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Research Article

Efficacy of ketamine in prevention of agitation in children undergoing magnetic resonance imaging under face mask sevoflurane: A randomized trial

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KEYWORDS

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Abstract *Background:* Emergence agitation (EA) is a common distressing problem in children after sevoflurane general anesthesia. The aim of the present study was to test the efficacy of ketamine in prevention of EA after sevoflurane general anesthesia in children undergoing magnetic resonance imaging (MRI) scan. Also, we evaluated the safety and efficacy of the face mask for administration of sevoflurane anesthesia in children.

Methods: In this randomized study, 120 children aged 2–7 years (ASA I or II) of either sex scheduled for elective MRI scan under sevoflurane anesthesia were enrolled in the study protocol. Patients were randomly allocated to one of 3 groups: saline group receiving normal saline (n = 40), ketamine 0.25 group receiving 0.25 mg/kg of ketamine intravenously 10 min prior the end of the procedure (n = 40), and ketamine 1.0 group receiving 1.0 mg/kg of ketamine intravenously before sevoflurane induction, (n = 40). Anesthesia was provided with sevoflurane in 100% oxygen. EA score, pausing of the scan, scan time, discharge time and any reported adverse events were recorded.

Results: No significant differences as regards age, weight, sex, or ASA score were found among the studied groups. Children in ketamine 1.0 group reported significant lower EA score in comparison with ketamine 0.25 and saline groups (P < 0.05). Ketamine 0.25 group reported significant lower

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EA score in comparison with saline group ($P < 0.05$). Children in ketamine 1.0 group reported significant lower incidence of pausing in comparison with ketamine 0.25 and saline groups ($P < 0.05$). No significant differences as regards nausea, vomiting, desaturation, scan and discharge times among the studied groups ($P > 0.05$) were found.

Conclusion: Ketamine premedication was effective in reducing EA without delay in recovery and significantly reduced the incidence of pausing of MRI scan.

1. Introduction

The provision of anesthesia and sedation for children undergoing procedures outside the operating room continues to evolve [1]. MRI scan requires prolonged immobilization that can only be provided by general anesthesia in pediatric patients [2]. EA is a common problem in children after sevoflurane general anesthesia [3]. The rapid emergence and recovery from sevoflurane general anesthesia are associated with high incidence of EA in children. However, the etiology of EA has not yet been identified clearly. The predisposing factors are preschool age, preoperative anxiety, lack of premedication and awakening in a strange environment [4]. The incidence of EA had been reported between 10% and 80% in different studies [5].

Sevoflurane is an inhalation anesthetic agent used frequently to induce and maintain outpatient or pediatric anesthesia due to its excellence in hemodynamic stability, less irritation of the mucous membranes and low blood solubility, which causes rapid induction and emergence from anesthesia [6]. The use of a face mask that is firmly secured to the face of the child, brings the concentration of sevoflurane needed to maintain general anesthesia at a lower levels, and the spread of sevoflurane throughout the environment is minimal [7]. Ketamine is an effective sedative analgesic and it does not cause respiratory depression at a small dose and does not affect heart rate and blood pressure significantly. It has strong preemptive analgesic effects, suppresses the occurrence of EA in children and is useful in sedating excited children before surgery [8].

In the present study, the aim was to test the efficacy of ketamine in prevention of EA after sevoflurane general anesthesia in children undergoing MRI scan. Ketamine was tested when administered as a premedicant before induction of anesthesia and when administered 10 min prior the end of the scan. Also, we evaluated the safety and efficacy of the face mask as a non-invasive method for administration of sevoflurane general anesthesia in children. Furthermore, pausing of the scan, respiratory problems, scan time, discharge time and reported other complications were evaluated.

2. Materials and methods

This randomized double blind study was performed in Urology and Nephrology Center, Mansoura University. The study protocol was approved by local ethics committee. Between May 2012 and September 2013, 120 children aged 2–7 years (ASA I or II) of either sex scheduled for elective MRI scan under sevoflurane general anesthesia through a face mask were enrolled in the study protocol. Written informed consent was obtained from at least one of the parents after explanation of the procedure and purpose of the study. Past and current medical records were checked for associated medical disorders and concomitant medication intake.

Exclusion criteria included patients with cardiopulmonary diseases, head and neck congenital anomalies, airway problems and patients with cognitive or developmental disorders were excluded from the study. Patients under treatment with sedatives or anticonvulsants, emergency indications, and parental refusal were also excluded from the study.

The patients were randomly allocated (by the use of sealed envelopes and computer-generated random tables) to one of 3 groups: saline group (control group) administered normal saline solution ($n = 40$), ketamine 0.25 group administered 0.25 mg/kg of ketamine intravenously 10 min prior the end of the procedure ($n = 40$) and ketamine 1.0 group administered 1.0 mg/kg of ketamine intravenously before sevoflurane induction ($n = 40$). All patients were premedicated with atropine 0.01 mg/kg injected intramuscularly 30 min before induction of anesthesia.

On arrival at the MRI scan room, an intravenous line was inserted and 10 ml/kg of normal saline solution was infused. Patients were monitored with the standard monitors including arterial blood pressure, electrocardiogram (ECG), pulse oximeter (SPO_2) and $ETCO_2$. $ETCO_2$ was monitored by the insertion of the capnography tube tip line inside the fitted face mask.

Patients in saline and ketamine 0.25 groups were administered normal saline while patients in ketamine 1.0 group were administered ketamine 1.0 mg/kg intravenously. All medications were administered by personnel who were not involved in this study.

Induction of anesthesia to all patients was provided with 8% sevoflurane in 100% oxygen. Anesthesia was maintained with sevoflurane 1–2% concentration in oxygen 5 L/min through firmly secured fitted pediatric face mask, while patients breathe spontaneously. The head and neck of the children were fixed in extension position and suitable oral airway was inserted to maintain airway patency. If the patient moved, the concentration of sevoflurane was incrementally increased by 0.5–1.0%. If apnea occurred, the concentration was decreased by the same percent.

Ten minutes prior the end of the procedure, patients in saline and ketamine 1.0 groups were administered normal saline and patients in ketamine 0.25 group were administered ketamine 0.25 mg/kg intravenously.

At the end of the procedure and when the radiologist declared that the MRI procedure would end in 2 min, the administration of sevoflurane was discontinued. After the completion of the procedure, the face masks were removed, and the children were allowed spontaneous recovery and transferred to the postanesthesia care unit (PACU). Arterial blood pressure and SPO_2 were monitored in the PACU. Parents were called to the bedside at that time.

The following variables were recorded for all patients:

- occurrence of respiratory adverse effects: apnea, laryngospasm, desaturation (SPO_2 below 92%),
- frequency of MRI scan pausing due to child movement or monitoring failure,
- scan time: time taken for MRI study,
- discharge time: time from shifting to PACU until discharge,
- occurrence of postoperative nausea and vomiting and
- EA according to pediatric anesthesia emergence delirium (PEAD) scale.

The quality of emergence was assessed using PAED by physician who was blinded to the group of the patients. The PAED scale was designed to measure EA in children [9]. In this study the PAED scale was used to measure EA based on five emergence behaviors. Each scale item was scored from 0 to 4 and the scores were summed to obtain a total score ranging from 0 to 20. We defined a low PAED score (0–3) as a calm child making eye contact, and a moderate PAED score (4–9) as a somewhat restless child aware of their surroundings and making purposeful actions. A high PAED score (10–20) corresponded to an inconsolable child who was crying, kicking, or screaming (Table 1).

3. Statistical analysis

The sample size of 30 patients was calculated in each group depending on the results from previous studies [10] assuming a reduction in the incidence of sevoflurane agitation from 60% to 30% with the α-error level was fixed at 0.05 and the power was set at 90%. Some exclusion was expected, so the number of the sample size was increased to 40 patients per group. Data were analyzed using SPSS (Statistical Package for Social Sciences) version 15. Qualitative data were presented as number and percent. Comparison between groups was done by Chi-Square test. Quantitative data were presented as mean ± SD. One Way Anova was used to compare between more than two groups. Post Hoc test (Fisher's Least Significant Difference (LSD) test) was used for two groups' comparison. *P*-value <0.05 was considered statistically significant.

4. Results

One hundred twenty preschool children were enrolled in this study. No significant differences as regards age, weight, sex, and ASA score were found among the studied groups (Table 2). Children in ketamine 1.0 group recorded significant lower EA score in comparison with ketamine 0.25 and saline groups ($P < 0.05$). Ketamine 0.25 group recorded significant lower EA score in comparison with saline group ($P < 0.05$) (Table 3). Children in ketamine 1.0 group recorded significant lower incidence of pausing and interruption of MRI procedure in comparison with ketamine 0.25 and saline groups ($P < 0.05$) where only one child moves during the scanning procedure and necessitates intervention by deepening the anesthesia while 6 children in ketamine 0.25 group and 7 children in saline group recorded pausing and interruption of MRI scanning (Table 3).

Children in the studied groups recorded no significant differences as regards scanning time and discharge time from PACU ($P > 0.05$) (Table 4).

Children in the studied groups recorded no significant differences as regards nausea, vomiting or desaturation ($P > 0.05$) (Table 4). Where only one child in saline group developed nausea but none of the children in ketamine 1.0 and ketamine 0.25 groups recorded nausea. Also two children in saline group suffered vomiting in comparison with one child in each of ketamine 1.0 and ketamine 0.25 groups. Three children in saline group developed desaturation in the postoperative period in comparison with two children in ketamine 0.25 group and one child in ketamine 1.0 group (Table 5). No children in the studied groups had other complications such as arrhythmia, hypotension or apnea. None of the children in the studied groups needed invasive airway and mechanical ventilation.

Table 1 Pediatric anesthesia emergence delirium (PAED) scale.

	Score
The child makes eye contact with the caregiver	4 = not at all
The child's actions are purposeful	3 = just a little
The child is aware of his/her surroundings	2 = quite a bit
	1 = very much
	0 = extremely
The child is restless	0 = not at all
The child is inconsolable	1 = just a little
	2 = quite a bit
	3 = very much
	4 = extremely

5. Discussion

In this study the preventive effect of ketamine 1.0 mg/kg administered as a premedicant was compared with ketamine 0.25 mg/kg administered 10 min prior the end of MRI scanning procedure in children undergoing MRI scan under sevoflurane general anesthesia through firmly secured fitted pediatric face mask with spontaneous breathing. This study shows that the incidence of EA measured by PAED scale was significantly lower in ketamine 1.0 group in comparison with both ketamine 0.25 and saline groups ($P < 0.05$) and the incidence of EA was significantly lower in ketamine 0.25 group in comparison with the saline group ($P < 0.05$) without delay in the recovery or discharge from PACU.

EA is characterized by self-limiting aggressive agitation developed in the early phase of awakening from general anesthesia. EA carries the risk of children injuring themselves and their healthcare providers causing delay of discharge from the PACU [4,8].

Sevoflurane is an inhalational anesthetic that is used widely in pediatric and outpatient anesthesia due to its hemodynamic stability and low blood solubility, which allows rapid induction and emergence from general anesthesia, with excellent control of the depth of anesthesia [11].

In this study the environmental sevoflurane pollution in the scanning room was minimized by firmly secured fitted face mask to the face of the child, thus keeping the needed sevoflurane concentration to maintain general anesthesia at the lowest levels.

However, the use of sevoflurane alone is associated with a higher incidence of EA in children due to its low blood solubility and consequently rapid removal of residual sevoflurane anesthetic [12].

Table 2 Patients demographics in the studied groups, values are presented as mean ± SD or number (*n*) and percentage (%).

	Saline group (*n* = 40 patients)	Ketamine 0.25 group (*n* = 40 patients)	Ketamine 1.0 group (*n* = 40 patients)	*P* value
Age	4.58 ± 1.36	4.33 ± 1.42	4.23 ± 1.48	0.526
Weight	17.08 ± 2.71	16.53 ± 2.91	16.53 ± 3.03	0.617
Sex				
Male	24 (60%)	22 (55%)	22 (55%)	0.873
Female	16 (40%)	18 (45%)	18 (45%)	
ASA				
I	18 (45%)	12 (30%)	15(38%)	0.383
II	22 (55%)	28 (70%)	25 (62%)	

Table 3 Emergence agitation score and pausing of MRI scanning in the studied groups, values are presented as mean ± SD or number (*n*) and percentage (%).

	Saline group (*n* = 40 patients)	Ketamine 0.25 group (*n* = 40 patients)	Ketamine 1.0 group (*n* = 40 patients)	*P* value
EA score	12.00 ± 1.59*	4.63 ± 0.95†	2.50 ± 0.99	<0.001*
Pausing	7 (17.5%)	6 (15%)	1 (2.5%)*	0.024*

* Significant ($P < 0.05$) in comparison with the other groups.
† Significant ($P < 0.05$) in comparison with the other groups.

Table 4 Scanning and discharge times in the studied groups, values are presented as mean ± SD.

	Saline group (*n* = 40 patients)	Ketamine 0.25 group (*n* = 40 patients)	Ketamine 1.0 group (*n* = 40 patients)	*P*-value
Scanning time (minutes)	35.93 ± 2.40	35.28 ± 2.80	34.31 ± 3.58	0.742
Discharge time (minutes)	22.28 ± 1.52	21.88 ± 1.68	21.35 ± 1.82	0.159

n = number of patients.

Table 5 Postoperative side effects in the studied groups, values are presented as number (*n*) and percentage (%).

	Saline group (*n* = 40 patients)	Ketamine 0.25 group (*n* = 40 patients)	Ketamine 1.0 group (*n* = 40 patients)	*P*-value
Side effects				
Nausea	1 (2.5%)	0 (0%)	0 (0%)	0.827
Vomiting	2 (5%)	1 (2.5%)	1 (2.5%)	0.761
Desaturation	3 (7.5%)	2 (5%)	1 (2.5%)	0.775

There have been several previous attempts to reduce the incidence of EA by ketamine [2,10], nalbuphine [2], propofol [13], fentanyl [14], melatonin [15], ketofol [16], dextromethorphan [17], etc., but the etiology and preventive treatments of EA remain unclear [11].

Ketamine suppresses the occurrence of EA in children [18]. It has strong analgesic effect at less than anesthesia-inducting doses, and does not cause respiratory depression at a small dose less than 1 mg/kg, with insignificant effects on the heart rate and blood pressure [19].

According to Kwak et al. [20] the incidence of EA was decreased without delay in the recovery time with intravenous injection of ketamine 1.0 mg/kg, administered after sevoflurane induction in young children undergoing tonsillectomy under sevoflurane general anesthesia.

In a study done by Lee et al. [11], the incidence of EA was decreased without any particular side-effects or delay in the recovery time after intravenous administration of ketamine 0.25 mg/kg or 0.5 mg/kg 10 min prior the end of surgery.

Dalens et al. [2] reported that the administration of intravenous ketamine 0.25 mg/kg at the end of the scanning procedure prevented EA in children undergoing MRI under sevoflurane general anesthesia.

Limited number of studies investigated sevoflurane general anesthesia for MRI scan using face mask with spontaneous breathing [7,21].

In this study anesthesia was maintained under firmly secured fitted pediatric face mask sevoflurane in a titrating concentration of 1–2% and the use of ketamine 1 mg/kg as a premedicant not only decreased sevoflurane concentration but also decreased significantly the incidence of EA and pausing of the scan ($P < 0.05$).

Kim et al. [22] recommended sevoflurane insufflation technique using nasal cannula as one of the sedation options in

managing uncooperative children for painful procedure, not only for nonpainful radiologic examination.

Ogurlu et al. [7] reported that sevoflurane could be reliably administered with a face mask at different concentrations. They also noted that with the reduction of sevoflurane concentration (1.5–1.25–1%) inadequate anesthesia did not come about. Adequate anesthesia in children at low sevoflurane concentrations was made feasible in that study by premedication with midazolam before the MRI scan. Thus, we hypothesized that utilization of ketamine as premedicant prior the scan will reduce the required sevoflurane concentration in addition to reduction of EA and pausing of the scan.

In this study, ketamine 0.25 mg/kg administered 10 min prior the end of the MRI scanning resulted in significant reduction in the incidence of EA. However, this did not result in reduction of the incidence of scan pausing as the anesthesia was maintained throughout the procedure by sevoflurane only. The incidence of scan pausing in this group was similar to the saline group.

With regard to scanning times, recovery times, hemodynamic and respiratory parameters and complications, no significant differences were observed among the studied groups.

Limitation of this study, premedication with sedatives or anxiolytics were not given to saline or ketamine 0.25 groups as preoperative anxiety may affect EA.

6. Conclusion

Ketamine 1.0 mg/kg administered intravenously as a premedicant and ketamine 0.25 mg/kg administered intravenously 10 min prior the end of MRI scan were effective in reducing the incidence of EA without delay in the recovery time or discharge from PACU with insignificant complications. Pre-scan ketamine 1.0 mg/kg significantly reduced the incidence of pausing of MRI scan. Administration of sevoflurane through face mask with spontaneous breathing provides safe and adequate anesthesia for children undergoing MRI scan.

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Conflict of interest

No conflict of interest emerged during the implementation of this work. The paper had not been presented at any congress before.

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