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Research Article

Sedation in children undergoing magnetic resonance imaging comparative study between dexmedetomidine and ketamine



Abeer M. Eldeek*, Sanaa Mohamed Elfawal, Mohamed Gaber Allam

Department of Anesthesia, Intensive Care and Pain Management, Faculty of Medicine, Ain Shams University, Cairo, Egypt

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KEYWORDS

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Abstract *Aim and background:* In this study we compared between sedative effect of dexmedetomidine and ketamine as regards their sedative, hemodynamic, respiratory effects and complication when given as infusions in children undergoing magnetic resonance imaging (MRI).

Methods: One hundred and ten children of both sex aged 3–7 years were randomly distributed into two groups. The first group ($n = 55$) received dexmedetomidine (D) $1 \mu\text{g}/\text{kg}$ as a loading dose followed by continuous infusion $0.5\text{--}0.75 \mu\text{g}/\text{kg}/\text{h}$ and the second group ($n = 55$) received ketamine (K) $1 \text{mg}/\text{kg}$ as a loading dose followed by continuous infusion $10\text{--}15 \mu\text{g}/\text{kg}/\text{min}$. Inadequate sedation was defined as difficulty in completing the procedure because of movement of the child during MRI. The children who were inadequately sedated were given a single dose of propofol $0.5 \text{mg}/\text{kg}$ in both groups intravenously (iv) as rescue doses. Mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO_2) and respiratory rate (RR) were monitored during this study.

Results: Inadequate sedation was observed in 6 children from (D) group and 4 children from (K) group during MRI examination. Onset of sedation was significantly shorter in (K) group, but the discharge time was longer in this group. MAP and HR decreased significantly from baseline during sedation in group (D). Nausea, vomiting, and dysphoria were observed in 3 children of group (K).

Conclusion: Dexmedetomidine provided adequate sedation in most of the children without hemodynamic or respiratory embarrassment, in comparison with ketamine which provided adequate sedation but with delayed discharge time and more side effects.

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1. Introduction

Sedation of children for imaging procedures is often challenging. While not painful, these procedures require patient immobility for as long as one to three hours. MRI examination is very sensitive to motion artifacts. If any movement occurs

* Corresponding author at: Al Rehab City, Group 109, Building 20, Cairo, Egypt. Tel.: +20 1001803754.

E-mail address: abeerluzo@gmail.com (A.M. Eldeek).

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during the imaging process for one sequence, the entire sequence must be repeated [1]. Children may be frightened by being in the magnetic resonance imaging (MRI) tunnel or duct and the loud noise generated during the imaging process. Thus sedation is required for children aged between 4 and 7 years. Children may not remain immobile for long enough to allow a sequence to be completed [2].

Consequently, a deep level of sedation is required during MRI. Deep sedation is defined as “a medically induced state of central nervous system depression in which the patient is essentially unconscious, and so does not respond to verbal command”. The potential complications of deep sedation include hypoventilation, apnea, airway obstruction, aspiration, hypotension, bradycardia, and increased intracranial pressure [3].

If any complications occur during an MRI examination, the nature of the set-up precludes easy access to the patient. Also, limited access to the patient may pose a safety risk during MRI examination [2,3]. There has been debate over the appropriate drugs and dosage regimens for MRI sedation in children.

Dexmedetomidine is a potent highly selective α 2-adrenoreceptor agonist with a distribution half-life of approximately 8 min and a terminal half-life of 3.5 h [4]. Dexmedetomidine, as a sedative agent, can provide easily controllable analgesia and sedation without respiratory depression and has been widely used in the intensive care unit (ICU) for sedation and postoperative analgesia [5].

Ketamine is an N-Methyl-D-Aspartate (NMDA) receptor antagonist used clinically as an anesthetic, sedative, and analgesic in pediatric patients.

In this preliminary study, the aim was to improve sedation and develop a regimen based on dexmedetomidine, and to evaluate the sedative, hemodynamic, respiratory effects and incidence of complication of dexmedetomidine compared with ketamine in children undergoing MRI examination in Ain Shams University hospitals from January 2014 to August 2015.

2. Methods

After departmental approval and written parents consent, 110 ASA (American Society of Anesthesiologists) I–II children aged 3–7 years undergoing MRI were included in this randomized prospective study from January 2014 to August 2015. Patients with heart, lung or neurological disease, central nervous system or extremity trauma, or contraindication or allergy to any of the drugs studied were excluded. Randomization was done using a computer-generated random number list in 1:1 ratio. The randomization list was concealed until the time of randomization. Allocation of patients to either group was done by a clinician not involved in the study and the randomization codes were kept concealed until after data collection and analysis were completed. All children were allowed to take clear liquids up to 2 h before sedation but food (including milk) intake was withheld for at least 8 h in children older than 3 years. To facilitate intravenous (i.v.) cannulation, EMLA cream was applied on the dorsum of both hands 1 h before transfer to the preparation room. Presedation behavior was assessed on a four-point scale (1 = calm, cooperative; 2 = anxious but reassuring; 3 = anxious and not reassuring;

Table 1 Ramsay sedation assessment scale.

Awake levels	Patient anxious or agitated or both	1
	Patient cooperative, oriented and tranquil	2
	Patient responds to commands only	3
Asleep levels	A brisk response to a light glabellar tap	4
	A sluggish response to a light glabellar tap	5
	No response	6

4 = crying or resisting). Categories 1 and 2 were classed as stressed # unstressed and categories 3 and 4 as distressed. Baseline values were recorded upon arrival in the preparation room. A 22G (gauge/size) or 24G venous cannula was inserted in the dorsum of the hand. Children were randomized using a computer generated random numbers table into groups: D and F; 55 patients each. Solutions of dexmedetomidine (Precedex, Abbott laboratories, Lake Forest, IL60045, USA), 1 ml at a concentration of 100 μ g/ml, were diluted with 49 ml normal saline to a concentration of 2 μ g/ml, and ketamine (Ketamine 50, Sigma-Tec Pharmaceuticals Industries, Egypt-SAE), 1 ml at a concentration of 50 mg/ml, was diluted with 49 ml normal saline to a concentration of 1 mg/ml. A loading dose (dexmedetomidine 1 μ g/kg was given over 10 min or ketamine 1 mg/kg with glycopyrrolate 5 μ g/kg) was given intravenously followed by continuous infusion (dexmedetomidine 0.5–0.75 μ g/kg/h or ketamine 10–15 μ g/kg/min). The sedation level of the children was measured every 10 min using the Ramsay sedation scale by evaluating response to sound, verbal commands or tactile stimulation. The Ramsay scale (Table 1) assigns a score of 1–6 based on the clinical assessment of the level of sedation (1 = anxious, agitated, restless; 2 = awake, but cooperative, tranquil, orientated; 3 = responds to verbal commands only). Scores 4–6 apply to sleeping patients and are graded according to the response to loud noise or a glabellar tap (4 = brisk response; 5 = sluggish response; 6 = no response). The children were taken into the MRI room after a Ramsay score of 6 and hemodynamic and respiratory stability were achieved. If a Ramsay score of 6 was not achieved after 25 ± 5 min of study drug infusion or inadequate sedation occurred during MRI examination, a single rescue dose of propofol 0.5 mg/kg i.v. was administered to the patients in both groups. Inadequate sedation was defined as difficulty in completing the procedure because of movement during MRI examination.

Mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO₂) and respiratory rate (RR) were monitored continuously and recorded at 5-min intervals during the study period. Spontaneous respiration was maintained in all children, and oxygen via a facemask was given as 8 L/min to maintain SpO₂ above 95%.

The quality of the MRI examination was evaluated using a three point scale (1 = no motion; 2 = minor movement; 3 = major movement necessitating another scan). At the end of the MRI, drug infusion was discontinued and the children were transferred to the recovery room. The onset of sedation time was defined as the time from starting drug infusion to achieving a Ramsay score of 6. Recovery time was the time between discontinuation of drug infusion and reaching a Ramsay score of 2. Discharge time was the time between discontinuation of drug infusion and discharge of the child from

the unit. Discharge criteria were the return of vital signs and level of consciousness to baseline, and the ability to maintain a patent airway.

2.1. Sample size

Prospective power analysis showed that a sample size of 55 patients per study group would have 80% power at the 10% significance level to detect the expected change.

The incidence of sedation failure was the primary endpoint of the study. The alpha-error level was fixed at 0.05.

3. Statistics

Analyses were done by IBM computer using statistical program for social science (SPSS), description of quantitative variables as mean, SD and range description of qualitative variable as numbers. The SPSS software used was version 20. The one-sided test with a shifted hypothesis was used in the confirmatory analysis. Analysis of variance for repeated measures was performed on hemodynamic and respiratory parameters, with compensation for post hoc comparisons using the Bonferroni correction. Intergroup statistical analyses were performed using the *t*-test, and non-parametric data were analyzed using the X^2 -test. Statistical significance was assumed at $P < 0.05$. Results are presented as mean (SD).

The power of the study was calculated based on the difference in the onset of sedation time between the two study groups. Setting a significance level of $P = 0.05$, it was calculated that a group size of 55 patients allowed detection of a difference between groups with a power of 80%.

4. Results

The patients' demographics, premedication behavior score, and the duration, type, and quality of MRI procedure were not statistically different between groups (Table 2).

Table 2 Patient characteristics, duration, and type of magnetic resonance imaging procedures.

Patient characteristic, procedure	Group D (<i>n</i> = 55)	Group K (<i>n</i> = 55)	Significant
Age (yr)	5 ± 1.67	5 ± 1.53	NS
Weight (kg)	14 ± 4.03	14 ± 4.73	NS
Sex (male/female)	33/22	26/29	NS
Premedication behavior score			
– Undistressed (scores 1 & 2)	29	28	
– Distressed (scores 3 & 4)	26	27	
Duration of MRI (min)	35 ± 32	38 ± 37.12	NS
Cranial MRI	32	30	NS
Extremity MRI	6	7	NS
Spine	7	9	NS
Thorax and abdomen	10	9	NS

Data are expressed as mean ± SD, numbers (*n*).

Group D (= dexmedetomidine); group K (= ketamine).

$P > 0.05$ = non-significant and N/S = non-significant.

Table 3 Results of sedation, duration of study drug infusion and adverse effects.

Inadequate sedation	Group D (<i>n</i> = 55)	Group K (<i>n</i> = 55)	<i>P</i> value
Sedation failure	6	4	
Onset of sedation time (min)	15 ± 3.0	5 ± 1.54	0.010
Duration of study drug infusion (min)	49 ± 14.81	52 ± 15.76	0.030
Adverse effects			
– Emesis	0	1	NS
– Agitation and dysphoric reaction	0	2	NS
– Apnea	0	0	
– Desaturation	6	5	NS
– Recovery time (min)	20 ± 4.65	21 ± 05.22	0.020
– Discharge time (min)	30 ± 18.35	50 ± 14.35	0.030

Data are expressed as mean ± SD, numbers (*n*).

$P > 0.05$ = non-significant while $P < 0.05$ is significant.

N/S = non-significant.

Adequate sedation, as defined by quality of the examination, was obtained in 49 children from group D and in 51 children from group K. Although, deep sedation (Ramsay score of 5) was obtained with the dexmedetomidine or ketamine infusion before MRI examination, inadequate sedation was observed in 6 children from group D and in 4 children of group K during MRI. MRI examination was successfully completed in all of these children with supplementary bolus doses of propofol in group D and group K. In group K, the onset of sedation was significantly shorter than in group D ($P < 0.05$), but the discharge time was longer in this group. The level of consciousness was the same in both groups at the time of discharge. The duration of drug infusion was not different between groups ($P > 0.05$) (Table 3).

MAP, HR, and RR were not statistically different between groups before sedation. MAP and HR decreased significantly from baseline during sedation in D group ($P < 0.001$), and maintained or even increased in K group.

HR at 5, 15 min was significantly more rapid in group K than in group D, and MAP was higher in this group; however, these differences were not clinically significant. The RR was statistically significantly less in group K than in group D but these differences were not clinically significant. Bradycardia was not observed in any child. Desaturation was observed in 6 children in group D and 5 children of group K, SpO₂ decreased below 93% (average 89%) during MRI examination, usually after giving bolus of propofol. In these children, oxygen desaturation was treated with chin lift and increasing the oxygen supplementation via facemask. Side effects such as nausea, vomiting or dysphoria were observed in 3 children of group K, while it did not appear in group D during or after sedation (Table 4).

5. Discussion

The main finding in the current randomized trial involving 110 ASA I–II physical status children (3–7 years) requiring sedation during MRI can be summarized as follows: Both sedative techniques (dexmedetomidine versus ketamine) can be used

Table 4 Hemodynamic and respiratory changes during study drug infusion.

Time (min)	Baseline	5	15	30	45	P Value
<i>MAP</i>						
Group K	90 ± 5.88	75 ± 7.53	74 ± 9.7	73 ± 8.35	76 ± 6.72 [§]	0.026
	84 ± 10.6	92 ± 9.34	88 ± 8.42	95 ± 7.54	91 ± 0.53	0.029
*P value	NS	0.024	0.014	0.026	0.021	
<i>HR</i>						
Group D	115 ± 11.69	92 ± 0.75	90 ± 0.86	94 ± 4.61	96 ± 4.3	0.038
Group K	109 ± 9.73	120 ± 8.59	119 ± 0.89	123 ± 5.57	119 ± 5.4	0.036
*P value	NS	0.029	0.033	0.034	0.027	
<i>RR (respiratory rate)</i>						
Group D	26 ± 2.68	24 ± 3.72	24 ± 3.64	24 ± 3.83	24 ± 3.32	N/S
Group K	25 ± 0.59	22 ± 4.35	19 ± 4.86	17 ± 0.5	18 ± 1.7	0.022
*P value	NS	NS	0.018	0.022	0.021	
<i>SpO₂</i>						
Group D	96 ± 3.76	98 ± 2.06	94 ± 5.47	96 ± 3.25	95 ± 2.79	N/S
Group K	95 ± 84.24	97 ± 3.43	95 ± 4.62	97 ± 2.93	96 ± 1.9	N/S
*P value	NS	NS	NS	NS	NS	

Data are expressed as mean ± SD, $P > 0.05$ = non-significant (NS) comparing with baseline.

* $P < 0.05$ is significant, comparing D group with K group.

safely in sedation for MRI. In group K, the onset of sedation was significantly shorter than in group D, but the recovery and the discharge time were longer in this group. The level of consciousness was the same in both groups at the time of discharge. MAP and HR decreased significantly from baseline during sedation in group (D). Nausea, vomiting, and dysphoria were observed in 3 children of group (K).

Sedation of children for MRI can be associated with difficulty in obtaining deep sedation while maintaining hemodynamic and respiratory stability [6]. The ideal pediatric sedative drug should maintain patient's ventilation, provide hemodynamic stability, provide patient immobility, and allow easy drug titration. It should also ensure rapid sedation induction time and recovery while providing minimal side effects such as nausea, vomiting, dysphoria or pain [7]. Previous studies indicate that infusion of dexmedetomidine 0.1–0.7 µg/kg/h provides effective sedation [8–10]. A sedation score between 2 and 4 was obtained with 0.5 µg/kg as loading and 0.25–0.5 µg/kg/h. as infusion dose of dexmedetomidine [11]. In our study, a dexmedetomidine loading dose of 1 µg/kg intravenously and infusion of 0.7 µg/kg/h were used. Adequate sedation was obtained with dexmedetomidine in most of the children and the others were effectively sedated with use of bolus dose of propofol 0.5 mg/kg.

Arian and colleagues [12] reported a sedation induction time of 25 min and recovery time of 34 min with dexmedetomidine in adults. The onset of sedation time and recovery time was shorter in our study. This could be explained by the fact that the subjects were children and that the duration of infusion was shorter.

As regards the use of intravenous ketamine, reports of outpatient ketamine use date back to the 1970s [13]. Dachs and Innes [14] first published on its use in the pediatric emergencies in 1997 [14]. In their case series of 30 children given intravenous ketamine (1–2 mg/kg) all were adequately sedated within two minutes. This consistency of effect was confirmed in our study, as we used a loading dose of 1 mg/kg intravenously followed by an infusion of 50–75 µg/kg/min for the

duration of the procedure. Children in their study were discharged at a mean time of 25 min after drug administration compared with a mean time in our study at ketamine group of almost 60 min.

There was prolonged recovery and discharge time in our study, because our discharge criteria were more conservative than those of Dachs and Innes [14], requiring that in addition to a return to a normal conscious level and appropriate verbalization, children needed to be free of nystagmus and ataxia.

Actually recovery agitation or emergence phenomena are common with intravenous ketamine in the form of clumsiness (evident as ataxic movements), dysphoric reaction hallucinations or nightmares. A recent report has suggested that the incidence of moderate to severe emergence phenomena associated with ketamine use is only 1.6%, considerably less than the previously described rate of up to 10% which is going with our study as there are two patients had signs of emergence phenomena [15].

Emesis is an important adverse event that can occur during or after procedural sedation. It is considered one of the side effects of ketamine, and actually, the rates of emesis in our study are consistent with the incidence reported in other studies [16]. In Sherwin et al. [17], the incidence of emesis was 12% in ketamine group. The dexmedetomidine group showed a hemodynamic stability, in spite the contradictory results related to its hemodynamic effects in some literature [18–20].

Hypotension and bradycardia have been reported particularly with large bolus dosing regimens, in patients with cardiac problems and in patients administered an initial dose in < 10 min [21,22]. In this study the initial dose of dexmedetomidine was administered over 10 min to minimize cardiovascular and respiratory depression related to initial dose, although MAP and HR decreased after 15 min from the start of dexmedetomidine infusion. This decreases because the patients were not premeditated and the baseline values may have been high and reflective of a time baseline value.

Because decreases in MAP and HR with dexmedetomidine infusion were < 20% of baseline and no bradycardia or

hypotension occurred in any child, there decreases were considered clinically insignificant. As regards ketamine infusion, there was hemodynamic stability, MAP and HR were maintained and even in the high side, and sometimes tachycardia occurs but no clinical significance clinically. Respiratory events make up a large proportion (5.5%) of the complications of the sedation in children. Some authors have reported that dexmedetomidine does not affect RR, SpO₂, and ETCO₂ [2]. However, some respiratory complications have been reported with large and rapid initial loading doses [19,21]. When a dexmedetomidine initial was administered rapidly (2 min), it caused irregular respiration, apnea, slight hypoxemia, and hypercapnia.

In this current study, the clinically insignificant decrease in RR during dexmedetomidine infusion may have been as a result of high baseline values. For ketamine group no patient had apnea or required the use of assisted ventilation. The routine use of anti-sialogogue could have reduced our incidence of adverse respiratory events.

Lion and Mathios [23] reported that no relevant respiratory effects of dexmedetomidine are known. Hemodynamic side-effects such as low blood pressure and low heart rate are common. A loading dose of 2–3 mg/kg over 10 min followed by 1–2 mg/kg/h as an infusion for sedation maintenance is recommended. Several studies investigating dexmedetomidine for sedation have been published. Mason and colleagues [24] reported MRI procedures for 747 children and showed successful imaging in 97.6%. Cardiovascular side-effects (bradycardia never exceeding a 20% range from standard values) were seen in 16%. Oxygen saturation was always above 95% [24]. In children with obstructive sleep apnea syndrome a comparison between dexmedetomidine and propofol for MRI sleep induction revealed effective sedation without the need for additional airway equipment in 88.5 versus 70% of scans [25]. Some other investigations found no difference in successful scanning between dexmedetomidine and propofol in 60 children between 1 and 7 years old but propofol showed advantages in induction, recovery and discharge time. No oxygen desaturation was seen in the dexmedetomidine-sedated children [26]. Similar results were reported by Heard and colleagues [27], who compared a midazolam–dexmedetomidine combination with propofol for sedation. The main finding in Waleed et al. [28] in a randomized trial involving 60 ASA I physical status children (4–10 years) requiring sedation during dentistry procedure at dentistry outpatient clinic can be summarized as follows: Both sedative techniques (dexmedetomidine versus propofol–midazolam) can be used safely in outpatient dentistry clinic. Propofol–midazolam combination can achieve rapid induction compared to dexmedetomidine alone, reflected by shorter duration required to achieve RSS P5. Dexmedetomidine had faster recovery compared to propofol–midazolam combinations reflected by rapid restoration of RSS of 2. Patients receiving dexmedetomidine requires less analgesia supplementation in the early recovery period compared to propofol–midazolam combination. Lubisch et al. [29] published a retrospective study of children with autism and other neurobehavioral disorders. Three hundred and fifteen patients with a mean age of 3.9 years were sedated with dexmedetomidine, most commonly for MRI, while 90% of patients received concomitant midazolam. Seven patients required intervention for cardiac events and one for a respiratory event. There were two episodes of recovery-related agita-

tion; 98.7% of sedations were successfully completed [29]. In the study of Tammam [30] was done on one-hundred and sixty-two children with ASA physical I–II were enrolled in a double-blind comparative study and assigned into three equal groups for sedation. Group D, patients received IM dexmedetomidine 3 ug/kg. Group K, patients received IM ketamine 4 mg/kg. Group DK, patients received a combination of IM dexmedetomidine 1.5 ug/kg and ketamine 2 mg/kg. The intramuscular mixture of dexmedetomidine and ketamine administration might avoid the adverse effects associated with dexmedetomidine and ketamine; and might reduce the need for titration, which is essential for IV sedation.

Thus, dexmedetomidine is suitable sedative agent and could be an alternative to ketamine for MRI sedation in children. Further studies with larger numbers of patients as structured multicenter studies are required, and also to assess intramuscular and transnasal administration of dexmedetomidine for MRI sedation.

In conclusion, dexmedetomidine provided adequate sedation at 1 µg/kg loading and 0.7 µg/kg/h infusion doses in most of children (aged between 3 and 7 years) without significant affection of hemodynamics, respiration, and with rapid smooth recovery.

In comparison, ketamine provides adequate sedation at 1 mg/kg intravenously as loading and 0.5–0.75 µg/kg/hr as infusion doses, but with delayed discharge time than dexmedetomidine and more side effects as emesis, dysphoric reactions and sometimes with emergence phenomena.

Conflict of interest

We have no conflict of interest to declare.

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