

## Effect of Magnesium Sulphate on Emergence Agitation in Children undergoing Adenotonsillectomy

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### ABSTRACT

**Background:** There is some evidence that intraoperative magnesium infusions prevent postoperative delirium in children.

**Objective:** The aim of the work was to study the effects of intra-operative magnesium sulphate administration on the children's risk of post-adenotonsillectomy post-agitation.

**Patients and Methods:** At Anesthesia & Surgical Intensive Care Department, Zagazig University Hospitals, this randomized, double-blind clinical trial included 90 children with American Society of Anesthesiologists (ASA) physical status classes I or II who were scheduled to undergo adenotonsillectomy. Patients were allocated randomly into two equal groups (45 for each group): Group C: received intraoperative 0.9% normal saline initial loading dose of 0.3ml/kg over 10 min as a bolus, then 0.1ml/kg/hr. of infusion for the length of the procedure. Group MG: Patients were given 30 mg/kg of a 10% solution of magnesium sulphate intraoperatively over the course of 10 minutes as an initial loading dose, then 0.1ml/kg/hr. of infusion for the length of the procedure.

**Results:** Group MG was significantly lower than Group C regarding fentanyl needed and also total dose of fentanyl. As regard Pediatric Anesthesia Emergence Delirium (PAED) score, we found that there was No significant difference regarding pre but at post group MG was significantly lower at post also agitation was significantly associated with Group C.

**Conclusion:** It could be concluded that sevoflurane anesthesia using magnesium sulphate is used for adenotonsillectomy surgery in children. A 30-mg/kg loading dose is given intraoperatively, followed by a continuous infusion at 0.1ml/kg/hr. for the duration of surgery. This combination reduces the incidence of emergent anxiety and the need for postoperative fentanyl.

**Keywords:** Magnesium Sulphate, Emergence Agitation, Adenotonsillectomy.

### INTRODUCTION

One of the most common surgical consequences after general anesthesia is emergent agitation (EA). Not only are parents and caregivers put through a difficult time when their children engage in EA, but it can also lead to unanticipated outcomes, such as the removal of drains or catheters, self-harm, and a delay in the patient's discharge. EA can occur at any age, however it is most common in children between the ages of 3 and 9<sup>(1)</sup>.

Literature on the prevalence of emergency agitation/delirium ranges from 10% to 80%<sup>(2)</sup>. In the early stages of emergence, delirium and agitation are common, but emergency agitation/emergency delirium has been observed as late as 45 minutes after the stoppage of general anesthesia, on average 14 minutes ( $\pm 11$  minutes)<sup>(3)</sup>.

Intravenous sedatives, anesthetics, and opioid drugs are the most commonly prescribed treatments for children with emerging agitation, but their success rates are inconsistent, recovery times are lengthy, and they can have unpleasant side effects as vomiting as well as nausea<sup>(4,5)</sup>. As the fourth most abundant cation in the human body, magnesium has been shown to influence ion transport and energy metabolism<sup>(6)</sup>.

Magnesium may block NMDA receptors and calcium channels in the central nervous system, brain, and spinal cord, hence modulating the transmission of

nociceptive impulses and pain perception. Analgesic effects of magnesium in abdominal, orthopedic, otolaryngological as well as cardiac surgery have been supported by that investigation<sup>(7)</sup>.

Increased sedation, analgesia, reduced usage of neuromuscular blockade medications, and avoidance of ischemic-reperfusion injury have been linked to the use of magnesium during the perioperative phase<sup>(8)</sup>.

Intraoperative magnesium infusions in children have been shown to minimize postoperative emergence delirium. Children's emerging delirium rates were unaffected by magnesium supplementation<sup>(9)</sup>.

The aim of the current work was to study the effects of intra-operative magnesium sulphate administration on the children's risk of post-adenotonsillectomy post-agitation.

### PATIENTS AND METHODS

This randomized double blind clinical trial included a total of 90 pediatric patients with ASA physical status classes I and II, scheduled for adenotonsillectomy, attending at Anesthesia & Surgical Intensive Care Department, Zagazig University Hospitals.

#### *Ethical Consideration:*

**This study was ethically approved by Zagazig University's research ethics committee. Written**



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**informed consent of all the participants' parents was obtained and submitted them to Zagazig University (ZU-IRB#6659). We adhered to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.**

**Inclusion criteria:** Children aged 3 – 9 years of both sexes. Under general anesthesia, children are scheduled for an adenotonsillectomy. I or II ASA physical status, and BMI  $\leq$  32 kg/m<sup>2</sup>.

**Exclusion criteria:** Family history of malignant hyperthermia or history of drug hypersensitivity. Use of sedative or antiepileptic medication. Alterations in behavior; physical or mental retardation. Myasthenic syndrome. Myasthenia gravis. Arrhythmia. Neuromuscular disease. Cardiovascular, respiratory, hepatobiliary and renal illness of moderate severity and abnormal electrolyte balance.

**The patients were divided into two equal groups based on a computer produced table (45 for each group):**

**Group C (n=45):** Patients were received intraoperative 0.9% normal saline as initial loading dose of 0.3ml/kg over 10min as a bolus, followed by a continuous infusion of 0.1ml/kg/hr. for entire duration of surgery.

**Group MG (n=45):** Patients were received intraoperative magnesium sulphate as initial loading dose of 30mg/kg of 10% solution over 10 min, followed by a continuous infusion of 0.1ml/kg/hr. for entire duration of surgery.

#### **Preoperative:**

1. One of the patients' parents was there at all times.
2. Full history taking.
3. Proper clinical examination.
4. Methods for obtaining anthropometric measurements such as height, weight, and waist circumference were followed. Using the patient's weight in kilograms divided by the square of their height in meters, the BMI was computed.
5. Blood sample was collected from each patient for Complete blood count (CBC), bleeding time, and Mg level.

This scale was used to measure the level of preoperative anxiety in patients (m-YPAS) <sup>(10)</sup>.

#### **Operative:**

Dextrose 5 percent infusion was started based on fasting time and body weight after sevoflurane was administered to induce general anesthesia. Tracheal intubation was performed without the use of neuromuscular blocking medicines when a sufficient depth of anesthesia had been achieved. Surgery began after an intravenous (IV) infusion of loading fluid (magnesium chloride or saline). As soon as the surgery is completed and anesthetic has been removed, the study drug infusion will be stopped.

To keep normocapnia, pressure support ventilation was used to increase the tidal volume of all patients during surgery. Maintaining a concentration of 2.5 to 3.5 percent end-tidal sevoflurane ensured that the heart rate and mean arterial blood pressure did not fall below 20 percent of their baselines. Fentanyl 1 micro gram/kg and paracetamol 30 mg/kg were administered intraoperatively as additional analgesia following anesthetic induction. For the prevention of postoperative nausea and vomiting, Dexamethasone 0.2 mg/kg was administered intravenously following anesthetic induction.

#### **After the operation has been completed:**

A gag reflex was confirmed to have returned before the patient was extubated from his or her trachea. After surgery, blood samples are drawn from the contralateral arm at the site of the study medication infusion and tested for postoperative serum magnesium levels.

#### **Postoperative:**

A blinded study investigation was to assess emergence agitation, and Once in the PACU, recovery parameters are assessed every 15 minutes for the next 45 minutes. The Pediatric Anesthesia Emergence Delirium Scale was used to assess agitation in the midst of anesthesia <sup>(11)</sup>; Scores lower than 10 were used to identify patients who were likely to develop agitation. Using this cut-off value, researchers found that agitation during emergence was reliably differentiated between the presence and absence of it <sup>(12, 13)</sup>.

#### **Statistical analysis**

When the data was obtained, it was entered into a computer and analyzed with SPSS, version 25, to provide the results. The findings were presented in the form of tables and graphs. Confidence intervals were presented in terms of the standard deviations and the mean. When presenting the data, frequency and percentage of qualitative data were employed. The student's t test (T) was used for quantitative independent data to assess the data as needed. For qualitatively distinct data, we utilised Pearson Chi-Square Test and Chi-Square for Linear Trend. Significant results were defined as those with a p value of 0.05 or lower.

#### **RESULTS**

Age was distributed as 6.13 $\pm$ 1.12 and 5.66 $\pm$ 1.21 years and ASA or sex had no effect on the differences between groups, nor did the duration of operation, anesthesia, sevoflurane dose, or M-YPAS have any meaningful effect on the differences between groups (**Table 1**).

There was no significant difference regard pre but regard post Group MG was significantly higher and regards change assessment Group MG significantly increased but there was no significant change in Group C (**Table 2**).

Group MG was significantly lower than Group C regarding fentanyl needed and also Total dose of fentanyl (**Table 3**).

MG group was significantly lower regard 20-, 30- and 40-minutes Heart Rate (HR.) (**Table 4**).

PAED score; although no significant differences existed between the groups at the beginning of the

study, the MG group's performance dropped dramatically and that of the other groups did as well (**Table 5**).

No significant difference regard pre but at post group MG was significantly lower at post also agitation was significantly associated with Group C (**Table 6**).

**Table (1): Basic demographic and clinical characters of studied group**

			Group MG (N=45)	Group C (N=45)	t/ X <sup>2</sup>	P
<b>Age (years)</b>			6.13±1.12	5.66±1.21	1.25	0.21
<b>BMI (kg/m<sup>2</sup>)</b>			22.10±2.26	21.52±1.58	1.15	0.25
<b>Duration of surgery (minutes)</b>			28.74±5.62	30.1±5.49	1.74	0.074
<b>Duration of operation</b>			48.94±6.43	51.0±7.23	1.82	0.061
<b>Sevoflurane dose (units)</b>			1.95±0.69	2.08±0.74	0.74	0.412
<b>M-YPAS</b>			12.31±3.80	11.24±3.65	1.358	0.178
<b>Gender</b>	<b>Female</b>	N	19	17	0.18	0.66
		%	42.2%	37.8%		
	<b>Male</b>	N	26	28		
		%	57.8%	62.2%		
<b>ASA</b>	<b>I</b>	N	34	36	0.25	0.61
		%	75.6%	80.0%		
	<b>II</b>	N	11	9		
		%	24.4%	20.0%		
<b>Total</b>	N		45	45		
	%		100.0%	100.0%		

**Table (2): Mg level pre and post distribution between studied groups**

	Group MG	Group C	T	P
<b>Mg level Pre</b>	2.17±0.62	2.16±0.47	0.762	0.448
<b>Mg level post</b>	3.06±0.68	2.23±0.50	4.352	0.00**
<b>P</b>	<b>0.02*</b>	<b>0.58</b>		

**Table (3): Total fentanyl distribution between studied groups**

			Group MG	Group C	t	P
<b>Total fentanyl</b>			7.55±2.87	16.33±3.59	12.047	0.00**
<b>Fentanyl post-operative needed</b>	<b>No</b>	N	35	20	10.58	0.001**
		%	75.6%	80.0%		
	<b>Yes</b>	N	10	25		
		%	24.4%	20.0%		
<b>Total</b>	N		45	45		
	%		100.0%	100.0%		

**Table (4): HR. distribution at different times pre and post OP between groups**

	Group MG (N=45)	Group C (N=45)	t	P
<b>HR. base line</b>	95.63±7.12	94.23±9.25	0.019	0.998
<b>HR. 10 M</b>	97.57±8.52	96.68±8.99	0.029	0.990
<b>HR. 20 M</b>	100.44±10.08	121.25±10.39	3.031	0.003*
<b>HR. 30 min</b>	97.88±11.11	119.11±10.77	2.245	0.015*
<b>HR. 40 min</b>	94.54±9.54	115.25±10.87	2.151	0.035*
<b>HR. 1H post OP</b>	90.58±2.97	91.25±4.21	0.025	0.979
<b>HR. 2H post OP</b>	92.11±3.25	93.14±3.25	0.018	0.998

**Table (5): PAED score distribution between studied groups at different times**

	Group MG	Group C	t	P
PAED_0	13.08±4.20	14.44±2.65	1.828	0.071
PAED_15	7.04±2.0	8.22±2.91	2.299	0.028*
PAED_30	6.78±0.89	7.60±1.42	2.251	0.031*
PAED_45	5.52±1.12	6.78±1.19	2.154	0.045*

**Table (6): Agitation distribution between studied groups**

		Group MG	Group C	t/ X <sup>2</sup>	P	
Agitation	-VE	N	42	34		
		%	88.9%	75.6%		
	+VE	N	3	11	5.42	0.019*
		%	11.1%	24.4%		
Total	N	45	45			
	%	100.0%	100.0%			

## DISCUSSION

One of the most common surgical consequences after general anesthesia is emergent agitation (EA). Parental and caregiver distress is compounded when a child engages in destructive behavior, such as removing drains or catheters, doing harm to oneself, or delaying the time at which a patient is ready to be discharged. Depending on the definition, research backdrop (patients' age group, surgical site or type of surgery etc.), evaluation method and monitoring duration employed in each study, the reported incidence of EA ranges from 30% to 80%. EA can occur at any age, however it is most common in children between the ages of 3 and 9<sup>(1, 14)</sup>.

Adenotonsillectomy-induced emerging delirium in children may be reduced by intraoperative magnesium infusion<sup>(14)</sup>.

As Hartman solution and regular saline don't include magnesium, it is typical to experience hypomagnesemia during the course of surgery<sup>(7)</sup>. It can thus reduce the amount of sedative, analgesic, or neuromuscular blocking medicine that is required during anesthesia, as well as improve postoperative consequences<sup>(15)</sup>.

Regarding basic demographic and clinical characters of studied group, the current study revealed that age was distributed as 6.13±1.12 and 5.66±1.21 for group MG and group C respectively, and ASA or sex had no effect on the differences between groups, nor did the duration of operation, anesthesia, sevoflurane dose, or M-YPAS have any meaningful effect on the differences between groups.

The present study was in line with the randomized, controlled, double-blind study by **Abdulatif et al.**<sup>(14)</sup> who investigated if magnesium sulphate infusion affected the emergence and degree of agitation in children having anesthesia with sevoflurane during adenotonsillectomy. There were 70 participants in the trial, with 20 boys (61 percent) in the magnesium sulphate group (n=33) and 13 boys (41 percent) in the saline group (n=33), with an average age of 5.8 years (0.9 years). The magnesium group was expanded to include more boys; baseline factors such as operation

length and anesthesia duration were similar in both groups, as were tracheal extubation times and the time it took for patients to interact.

For pre-post comparison, we found no significant differences, however the change evaluation for Group MG was much greater after the study ended. Group MG showed a large rise, but Group C showed no such shift.

**Abdulatif et al.**<sup>(14)</sup> found that there was no difference in pre-operative serum magnesium levels between the two groups. Serum magnesium levels in the magnesium sulphate group, on the other hand, rose 0.9 to 1.6 mmol. l-1 after surgery (p < 0.001).

We found also that Group MG was significantly lower than Group C regard fentanyl needed and also Total dose of fentanyl.

Our results were supported by **Abdulatif et al.**<sup>(14)</sup> as they revealed that Fentanyl rescue doses for emerging agitation or postoperative pain in the PACU were administered to 23 (72 percent) of the children in the control group and 15 (45 percent) of the children in the magnesium group (p = 0.03).

Also, in agreement with our results **Elsharnouby et al.**<sup>(16)</sup> revealed that in the PACU, time to first analgesic requirement (P = 0.0001) was significantly longer, with significantly reduced doses of rescue analgesic (fentanyl) requirement (P = 0.02) and rescue antiemetic in group M than group C.

Regarding HR. distribution at different times pre and post OP between groups, we found that MG group was significantly lower regard 20-, 30- and 40-minutes HR. In line with our results **Abdulatif et al.**<sup>(14)</sup> study found that Heart rates were lower in children who received magnesium supplementation than those in the control group. The heart rate of the control group was significantly greater than that of the experimental group at 10 minutes following tracheal intubation. (p < 0.001).

While the study by **Marzban et al.**<sup>(17)</sup> indicated that the trend of increases in children's mean heart rates did not demonstrate a statistically significant difference between the two groups and followed the same pattern (P = 0.097) utilizing general linear model

and repeated measurement. When the endotracheal tube was removed, the heart rate increased less in magnesium sulphate, which was statistically significant ( $P = 0.0001$ ).

As regard PAED score distribution between studied groups at different times, we found that There was no significant difference among groups at baseline but from 15 until the end MG group was significantly lower and both groups significantly decreased.

In agreement with our results **Elsharnouby et al.** <sup>(16)</sup> reported that The median PAED score was significantly reduced in group M than group C, respectively, at T0 (on admission) ( $P < 0.0001$ ), T1 (5 min) ( $P < 0.0001$ ), T2 (15 min) ( $P < 0.0001$ ), T3 (30 min) ( $P = 0.04$ ), T4 (45 min) ( $P = 0.04$ ), and T5 (60 min) ( $P = 0.03$ ), but not significantly differently at T6 (75 min) ( $P = 0.1$ ), (45 min) ( $P = 0.001$ ), T5 (60 min) ( $P = 0.04$ ) but not significantly different at T6 (75 min) ( $P = 0.2$ ), T7 (90 min) ( $P = 0.5$ ), T8 (105 min) ( $P = 0.3$ ), and T9 (120 min) ( $P = 0.7$ ).

As regard agitation distribution between studied groups, we found that there was No significant difference regard pre but at post group MG was significantly lower at post also agitation was significantly associated with Group C.

With our findings, **Apan et al.** <sup>(18)</sup> showed that in the magnesium treatment group, Time-dependent Agitation Scores remained unaltered in comparison with saline controls and significant only at the 60th minute in the recovery (Group C:  $1.3 \pm 0.7$ , Group M:  $1.0 \pm 0.3$ ,  $p = 0.005$ ).

Also, **Elsharnouby et al.** <sup>(16)</sup> reported that After discharge from the recovery room, no patient had any episode of agitation defined by PAED greater than 10 or bleeding; only thr.ee (13%) patients in group C and one (4.2%) patient in the group M had nausea, retching, and vomiting ( $P = 0.3$ ).

While **Abdulatif et al.** <sup>(14)</sup> stated that the magnesium group had significantly higher Emergence delirium scores than the control group did at all of the PACU's assessment points. There were 23 (72%) and 12 (36%), respectively, children who showed emerging agitation ( $p = 0.004$ ).

## CONCLUSION

It could be concluded that sevoflurane anesthesia using magnesium sulphate is used for adenotonsillectomy surgery in children. A 30-mg/kg loading dose is given intraoperatively, followed by a continuous infusion at 0.1ml/kg/hr. for the duration of surgery. This combination reduces the incidence of emergent anxiety and the need for postoperative fentanyl.

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