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# Dexmedetomidine or magnesium to control agitations in patients undergoing tonsillectomy: randomised controlled study

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## Abstract

**Background** Preoperative time is a very stressful time for most patients undergoing surgery, particularly young patients. The primary goal of an anaesthesiologist is to reduce patients' anxiety before surgery. To lessen this stress response, many anaesthetic pre-medications are used. Magnesium chloride and dexmedetomidine are two of these pre-medications that work well as sedatives. This study examined dexmedetomidine and magnesium sulphate as a pre-anaesthetic medication for kids. Dexmedetomidine and magnesium will be compared for their efficacy and safety in treating children who experience emerging anxiety after having their tonsils removed in this trial. Forty-five children between the ages of 4 and 12 years who were having elective adenotonsillectomy surgery in this comparative prospective, double-blind, randomised controlled clinical research. Children were split up into three groups: group A was given dexmedetomidine, group B was given magnesium infusion, and group C was given normal saline 0.9% infusion.

**Results** Ramsay and Cravero scores revealed that children who got dexmedetomidine infusion were less agitated than those who received magnesium sulphate or normal saline infusion (*p* value 0.01).

**Conclusions** When comparing dexmedetomidine to magnesium sulphate, there are a few advantages to its use. It can be administered as an anaesthetic medication to minors undergoing adenotonsillectomy under general anaesthesia in order to lessen postoperative agitation.

**Keywords** Dexmedetomidine, Magnesium sulphate, Paediatric, Adenotonsillectomy

## Background

Adenotonsillectomy is one of the operations that otorhinolaryngologists perform on kids the most frequently. The main reason for postoperative morbidity after tonsillectomy is emergent agitation (EA), which can postpone discharge and make it difficult for the patient to resume normal activity. Additionally, this condition is followed by inadequate oral intake, severe pain, vomiting, and nausea (Rosenfeld and Green 1990).

Children coming up from general anaesthesia frequently experience emergent agitation (EA) following operation. Agitation is a common problem in young infants, and it usually starts right after they come out of general anaesthesia (GA). Studies show that children can become agitated while being treated in the postoperative care unit (PACU) at any moment. There are various aetiologies for postoperative emerging agitation, like pain, tension, physiologic impairment, and negative anaesthetic effects (Mohkamkar et al. 2014).

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Dexmedetomidine is a potent, 2-adrenergic agonist that has no apparent respiratory depression and dose-dependent sedative, analgesic, and anaesthetic-sparing effects. The Food and Drug Administration (FDA) has recently authorised the continuous infusion of dexmedetomidine for up to 24 h by intravenous (IV) administration for the sedation of people using mechanical ventilation in an intensive care unit (ICU) environment. In a dose-dependent manner, it lowers cardiac output, blood pressure, and heart rate (Shukry et al. 2005).

As an N-methyl-D-aspartate receptor (NMDA) antagonist with dubious therapeutic efficacy, magnesium sulphate is being used more frequently in adults as an anaesthetic and analgesic substitute. In the literature on paediatric anaesthesia, there are not many papers that detail the same use of magnesium sulphate (Odochian 2011).

## Methods

### Ethics statement

Between January 2021 and December 2021, this randomised clinical research was carried out at Ain Shams University Hospitals. The identification code in the clinical trials.gov data base is NCT05164627. Our work received approval from the Ain Shams University's research ethical committee under grant number FWA A00017585. Before enrolling patients, parents' signed informed permission was collected.

### Randomisation

Randomisation was conducted utilising opaque, sealed envelopes containing computer-generated random number tables that were developed by an anaesthesiologist not involved in the study. A 1:1:1 ratio was used for the randomisation. The group assignments were placed in sealed, opaque, sequentially numbered envelopes by a junior anaesthesiologist who was not involved in the trial. Throughout the duration of the study, all attending anaesthesiologists, patients, and data collectors were kept in the dark regarding group memberships. On the day of the procedure, the junior anaesthesiologist opened each package immediately before general anaesthesia was induced and prepared the infusion solutions of dexmedetomidine, magnesium sulphate, and normal saline and then gave them to the anaesthesiologist who was going to gather the perioperative information. The anaesthesiologist was informed about the results of our investigation at the conclusion.

### Study protocol

A double-blind, randomised clinical trial (pilot study) was done. Forty-five patients with ASA I to II and ages 4 to 12 were scheduled for elective adenotonsillectomy. Patients' liver and kidney function tests were also normal. Patients with known adverse effects to dexmedetomidine, mental retardation, developmental delay, and neurological or psychiatric conditions that may cause agitation were not included.

#### *Inclusion criteria*

- ASA status I or II
- Age range: 4 to 12 years
- The procedure expected to be completed within 1 h

#### *Exclusion criteria*

- Patients with challenging airway management
- No consent obtained
- Dexmedetomidine side effects
- Mental retardation, developmental delay, or psychiatric or neurological conditions (such as cerebral palsy and seizures) that may be related to agitation
- Cough or airway secretions at time of surgery
- Active infection disease
- INR > 1.5
- BMI > 30 $kg/m^2$
- Surgical complication

In the ward, intravenous access was obtained using EMLA cream, in compliance with the American Academy of Pediatrics' recommended standards for procedural sedation and hospital policy. Children were required to fast for 6 h prior to the operation, but they were allowed clear liquids up until 2 h before being admitted to the operating room. The child was given details on the GA, OR, and surgery. Pictures of the staff, the OR, a facemask, and a blood pressure cuff were all included in this material. In order to foster bonding, the infant was transferred from the ward to the pre-anaesthesia care unit with his or her parents and anaesthesia doctor. Using a four-point measure, cooperation during induction was scored as satisfactory between 1 and 2 and unsatisfactory between 3 and 4. If the infant became agitated (score 3 or score 4), an emergency dose of 0.1 mg/kg midazolam was administered, and the child was removed from the study. There were monitors for non-invasive heart rate, electrocardiogram (ECG), pulse oximetry ($SpO_2$), and blood pressure. In order to enable tracheal intubation, the induction of anaesthesia was carried out using 8% sevoflurane in oxygen gas along with atracurium 0.5 mg/kg and fentanyl 0.5 mcg/kg.

Lactated Ringer's solution was administered as part of the treatment of intravenous fluids. Replacement fluid was calculated based on fasting durations, and maintenance fluid was determined based on patients' weights.

The patients were divided into three groups:

- *Group A (dexmedetomidine group)*: patients received dexmedetomidine infusion (0.2 mcg/kg/h) from the start of the surgery till the end of it
- *Group B (magnesium group)*: patients received magnesium infusion (10 mg/kg/h) from the start of the surgery till the end of it
- *Group C (control group)*: patients received normal saline 0.9% infusion

Sevoflurane 2% in oxygen gas was used to maintain anaesthesia. To keep normocapnia, controlled artificial ventilation was used. If the patient experiences discomfort, rescue doses of fentanyl (0.5 mcg/kg) were administered. Tachycardia (> 20% of baseline heart rate measurement) and hypertension (> 20% of baseline mean arterial blood pressure reading) are two conditions that indicate the onset of intraoperative pain.

Patients will be observed for any complication either related to the procedure, e.g., bleeding or related to drugs injected, e.g., hypotension, bradycardia, hypoxemia, nausea, vomiting, or any other adverse effects and were managed. The time range for procedures was 30–45 min from the start of surgery till extubation occurred.

The total anaesthesia time, the total surgery time, the time from anaesthesia off to open the eyes, the time from anaesthesia off to extubation, and the time from anaesthesia off to PACU discharge did not significantly differ between the three groups ($p$-value > 0.05).

In case of hypotension (drop of blood pressure > 20% of baseline reading), 3 mg of ephedrine increments was given intravenously by titration according to the blood pressure.

In case of bradycardia (drop of heart rate > 20% of baseline reading) when it is associated with hypotension or any signs of impaired perfusion, 0.01 mg/kg of atropine was given and can be repeated every 3–5 min.

Medication for agitation due to pain in PACU was IV paracetamol (10 mg/kg) as a part of multimodal analgesia.

Intravenous fentanyl 1 μg/kg was used as a rescue treatment for agitation.

### Primary outcome

The Cravero scale, Ramsay Sedation Scores (RSS), emerging agitation, heart rate (HR), and mean arterial blood pressure (MAP) were monitored after the patient arrived at the PACU every 5 min for the first 30 min and then every 10 min for the final 30 min of the recovery room stay. Then, the patients were brought to the ward. The same anaesthesiologist, who was unaware of the group assignment, conducted all postoperative observations and scoring.

The study had 45 participants, with 15 patients in each group: dexmedetomidine group (group A), MgSO4 group (group B), and control group (group C).

### Statistical analyses

#### *Sample size*

Since there are no studies that compare the effectiveness and safety of dexmedetomidine and magnesium sulphate for emergence agitation following adenotonsillectomy in children, no sample size calculations will be made, so a total sample size of 45 patients will be enrolled to investigate the variations in agitation incidence. The patients will be recruited into 3 distinct groups, 15 patients each group based on expert recommendation with field of anaesthesiology.

#### *Statistical method*

The data were examined using SPSS version 22.0. The mean, standard deviation (SD), or median and interquartile range (IQR) were used to report quantitative data. The qualitative data were expressed using frequency and percentage.

## Results

In terms of age, sex, BMI, and ASA, as well as the length of surgery, groups were roughly comparable and did not differ statistically significantly from one another ($p$-value > 0.05) (Table 1).

In terms of mean arterial blood pressure (MABP), heart rate (HR), and cooperation score, the three groups were comparable preoperatively and did not differ statistically significantly from one another ($p$-value > 0.05) (Table 2).

**Table 1** Comparison of demographic information between groups

| Demographic data | Group A ($n=15$) | Group B ($n=15$) | Group C ($n=15$) | $F/\chi^2$ | $p$-value |
|---|---|---|---|---|---|
| **Age (years)** | 6.6 ± 2.7 | 7.6 ± 2.4 | 6.7 ± 2 | $0.8^{f}$ | 0.45 |
| **BMI (kg/m$^2$)** | 23.7 ± 2.7 | 23.1 ± 2.7 | 24.8 ± 2.6 | $1.5^{f}$ | 0.23 |
| **ASA** | | | | | |
| **I** | 7 (46.7%) | 7 (46.7%) | 7 (46.7%) | $0^{X2}$ | 1 |
| **II** | 8 (53.3%) | 8 (53.3%) | 8 (53.3%) | | |
| **Sex** | | | | | |
| **Male** | 8 (53.3%) | 8 (53.3%) | 7 (46.7%) | $0.18^{X2}$ | 0.9 |
| **Female** | 7 (46.7%) | 7 (46.7%) | 8 (53.3%) | | |
| **Duration of surgery** | 52.5 ± 3.9 | 54.8 ± 4.1 | 51.9 ± 4.4 | $1.99^{f}$ | 0.15 |

Data expressed as mean ± SD, proportion. $F$ ANOVA test, $\chi^2$ chi-square

**Table 2** Comparison of the groups' preoperative vital signs

| Preoperative | Group A ($n=15$) | Group B ($n=15$) | Group C ($n=15$) | $F/\chi^2$ | $p$-value |
|---|---|---|---|---|---|
| **MABP** | 65.1 ± 3.97 | 68.1 ± 5.8 | 64.6 ± 3.4 | 2.7 | 0.08 |
| **HR** | 122 ± 16.7 | 125.8 ± 13.2 | 121 ± 14.1 | 0.44 | 0.65 |
| **Cooperation score** | | | | | |
| **1** | 7 (46.7%) | 7 (46.7%) | 7 (46.7%) | $0^{\chi 2}$ | 1 |
| **2** | 8 (53.3%) | 8 (53.3%) | 8 (53.3%) | | |

Data expressed as mean ± SD, proportion. *F* ANOVA test, $\chi^2$ chi-square

The three groups' mean arterial blood pressure (MABP) and heart rates (HR) were comparable following surgery, with group A showing the biggest decline in both (MABP and HR); however, it was still within the normal range before we classified it as a problem (Figs. 1 and 2).

The Ramsay Sedation Scores for the three groups were equivalent, and there was statistically significant variation across groups ($p$ value < 0.01) (Table 3).

On the Cravero scale, the three groups were comparable, and they varied statistically significantly from one

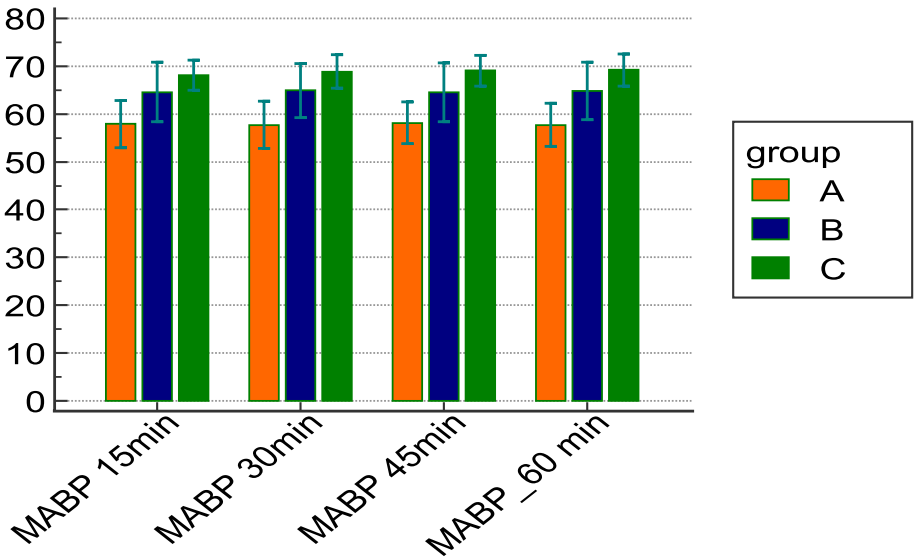


**Fig. 1** Comparison of three groups' MABP results

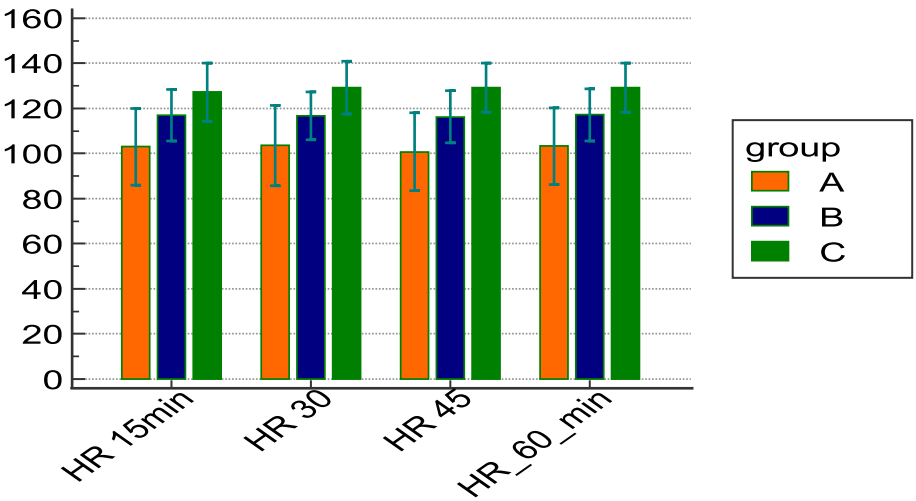


**Fig. 2** Comparison of HR data from three groups

**Table 3** Ramsay Sedation Score (SSS) comparison between groups

| | Group A ($n=15$) | Group B ($n=15$) | Group C ($n=15$) | *F* | *p*-value |
|---|---|---|---|---|---|
| RSS | 3 (2–3) | 2 (1–2) [a] | 1 (1–1)[bc] | 24.4 | **< 0.001** |

Data expressed as median (IQR), *f* Kruskal–Wallis test

[a] Conover post hoc test level of significance between groups A and B

[b] Conover post hoc test level of significance between groups A and C

[c] Conover post hoc test level of significance between groups B and C

another ($p$ value < 0.01), which was in favour of group A in controlling agitations (Fig. 3).

## Discussion

Around 26% of children who undergo otorhinolaryngology surgery experience postoperative agitation. This condition is one of the risk factors for postoperative agitation in children. The most common symptoms are thrashing and kicking (86% and 64%, respectively), while only a very small percentage (14%) display restless and disorganised behaviour (Voepel-Lewis et al. 2003). According to Eckenhoff et al. (Eckenhoff et al. 1961), suffocation may be a factor in the high incidence of postoperative agitation in otorhinolaryngology procedures.

The results of our present study were noted. Meng et al. concluded that following a tonsillectomy, dexmedetomidine seems to be both safe and beneficial at lowering the incidence of early emergence agitation in children. For children who have undergone tonsillectomy, a loading dosage of 1.0 g $kg^{-1}$ followed by a maintenance infusion of 0.4 g $kg^{-1}$ $h^{-1}$ is preferable (Meng et al. 2012). The same outcomes were shown by Yang et al. Dexmedetomidine can minimise emerging agitation, treat postoperative pain, reduce the need for rescue analgesics, and reduce postoperative nausea and vomiting episodes (Yang et al. 2020).

In contrast to Salman et al., who claimed that dexmedetomidine and magnesium sulphate infusion are both equally efficient in lowering the incidence of EA in obese people after nose surgery, extubation and PACU time took dexmedetomidine patients a little longer than patients who took magnesium sulphate or were in the control group (Salman and Ali Mohamed 2022). Also, according to Zarif et al., during laparoscopic colectomy under pneumoperitoneum in the 30° Trendelenburg position, intraoperative administration of either dexmedetomidine or magnesium sulphate could improve the pressor responses to anaesthesia and surgical manoeuvres (Zarif et al. 2016a).

No matter the clinical circumstance, sedative medications like dexmedetomidine can damage cardiorespiratory function. The latter may be particularly concerning in individuals with underlying respiratory insufficiency or in the immediate aftermath of surgery, given the potential respiratory depressing effects of residual anaesthesia medicines. As of now, there does not appear to be much of a risk that dexmedetomidine would cause respiratory depression.

In healthy participants, Hall et al. found that dexmedetomidine infusions (0.6 μg/kg followed by either 0.2 or 0.6 μg/kg/h) resulted in drowsiness, memory impairment, and impaired psychomotor performance (age range, 23–31 years). Little changes in hemodynamic indicators or respiratory function were observed in their investigation (end-tidal $CO_2$, oxygen saturation, respiratory rate) (Hall et al. 2000).

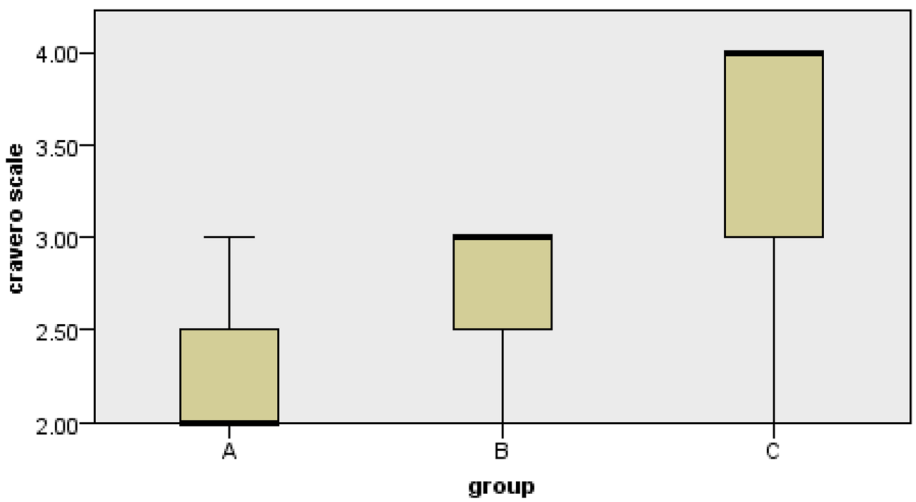


**Fig. 3** Box and whisker comparison chart comparing various groups according to the Cravero scale

Two patients in the Peden et al. study who had previously received dexmedetomidine briefly went into sinus arrest following the administration of propofol and a laryngoscopy, raising the possibility that slow heart rate increases could be caused by medications or procedures that stimulate the vagus nerve (propofol, fentanyl). Consequently, despite the agent's effectiveness, continuous cardiorespiratory monitoring is advised while it is being administered (Cravero et al. 2003).

Although postoperative agitation after general anaesthesia may be brought on by pain, this is not the only reason of agitation (Sandner-Kıeslıng et al. 2002). A little amount of fentanyl added to inhaled sevoflurane anaesthesia reduced the incidence of emergence agitation without having any impact on pain control, according to the findings of Cravero et al. EA was observed in 56% of paediatric patients following sevoflurane anaesthesia without surgery (Sandner-Kıeslıng et al. 2002). Agitation was observed in 31% of paediatric MRI patients who had undergone sevoflurane anaesthesia, according to Sandner-Kiesling et al. (Hussein et al. 2019).

According to Hussein et al.'s work (Zarif et al. 2016b), we also investigated whether intraoperative magnesium sulphate can successfully prevent EA in patients undergoing nose surgery while under sevoflurane anaesthesia. No adult participants with ASA physical status I or II between the ages of 20 and 40 who were nonsmokers and had a BMI of less than or equal to 30 were enrolled in the study. Except for the ASA classification, which showed a rise in cases of ASA 2 in the magnesium sulphate group compared to the control group regarding the demographic data of the patients under study, there was no statistically significant difference between the magnesium sulphate and control groups ($p$-value = 0.041).

Rashwan et al. (Peden et al. 2001) reported that there was no statistically significant difference in the mean systolic and diastolic arterial blood pressure between the two analysed groups at baseline, which is consistent with our findings. However, the intraoperative systolic arterial blood pressure in the D group was statistically significantly lower than in the P group at 60, 105, 120, and 135 min. The intraoperative diastolic arterial blood pressure was statistically significantly lower in the D group than the P group, with the exception of at 75 and 135 min.

Limitation to our study were only 15 participants each group made up the small sample size, so we advise increasing the number of participants in future research to improve the validity of the findings. The single-centre study design might have compromised the study's objectivity. Also recording but not analysing the intraoperative data as our main target is the agitation caused by many factors and how to be treated.

## Conclusions

Dexmedetomidine offers some advantages compared with magnesium sulphate. In order to lessen postoperative agitation in children having an adenotonsillectomy under general anaesthesia, it can be used as an anaesthetic medicine in a safe and effective manner.

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Not applicable.

**Authors' contributions**
BGS designed the study, revised the literature, performed the analysis, followed up the patients, measured and calculated the blood loss, and wrote the manuscript. BBG designed the study, performed the analysis, and wrote and critically revised the manuscript. AE revised the literature, performed the analysis, and critically reviewed the manuscript. MA revised the literature, followed up the patients, measured and calculated the blood loss, collected the data, performed the analysis, and critically reviewed the manuscript. KK followed up the patients, measured and calculated the blood loss, collected the data, and performed the analysis. All authors approved the final version of the manuscript.

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None.

**Availability of data and materials**
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Ethics approval and consent to participate**
After approval of the ethical committee in Faculty of Medicine, Ain Shams University number, this randomised controlled study was conducted in over 45 children from January 2021 to December 2021. The identification code in the ClinicalTrials.gov data base is NCT05164627. Written informed consent was obtained from patients' legal guardian(s) after explaining the procedure and its potential complications.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare that they have no competing interests.

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## Publisher's Note