials.

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Key Words: magnesium, postoperative arrhythmias, congenital heart surgery, junctional ectopic tachycardia, atrial tachycardia, ventricular tachycardia, atrioventricular block

TABLE E1. Baseline characteristics in prematched cohorts

Variable	No-Mg control group (n = 750)	Mg-25 mg/kg (n = 338)	Mg-50 mg/kg (n = 783)	P value (control vs Mg-25 mg/kg)	P value (control vs Mg-50 mg/kg)
Age, mo	5 (1-18)	6 (2-32)	8 (4-41)	<.001*	<.001*
Weight, kg	5.5 (3.7-9.8)	6.4 (4-12.1)	7.3 (4.4-14.5)	<.001*	<.001*
BSA, m ²	0.31 (0.23-0.46)	0.34 (0.25-0.55)	0.37 (0.26-0.61)	<.001*	<.001*
Male sex, n (%)	406 (54)	177 (52)	411 (53)	.589	.519
Race, n (%)				.939	.063
White	329 (44)	146 (43)	335 (43)		
African American	210 (28)	102 (30)	236 (30)		
Hispanic	103 (14)	44 (13)	75 (10)		
Asian	32 (4)	12 (4)	20 (3)		
Other	76 (10)	34 (10)	117 (14)		
Cardiac defect, n (%)				.009*	<.001*
Conotruncal/VSD	391 (52)	144 (43)	315 (40)		
Single ventricle	200 (27)	108 (32)	155 (20)		
Atrial septal defect	63 (8)	24 (7)	84 (11)		
Outflow obstruction	46 (6)	24 (7)	79 (10)		
Miscellaneous/valve	50 (7)	38 (11)	150 (20)		
Aristotle score, n (%)				.015*	.012*
1 or 2	394 (53)	204 (60)	461 (59)		
3 or 4	356 (47)	134 (40)	322 (41)		
Crossclamp time, min	41 (30-55)	35 (18-48)	39 (21-59)	<.001*	.051
CPB time, min	84 (67-109)	83 (65-107)	86 (67-120)	.438	.003*
Surgical time, min	190 (165-227)	210 (175-240)	230 (190-280)	<.001*	<.001*

Continuous data are represented by the median (interquartile range). *No-Mg*, No magnesium given; *Mg-25*, 25 mg/kg; *Mg-50*, 50 mg/kg; *BSA*, body surface area; *VSD*, ventricular septal defect; *CPB*, cardiopulmonary bypass. *Statistically significant imbalance.