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Dexmedetomidine/propofol versus dexmedetomidine/ketamine versus dexmedetomidine as a sole agent for pediatric sedation during MRI

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Abstract

Background: Propofol use in MRI procedures is growing worldwide especially for infants and children. Propofol causes unintended deep sedation and respiratory depression. The safety and efficacy of dexmedetomidine–propofol versus ketamine–dexmedetomidine versus dexmedetomidine alone as a based sedation regimen in specific age range of children is the study concern.

Objective: The aim of this study is to compare the efficacy of dexmedetomidine/propofol mixture, dexmedetomidine/ketamine, and dexmedetomidine alone for pediatric MRI sedation.

Patients and methods: Ninty infants and children whose body weight is more than 10 kg were enrolled in a double-blind comparative study and assigned into three equal groups for sedation, group (DK) dexmedetomidine/ketamine, group (DP) dexmedetomidine/propofol, and group (D) dexmedetomididne alone. All patients were given premedication in the form of oral midazolam 0.5 mg/kg 30 min before the procedure. Sedation was according to group: Group (DK) received ketamine 1.5 mg /kg intravenous bolus as a loading dose and maintenance dose done by dexmedetomidine infusion with a concentration of 0.004 mg/ml and infusion rate of 1 μg/kg/h for the first 10 min then reduced infusion dose to be in between 0.6 and 1 μg/kg/h to keep the patient sedated to a Ramsay sedation score more than 4. Group (DP) received propofol 1.5 mg/kg intravenous bolus as a loading dose, then maintenance dose infusion was a mixture of dexmedetomidine with a concentration of 0.004 mg/ml and propofol 4 mg/ml; this combination is compatible (Trissel et al., 2002; Cayo, 2013). This combination will be started by a loading dose of 1 μg/kg/h for the first 10 min then 0.6 to 1 μg/kg/h, sedated with a Ramsay sedation score of more than 4. Group (D) received dexmedetomidine with a dose of 2–3 μg/kg/h as loading for 10 min then 0.6 to 1 μg/kg/h to keep the patient sedated with a Ramsay sedation score of more than 4.

Results: There was a significant difference between the DP group induction recovery time, hemodynamics, and Ramsey sedation score up to 5 min after the induction to the other two groups, and there was a significant difference between the DK group to the other two groups concerning emergence phenomena (agitation, altered perception, hallucination) and sedation failure.

Conclusion: The combination of dexmedetomidine to propofol with a low dose for sedation during MRI gives better induction + recovery time, improves hemodynamics, and decreases incidence of emergence phenomena and sedation failure.

Keywords: Dexmedetomidine infusion, Propofol infusion, Ketamine infusion, Pediatric sedation, MRI

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Background

The sedation challenge with MRI patients is to withstand a noisy and claustrophobic environment till the end of the procedure especially for pediatric. A variety of concepts are used by nurses, pediatricians, and anesthesiologists. Each concept has advantages and disadvantages (Dearlove and Corcoran 2007). Propofol was raised over all intravenous drugs for pediatric sedation. However, the narrow therapeutic window is associated with unintended deep anesthesia with loss of protective reflexes even after a small dosage. Thus, an appropriate low dosage of propofol is the target to ensure sedation for successful MRI completion, to avoid its risky adverse effects (Sury and Smith 2008).

Aim

The aim of this study is to compare the efficacy of dexmedetomidine/propofol mixture, dexmedetomidine/ketamine, and dexmedetomidine alone for pediatric MRI sedation.

Methods

After approval of the institutional ethical committee of King Faisal Specialized Hospital and Research Center and written informed consent was obtained from the parents, ninety infants and children whose body weight is more than 10 kg scheduled for elective MRI since December 2014 till June 2015 were randomly assigned to one of the study groups by use of a computer-generated list compiled before the start of the study. Exclusion criteria were pulmonary or cardiovascular disorders, congenital heart disease, anatomic airway abnormalities or extreme tonsillar hypertrophy, head trauma, increase intracranial tension, AV node block, receiving drugs as BB or digoxin, a history of propofol intolerance, and known fat metabolism disorder.

In a pre-procedure interview, all parents were instructed about the patient fasting hours as recommended by the "American Society of Anesthesiologists Pre procedure Fasting Guidelines": clear liquids were withheld for at least 2 h, breast milk for 4 h, and infant formula and solid food for 6 h. The fasting periods were applied to all ages.

On the day of the procedure, all patients were admitted with their parents at the day care unit. Patients received midazolam 0.5 mg/kg orally 30 min before the procedure. An intravenous cannula was inserted and then the patient was transferred to the MRI suite accompanied by his/her parents.

The induction time is calculated since loading dose of the sedative drug is given till the patient's Ramsay sedation score became more than 6.

Group (DK) received ketamine 1.5 mg/kg intravenous bolus as a loading dose and maintenance of sedation done by dexmedetomidine infusion with a concentration of 0.004 mg/ml and infusion rate 1 μg/kg/h for the first 10 min then 0.6 to 1 μg/kg/h to keep the patient sedated with a Ramsay sedation score of more than 4. Group (DP) received propofol 1.5 mg/kg intravenous bolus as a loading dose then infusion by a mixture of dexmedetomidine with a concentration of 0.004 mg/ml and propofol 4 mg/ml; this mixture is compatible according to pharmacological recommendations (Trissel et al., 2002; Cayo, 2013). The mixture infusion will start by a loading dose of 1 μg/kg/h for the first 10 min then 0.6 to 1 μg/kg/h to keep the patient sedated with Ramsay sedation score of more than 4. Group (D) received dexmedetomidine with a dose of 2–3 μg/kg/h as a loading dose for 10 min then a maintenance infusion dose to be in between 0.6 and 1 μg/kg/h to keep the patient sedated with a Ramsay sedation score of more than 4. The maintenance of spontaneous respiration was verified. Then soft supports were placed under the patient's neck and shoulders to position the patient with the head forward and the neck slightly extended to maximize airway patency. Supplemental oxygen was delivered by pediatric face mask with a gas flow rate of 2 l/min. Sedation was maintained with medication according to the group regimen, using an MRI-compatible syringe pump and MRI-compatible monitors. Heart rate, mean arterial blood pressure, peripheral oxygen saturation (SpO2), and end-tidal carbon dioxide were monitored continuously during the procedure and recorded by the monitor at 5-min intervals; sedation failure was monitored by a Ramsay sedation score (RSS) all over the procedure to keep the score more than 4. Patient experienced sedation failure if the patient wakes up (RSS less than 4) or has inability to complete the planned procedure secondary to unacceptable motion artifacts. Supplemental sedation was provided by using titrated doses of IV propofol 1.5 mg/kg one time only, and then the infusion is resumed according to the group; if it failed to continue with the maintenance infusion, the patient will receive general anesthesia and excluded from the study. Incidence of complications during and after the procedure was documented by the anesthetists. Airway complications, emergence phenomena, and unplanned admission were recorded. Hypotension after sedation was defined as a decrease in arterial pressure of 20% from baseline values. Intervention was considered necessary when there is a decrease in SpO2 to 94%, an increase in EtCO2 of more than 50 mmHg, apnea (cessation of spontaneous respiration for 20 s), bradycardia (20% decrease in heart rate from baseline), and also occurrence of arrhythmia. For safety, the anesthesiologist closely observed the patients and provided interventions as needed. Discharge readiness was achieved when a modified Aldrete score is 8.

Definitions used are as follows:
Ramsay sedation score:

Score	Response
(1)	Anxious, agitated, and restless
(2)	Cooperative, oriented, and tranquil
(3)	Responsive to command only
(4)	Brisk response to light glabellar tap or loud auditory stimulus
(5)	Sluggish response to light glabellar tap or loud auditory stimulus
(6)	No response to light glabellar tap or loud auditory stimulus

Ramsay sedation score by Ramsay et al. (1974).

Induction time: time recorded since the patient receives the loading dose of the sedating drug till patient RSS is *6*.

Recovery time: time recorded since the procedure is finished till patient RSS becomes less than 4 (Trissel et al., 2002) and patient is ready to transfer to the day care unit.

Induction + recovery time: the summation of the induction and the recovery time.

Emergence: the return to baseline physiologic function of all organ systems after the cessation of general anesthetics. It may be accompanied by temporary neurologic phenomena, such as agitated emergence (acute mental confusion), aphasia (impaired production or comprehension of speech), or focal impairment in sensory or motor function. Shivering is also fairly common and can be clinically significant because it causes an increase in oxygen consumption; carbon dioxide production; cardiovascular events such as increased or decreased blood pressure, rapid heart rate, and cardiac dysrhythmias; and respiratory symptoms such as dyspnea Stoelting and Miller (2006).

Sedation failure: the patient wakes up (RSS less than 4) or has inability to complete the planned procedure secondary to unacceptable motion artifacts Tammam (2013).

Statistical data analysis

Data were analyzed using SPSS version 16.0 computer software (Chicago, IL, USA). Numerical variables were presented as mean and standard deviation (SD), while categorical variables were presented as frequency (%). One-way ANOVA was used for between-group comparisons of numerical variables. Chi-square test was used for comparisons of categorical variables. Tukey's HSD test was used as post hoc test for pairwise comparisons. A p value of 0.05 was considered statistically significant. Sample size calculation revealed that at least 27 patients are needed in each group for detecting a difference in induction, and recovery time of at least 5 min, assuming the standard deviation of this time is 5 min, with a power and significance level of 0.9 and 0.05 respectively. Sample size was increased by 10% making it to be 30 patients in each group for compensation of possible data skewness.

Results

The demographic data as age and weight showed no significant difference between the three groups as shown in Table 1, with a p value of 0.22 for age and a p value of 0.508 for the body weight.

Hemodynamics parameters (heart rate and mean blood pressure) presented in Table 2 showed a significant difference in the dexmedetomidine group compared to the other two groups with a p value of < 0.001, and the dexmedetomidine/propofol group shows a significant difference compared to the dexmedetomidine/ketamine group with a p value of < 0.001.

Oxygen saturation as showed in Table 3 represents no significant difference between the three groups with an actual p value of 0.009.

Emergence as shown in Table 4 showed a significant difference between DK group (7 patients) and the other two groups with a p value of < 0.001.

Discussion

Dexmedetomidine is a specific and selective alpha-2 adrenoceptor agonist. By binding to the presynaptic alpha-2 adrenoceptors, it inhibits the release of norepinephrine, terminating the propagation of pain signals. Activation of the postsynaptic alpha-2 adrenoceptors inhibits the sympathetic activity decreasing the blood pressure and heart rate. Its common adverse events related to its IV administration include bradycardia, hypotension, and easy arousal by minimal stimulants such as MRI noise (Fairbanks et al., 2002; Scheibner et al., 2002).

Propofol has a narrow therapeutic, unintended deep anesthesia with loss of protective reflexes even after a small dosage.

Gunduz et al. (2011) compared the sedoanalgesic effects of intravenous ketamine–dexmedetomidine and ketamine–midazolam on dressing changes of adult burn

Table 1 Demographic data (age, weight)

	Groups	Number	Mean	Standard deviation	p value
Age (years)	D	30	4.51	.9239	0.222
	DK	30	4.86	.6806	
	DP	30	4.75	.7114	
Body weight (kg)	D	30	14.27	1.4355	0.508
	DK	30	14.18	1.0160	
	DP	30	14.54	1.2615	

The demographic data as age and weight showed no significant difference between the three groups, with a p value of 0.22 for age and a p value of 0.508 for the body weight

Table 2 Hemodynamic parameters (heart rate, mean blood pressure)

	Groups	Number	Mean	Standard deviation	*p* value
Heart rate (bpm)	D	30	51.2	3.761	< 0.001
	DK	30	102.6	7.297	
	DP	30	70.6	8.182	
Blood pressure (mmHg)	D	30	57.6	3.7568	< 0.001
	DK	30	76.7	4.3179	
	DP	30	60.3	3.7788	

Hemodynamics parameters (heart rate and mean blood pressure) showed a significant difference in the dexmedetomidine group compared to the other two groups with a *p* value of < 0.001, and the dexmedetomidine/propofol group shows a significant difference compared to the dexmedetomidine/ketamine group with a *p* value of < 0.001

Table 4 Emergence (agitation, altered perception, and hallucination)

			Group			Total
			D	DK	DP	
Emergence	(No)	Count	30	23	30	83
		% within group	100.0%	76.7%	100.0%	92.2%
	(Yes)	Count	0	7	0	7
		% within group	.0%	23.3%	.0%	7.8%
Total		Count	30	30	30	90
		% within group	100.0%	100.0%	100.0%	100.0%

Emergence showed a significant difference between DK group (7 patients) and the other two groups with a *p* value of < 0.001

patients. They noted both combinations offered an effective sedoanalgesia without causing any significant side effect, but the ketamine–dexmedetomidine regimen resulted in higher sedation scores.

In this study, the demographic data as age and weight showed no significant difference between the three groups as shown in (Table 1) patients given the mixture of IV dexmedetomidine and propofol showed less adverse effects and high radiologist satisfaction of sedation compared to the other sedatives. The duration of the procedure showed no significant difference between the three groups (Table 5). The induction, recovery and combination of induction, and recovery time was much lower in the dexmedetomidine–propofol group which showed a significant difference compared to the other two groups (Table 6). The DP group showed induction, recovery, and total induction + recovery time of 12.2, 10, and 22.2 min respectively with 3.1 SD. The DK group showed induction, recovery, and total induction + recovery time of 18, 21.1, and 49.2 min respectively with 4.5 SD, while group D showed 20, 29.2, and 39.1 min respectively with SD 3.4; DK leads to a higher sedation score and leads to a long arousal time, these results correspond to those of Gunduz et al. (2011) and Tarek F. Tammam whose study detected longer duration of sedation in the ketamine group compared to the dexemedetomidine–ketamine group (Tammam, 2013).

In this study, the sedation failure (Ramsay sedation score of ≤ 4 or movement (Table 7)) was higher in the dexmedetomidine–ketamine group (20%) in comparison to that in the dexmedetomidine–propofol group (6.7%) and dexmedetomidine group (6.7%), with the need of extra dose of sedative drug; this is corresponding with Gunduz et al. (2011) and corresponds to Sheikh Sohail who used dexmedetomidine as a sole agent in pediatric sedation during MRI (Mason et al., 2008).

In this study, concerning Ramsay sedation, 5 min post induction (Table 8) showed a score of 6 with a significant difference between the three groups with 96.7% for the dexmedetomidine–propofol group, 0% for the dexmedetomidine group, and 3.3% for the dexmedetomidine–ketamine group. Regarding Ramsay sedation score during the procedure (Table 9), there was no significant difference between the three groups. The Ramsay sedation score for 20 min post procedure showed a significant difference between the three groups (Table 10); the dexmedetomidine–ketamine group showed 20% of the patients' RSS (Trissel et al., 2002) detecting a restless patient due to emergence which is common with ketamine, showing a significant difference compared to the other two groups. These results correspond to those of Gunduz et al. (2011).

Regarding hemodynamics, there is a significant difference between the three groups. The dexmedetomidine–ketamine group showed the highest blood pressure and heart rate, and the dexmedetomidine–propofol group showed the minimal alteration in hemodynamic state (Table 2).

Table 3 Oxygen saturation

	Groups	Numbers	Mean	Standard deviation	*p* value
O_2 saturation %	D	30	98.07	.944	0.009
	DK	30	97.29	1.039	
	DP	30	97.43	1.073	

Oxygen saturation represents no significant difference between the three groups with an actual *p* value of 0.009

Table 5 Duration of the procedure

	Groups	Numbers	Mean	Standard deviation	*p* value
Duration of procedure (min)	D	30	61.2	3.640	0.165
	DK	30	59.5	1.503	
	DP	30	59	4.564	

The duration of the procedure showed no significant difference between the three groups with a *p* value of 0.165

Table 6 Induction, recovery, and induction + recovery time

	Groups	Numbers	Mean	Standard deviation	*p* value
Induction time					
	D	30	18	3.424	< 0.001
	DK	30	20	4.025	
	DP	30	12.2	3.034	
Recovery time					
	D	30	21.1	3.513	< 0.001
	DK	30	29.2	4.364	
	DP	30	10	3.237	
Induction + recovery time (min)	D	30	39.1	3.468	< 0.001
	DK	30	49.2	4.580	
	DP	30	22.2	3.104	

The induction, recovery and combination of both times showed a significant difference between dexmedetomidine–propofol group and the other two groups with a *p* value of < 0.001 with a lower induction time of 12.2 min and a recovery time of 10 min and a total combination time of 22.2 min, while the dexmedetomidine group (18 min, 21.1 min, and 39.1 min, respectively) shows significant difference to dexmedetomidine/ketamine group (20 min, 29.2 min, and 49.1 min respectively) with a *p* value of < 0.001

The limitation of the study was the need to increase the number of cases to get more significant results. The dexmedetomidine group showed the lowest heart rate and blood pressure among the three groups and this is corresponding to the study of Mason et al. (2008), who used high-dose dexmedetomidine as a sole sedative for pediatric MRI, wherein the cardiovascular side effects were noted in 16% of patients, and also corresponds to Sheikh Soheil et al. who used the dexmedetomidine as a sole agent in pediatric sedation for MRI by 2 μg/kg/h followed by 1 μg/kg/h, wherein he documented bradycardia and hypotension in 86 (26%) of patients but all the patients were normotensive (Ahmed et al., 2015).

Table 7 Sedation failure (yes/no)

			Group			Total
			D	DK	DP	
Sedation failure (yes/no)	No	Count	28	24	28	80
		% within group	93.3%	80.0%	93.3%	88.9%
	Yes	Count	2	6	2	10
		% within group	6.7%	20.0%	6.7%	11.1%
Total		Count	30	30	30	90
		% within group	100.0%	100.0%	100.0%	100.0%

Group DK showed a significant difference regarding sedation failure (six patients) in comparison to the two groups (two patients) with a *p* value of < 0.001

Table 8 Ramsay sedation score 5 min post induction group

			Group			Total
			D	DK	DP	
RSS 5 min post induction	(4)	Count	30	29	1	60
		% within group	100.0%	96.7%	3.3%	66.7%
	(6)	Count	0	1	29	30
		% within group	.0%	3.3%	96.7%	33.3%
Total		Count	30	30	30	90
		% within group	100.0%	100.0%	100.0%	100.0%

Ramsay sedation score (5 min post induction) showed significant difference in DP group to the other two groups where 29 patients reaches RSS (Stoelting & Miller, n.d.) detecting faster induction

The incidence of sedation failure was higher in the dexmedetomidine–ketamine group (6 patients) with significant statistical difference to the other two groups; this result corresponds to the results of Tammam (2013) that documented that incidence of sedation failure in ketamine group was higher than in the dexmedetomidine–ketamine group, and also corresponds to the results of Ahmed et al. (2015) that documented the usage of extra medications for sedation maintenance during pediatric sedation in MRI.

The respiratory events make up a large proportion (5.5%) of sedation complications in children according to Hasan et al. (2003). In some studies, rapid administration of large loading doses has been described to cause respiratory complications according to Belleville et al. (1992) and Bhana et al. (2000). A loading dose of dexmedetomidine given over 2 min has been reported to cause irregular respiration, apnea, slight hypoxemia, and hypercapnia Ebert et al. (2000). However, similar to our study, several other studies have reported a trivial effect of dexmedetomidine on respiration which is consistent with the notion that the risk of respiratory depression is minimal with dexmedetomidine–propofol sedation this

Table 9 Ramsay sedation score during the procedure

			Group			Total
			D	DK	DP	
RSS procedure	≤ 4	Count	2	6	2	10
		% within group	6.7%	20.0%	6.7%	11.1%
	6	Count	28	24	28	80
		% within group	93.3%	80.0%	93.3%	88.9%
Total		Count	30	30	30	90
		% within group	100.0%	100.0%	100.0%	100.0%

Ramsay sedation score during the procedure showed no significant difference between the three groups detecting same sedation potency between the three groups

Table 10 Ramsay sedation score 20 min post procedure

			Group			Total
			D	DK	DP	
RSS 20 min post procedure	(RSS 1)	Count	2	6	2	10
		% within group	6.7%	20.0%	6.7%	11.1%
	(RSS 2)	Count	28	24	28	80
		% within group	93.3%	80.0%	93.3%	88.9%
Total		Count	30	30	30	90
		% within group	100.0%	100.0%	100.0%	100.0%

The Ramsay sedation score (20 min post procedure) showed significant difference between the DK group and the other two groups where six patients showed a RSS (Trissel et al., 2002) in comparison to two patients in the other two groups, with a p value of < 0.001

is corresponding to the results of Mason et al. (2008), Belleville et al. (1992) and Heard et al. (2007). Regarding emergence (Table 4), there was a significant difference between the DK group with 7 patients and 0 in the other two groups.

Conclusion

The combination of dexmedetomidine–propofol for sedation during MRI gives better induction + recovery time and decreases incidence of emergence phenomena and sedation failure.

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Availability of data and materials

All data and material is available on the main manuscript and additional information will be provided upon request.

Authors' contributions

MKA is responsible for data collection, data analysis, and writing of the manuscript. THI is responsible for data collection and helped in writing the manuscript. Both authors read and approved the final manuscript.

Ethics approval and consent to participate

After approval of the institutional ethical committee of King Faisal Speciaclized Hospital and Research Center and written informed consent was obtained from the parents.

Consent for publication

Authors agree for publication of this research article in your journal. All data and materials are available in the mainscript. Funding was the responsibility of the authors.

Competing interests

The authors declare that they have no competing interests.

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