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A COMPARISON OF THE SEDATIVE, HEMODYNAMIC, AND RESPIRATORY EFFECTS OF DEXMEDETOMIDINE AND PROPOFOL IN CHILDREN UNDERGOING MAGNETIC RESONANCE IMAGING

Anaesthesiology

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ABSTRACT

Sedation of children for MRI is usually associated with inadequate or failed sedation because of difficulty in achieving complete immobility while maintaining hemodynamic and respiratory stability.

30 children each in two groups Group D receiving intravenous (iv) dexmedetomidine a potent, highly selective $\alpha_2$adrenoreceptor agonist and Group P receiving iv propofol were compared for efficacy in MRI sedation.

Dexmedetomidine was effective in 78.5% of cases with 21.5% of children required additional medications. Side effects occurred in approximately 25% of cases, bradycardia (3.9%) and hypotension (18.4%) that resolved spontaneously. In group P, the onset of sedation, recovery, and discharge time were significantly shorter than in group D ($P< 0.05$). 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 ($P> 0.05$).

100% of the children in both treatments completed their MRI scans without interruption or interventions (i.e., no failures) and without complications. Heart rate and systolic blood pressure changes were transient and statistically significant, but not of sufficient magnitude to warrant interventions.

KEYWORDS

MRI, sedation, pediatric

INTRODUCTION

The MRI unit is a work station where all procedures have to be well planned by staff trained to guarantee maximum patient safety and superior quality of imaging. The crucial role of MRI in emergencies, and also in the diagnosis of various diseases is invaluable. Those who are most in need of sedation or general anesthesia include children who are young (<6 yr of age), those who are unable or unwilling to remain still during the scan and those who are developmentally or cognitively challenged or severely claustrophobic. Because procedural sedation is unable to guarantee patient compliance in these cases, a deeper level of sedation is often required. [1,2]

The success of sedation for MRI is measured by two factors: the safety of the sedation procedure (lack of adverse events) and the effectiveness of the procedure (successful completion of the diagnostic examination.[3]

Sedation of children for MRI is usually associated with inadequate or failed sedation because of difficulty in achieving complete immobility while maintaining hemodynamic and respiratory stability. Limited access to the patient also poses a safety risk.(4)

Appropriate drugs have to be selected, administered, and titrated to achieve these objectives. [5] Although many healthy young children have been managed by radiologists and nursing staff with oral or intravenous sedation, the efficiency of these techniques are poor and the failure rate is substantial.

Dexmedetomidine is a potent, highly selective $\alpha_2$adrenoreceptor agonist having a distribution half-life of approximately 8 min and a terminal half-life of 3.5 h [6,7] At therapeutic doses, dexmedetomidine provides profound levels of sedation without affecting cardiovascular and respiratory stability. [8,9]

Propofol for sedation in children in the MRI setting is also popular because of its predictability, rapid onset, and offset of action. [10,11]

Failure rates (as evidenced by movement during the scan) with dexmedetomidine and propofol are in the range of 16% and 10% respectively.

METHODS

Selection & Description of Participants

After local Institutional Ethics Committee approval and written parental consent, ASA physical status I-II children aged between 1–7 yrs undergoing MRI at the NRI Institute of Medical Sciences, Visakhapatnam were included in this randomized and prospective study.

Children above 7 years of age can usually comprehend details of the MRI procedure and cooperate without need for any sedative medications.

Exclusion criteria

(a) Age <1 year
(b) The presence of congenital heart disease
(C) A recent upper respiratory infection or acute asthma in the preceding 2 weeks
(d) Behavioral problems (i.e., attention deficit hyperactivity disorder),
(e) Difficult airway or one that requires tracheal intubation or laryngeal mask airway
(f) Central nervous system or extremity trauma
(g) Scan expected to last more than 90 min.

MATERIAL & METHODS

The children were randomly assigned to receive either dexmedetomidine or propofol and randomization was ensured by using random number tables to assign the numbers between 1 and 60 to the 2 groups. The randomization assignment was concealed until the parents consented to the study.

Children older than 3 yr of age were NPO for solids and milk for at least 4 h and children 1–3 yr of age were NPO for solids and milk for 3 h. All the children were allowed to take clear liquids up until 2 h before the beginning of the sedation.

Presedation behavior was assessed on a 4-point scale, by an anesthesiologist blinded tothe drug selected, where 1 = calm, cooperative 2 = anxious but reassurable 3 = anxious and not reassurable 4 = crying or resisting. Categories 1 and 2 were called "undistressed behavior," and categories 3 and 4 were defined as "distressed behavior." Baseline values were recorded upon the arrival of the unpremedicated children to the preparation room before the 22 or 24-gauge venous cannula was inserted into the dorsum of the hand.

Children were allocated according to a random number table to receive either dexmedetomidine (group D, $n = 30$) or propofol (group P, $n = 30$). Solutions of dexmedetomidine, 1 mL at a concentration of 100 μg/mL, was diluted with 49 mL normal saline to a concentration of 2 μg/mL.All children in Group P were administered 1 ml of 1% preservative free lignocaine IV to reduce propofol injection pain. After administration of atropine, 2mcg/kg iv, a loading dose of dexmedetomidine (2 $\mu g \cdot kg^{-1}$ iv) was administered over ten minutes followed by a continuous infusion of 1.0 $\mu g \cdot kg^{-1} \cdot hr^{-1}$by syringe pump for maintenance. In the propofol group, the drug was infused IV at 300 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for the first 10 min and then at 250 $\mu g \cdot kg^{-1} \cdot min^{-1}$by syringe pump for the remainder of the MRI procedure. Once the infusion of dexmedetomidine (initial loading dose) or propofol was established, the child entered the MRI scanner. After 10 min procedure time, 0.1 mg/kg midazolam was given IV to children in the dexmedetomidine group and a similar volume of saline was given IV to those in the propofol group.

The sedation level of the children was measured by another anesthesiologist using the Ramsay sedation scale every 10 min. The Ramsay scale assigns a score of 1–6 based on the clinical assessment of the level of sedation as follows: 1 = anxious, agitated, restless; 2 = awake, but cooperative, tranquil, orientated; 3 = responds to verbal commands only. Scores 4–6 are used for sleeping patients and are graded according to the response to glabellar taps as follows: 4 = brisk response; 5 = sluggish response; 6 = no response. Score 3 was accepted as procedural sedation and 5 was accepted as deep sedation.

Children were transferred and positioned on the scanning table with a shoulder roll under the neck (either a rolled up towel or sheet) after both a Ramsay score of 5 was achieved and hemodynamic and respiratory stability was ensured.

The onset of sedation time was defined as the period of time between the beginning of study drug infusion and reaching a Ramsay score of 5.

If a Ramsay score of 5 was not achieved after infusion of the study drug, the infusion rate of the study drugs was increased to 0.7 $\mu g \cdot kg^{-1} \cdot h^{-1}$ in group D and to 150 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in group P for 5 min . If a Ramsay score of 5 was still not achieved, a supplementary bolus dose of midazolam (0.05 mg/kg) in group D or 1 mg/kg propofol in group P was given. Inadequate sedation was defined as difficulty in completing the procedure as a result of the child's movement during MRI examination.

Mean arterial blood pressure (MAP), heart rate (HR), peripheral oxygen saturation (Spo_2), and respiratory rate (RR) were monitored continuously and recorded at 5-min intervals during the study period by an anesthesiologist. Patients were allowed to breathe spontaneously without an artificial airway throughout the procedure. Ventilatory function was assessed by observation of respiratory activity by the anesthesiologist present. If the Spo_2 level decreased below 93% for 30 s the imaging process was interrupted and the patient taken out of the MRI tunnel. After airway patency was assessed, the neck was extended slightly and oxygen was administered via facemask.

At the end of the MRI, the drug infusion was discontinued and the children transferred to the recovery room.Recovery time was taken as the period of time between discontinuation of study drug infusion and reaching a Ramsay score of 2.

Quality of the MRI was evaluated by a radiologist using a three-point scale (1 = no motion; 2 = minor movement; 3 = major movement necessitating another scan). [Table 1]

The criterion of the discharge was the return of vital signs and level of consciousness to baseline, and the ability to maintain a patent airway. Side effects (e.g., nausea, vomiting, dysphoria) that occurred during and after sedation were recorded.

Statistical analyses were made with SPSS® 10.0 (SPSS Inc., Chicago, IL). Results are presented as mean (sd) or their confidence interval (CI).. Intergroup statistical analyses were performed using Student's *t*-test, and nonparametric data were analyzed using χ^2 test. Statistical significance was considered at $P< 0.05$. The power of the study was calculated based on the onset of sedation time. Setting a significance level of $P = 0.05$, it was calculated that a group size of 30 patients allowed detection of a difference of 4 min between groups with a power of 100%.

RESULTS

In Group D, dexmedetomidine was effective in 78.5% of cases; 21.5% of patients required additional medications. Side effects occurred in approximately 25% of cases, bradycardia (3.9%) and hypotension (18.4%) that resolved spontaneously.

In group P, the onset of sedation, recovery, and discharge time were significantly shorter than in group D ($P< 0.05$). 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 ($P> 0.05$)

MAP, HR, and RR were not statistically different between groups before sedation. MAP and HR decreased significantly from baseline during sedation in both groups ($P< 0.001$). HR at 10, 20, 25 min was significantly more rapid in group P than in group D, and MAP at 10, 15, 20, 35 and 50 was lower in group P than group D; however, these differences were not clinically significant. MAP in group P decreased below 20% from baseline only at 50 min. [Fig 1 & 2] Bradycardia was not observed in any child. The maximum decreases in MAP during sedation in groups D and P were 17% and 21%, where the maximum decreases in HR during sedation were 15% and 17%, respectively. The RR was statistically significantly lower in group P than group D but these differences were not clinically significant. [Fig 3], and the maximum decreases in RR during sedation in groups D and P were 8% and 17%, respectively. [Table 2]

No side effects such as nausea, vomiting, or dysphoria were observed in either group during or after sedation. However, desaturation was observed in 4 children of group P in whom Spo_2 decreased below 93% during MRI examination. In these children, oxygen desaturation was treated with chin lift, temporary cessation of the propofol infusion, and oxygen supplementation via facemask. (Fig 3)

Recovery of full responsiveness, the primary outcome variable, after dexmedetomidine-midazolam was significantly greater than that after propofol by 50% or 15 min ($P< 0.05$). This accounted for the excess time in the PACU after dexmedetomidine-midazolam administration compared with propofol. Once discharged from the PACU though, the times to discharge from the hospital for both treatment groups were similar. 100% of the children in both treatments completed their MRI scans without interruption or interventions (i.e., no failures) and without complications. Heart rate and systolic blood pressure changes were transient and statistically significant, but not of sufficient magnitude to warrant interventions.

Table 1
Patient biophysical profile, Duration, Type, and Quality of Magnetic Resonance Imaging Procedures

	Group D (n=30)	Group P (n=30)
Age (yr)	4+-1.88	3+-2.03
Weight (kg)	14+-4.14	14+-4.57
Sex (Male/Female)	17/13	10/20
Presedation behavior score		
Undistressed (1 & 2)	22	20
Distressed (3 & 4)	8	10
Duration of cranial MRI (min)	22+-7.14	25+-10.14
Quality of MRI		
1	19	20
2	6	7
3	5	3
Inadequate sedation	5	3
Onset of sedation (min)	11+-4.00	4+-1.94 (P<0.01 between groups)
Recovery time(min)	27+-19.05	18+-4.72 (P,0.05 between groups)

Table 2
Hemodynamic and Respiratory Changes During Study Drug Infusion

Time (min)	Group D (n = 30)			Group P (n = 30)		
	MAP (mm Hg)	RR (bpm)	RR (breath/min)	MAP (mm Hg)	RR (bpm)	RR (breath/min)
Baseline	83 ± 7.92†	110±12.09†	25±3.96†	82± 7.69†	114±8.96†	24±3.67†
5	77 ± 8.42	104± 13.01	24 ± 3.89	73 ± 8.71	109 ± 9.27	22 ± 4.32*
10	75 ± 9.06	97 ± 13.69	23 ± 4.72	70 ± 8.69*	104 ± 9.26*	21 ± 4.35*
15	74 ± 9.87	97± 12.61	24± 4.27	68 ± 7.50*	102± 9.55	21 ± 4.35*
20	74 ± 8.59	95± 12.88	24 ± 3.75	69 ± 6.81*	102± 9.89*	21 ± 4.35*
25	72 ± 10.60	93 ± 11.81	23± 3.82	68 ± 7.07	101 ± 10.53*	20± 4.45*
30	70 ± 7.29	95± 12.90	24 ± 3.04	67 ± 7.56	99 ± 10.40	20 ± 4.33*

35	74 ± 9.34	97± 12.59	24 ± 3.20	67± 5.94*	98± 9.45	20 ± 4.01*
40	72 ± 9.87	96 ± 14.03	24 ± 3.73	68± 8.85	97± 8.16	20 ± 3.97*
45	70± 7.83	96 ± 11.71	24 ± 3.68	67 ± 8.75	96± 8.30	20 ± 4.03*
50	69 ±6.22	96 ± 11.42	24 ± 3.29	65± 8.33*	95± 7.35	20 ± 3.89*

Values are mean ± SD
MAP + Mean arterial blood pressure; HR = Heart Rate; RR = Respiratory Rate
*P < 0.05 between group; †P < 0.01 compared with duration sedation

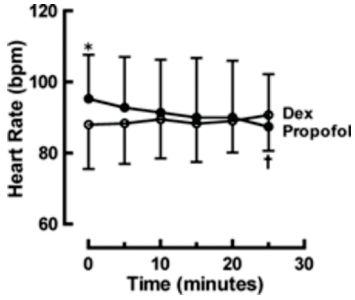

Fig 1. Effects of Dexmedotomidine and Propofol on heart rate

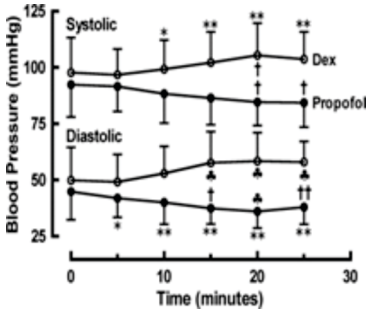

Fig 2. Effects of Dexmedetomidine and Propofol on blood pressure

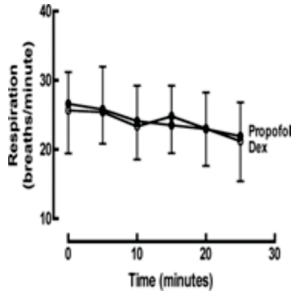

Fig 3. Effects of Dexmedetomidine and Propofol on respiration

DISCUSSION

The ideal pediatric sedative drug should not adversely affect a child's ventilation, provide hemodynamic stability and immobility, and permit easy drug titration. The sedation used should ensure rapid anesthetic induction and recovery while producing minimal side effects such as nausea, vomiting, dysphoria, or pain. [12]

The elimination half-life of dexmedetomidine in children is prolonged, lasting approximately 2 h. [13]

Inadequate sedation is the most common adverse event (5%–15%) resulting in failure (3.7%) of MRI procedures. Inadequate sedation was more frequent in hyperactive, uncooperative, and older children. [14]

Previous studies indicate that infusion doses of dexmedetomidine ($0.1–0.7\ \mu g \cdot kg^{-1} \cdot h^{-1}$) have provided effective sedation. [15,16,17,18]

Infusion of propofol at a rate of 100–150 $\mu g \cdot kg^{-1} \cdot min^{-1}$ effectively prevents movement in at least 90% of children during elective MRI. [19]

These dosage guidelines were incorporated in our studies and results similar. The inadequate sedation rate observed with dexmedetomidine and propofol in this study was also similar to that previously reported. Onset of action with propofol, discharge, and recovery times are also compatible with previously published studies. Adequate sedation was obtained with dexmedetomidine and propofol in most of the children. [20]

The onset of sedation (Ramsay score=5) time was 19 minutes for dexmedetomidine in MRI sedation. Propofol provided faster onset of sedation, recovery, and discharge times than dexmedetomidine.

Although the advantage of dexmedetomidineis hemodynamic stability, hypotension and bradycardia have been reported, particularly with large bolus dosing regimens, in patients with preexisting cardiac problems and in patients administered an initial dose in <10 minutes. [21]

Hypotension and bradycardia are observed occasionally when propofol infusion, used as a single drug, is titrated to achieve adequate sedation. It has been reported that the decrease in MAP and HR after propofol induction was 15%–31% and 17%–24%, respectively. [22,23]

In this study, an initial dose of propofol was administered for 10 minutes to match the time taken in Group D and also to minimize cardiovascular and respiratory depression related to the initial dose. MAP and HR decreased significantly after dexmedetomidineto <20% of baseline and >20% with propofol infusion.

Respiratory events make up a large proportion (5.5%) of the complications of the sedation in children. Dexmedetomidine doesnot , in clinical doses, affect RR, Spo_2, and $ETco_{2.[24]}$

However respiratory depression is more likely with large and rapid initial loading doses. [25]

Propofol may depress ventilation, suppress pharyngeal and laryngeal reflexes, and cause transient apnea, but this is not a consistent finding. In this current study, the clinically insignificant decrease in RR during dexmedetomidine or propofol infusion may have been a result of high baseline values. Although RR decreased more with propofol than dexmedetomidine, propofol was associated with more respiratory events (desaturations).

CONCLUSION

Both dexmedetomidine and propofol provide adequate sedation in most children aged 1–7 years. Both drugs prevented undesired movement in most of the children and propofol provides more rapid rates of induction, recovery, and discharge. MAP, RR and oxygen saturations are however, better preserved with dexmedetomidine, making it a good and safe alternative to propofol for MRI in selected pediatric patients.

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