ORIGINAL RESEARCH PAPER

Volume-7 | Issue-4 | April-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

TO COMPARE THE SEDATIVE EFFECT OF DEXMEDETOMIDINE IN COMPARISON TO PROPOFOL+MIDAZOLAM IN CHILDREN UNDERGOING MRI.

Anaesthesiology

Dr. Rohit Malhotra Assistant Professor, Dept. of Anaesthesia, Armed Forces Medical College Pune, Maharashtra

Dr. Santosh Kumar Singh* Assistant Professor, Dept. of Pharmacology, Armed Forces Medical College, Pune, Maharashtra *Corresponding Author

ABSTRACT

Background: The number of diagnostic and therapeutic procedures done outside the operating room has increased dramatically in recent years. While most of these procedures themselves pose little risk to the child, the administration of sedation or analgesia may add substantial risk.

Objective: To compare the sedative effects of Dexmedetomidine in comparison to Propofol+Midazolam in children undergoing MRI.

Materials and methods : A prospective, randomized, single blinded comparative study between two anaesthetic agents in a teaching hospital. A sample size of 30 patients in each group, as calculated from the power of previous studies was taken, setting a significance level of P = 0.05, it was calculated that a group of 30 patients allowed the power of the study to be 95 %.Group "P": Patients receiving Midazolam+ Propofol combination**.** Group "D": Patients receiving Dexmedetomidine alone

Results : Propofol+Midazolam provided faster onset of sedation, recovery, and discharge times than dexmedetomidine.The time to Ramsay Sedation Scale =5 was significantly higher in Group D (Mean=12.20 minutes, SD=2.01 minutes) as compared to Group P (Mean = 6.30 min, SD =1.32 minutes), P value=0.001(P value significant if <0.05).The time to Aldrete Score 10/10 was also significantly higher in Group D(Mean = 21.10 minutes SD = 1.84 minutes) as compare to Group P (Mean = 13.73 minutes SD = 1.89 minutes),P value=0.001(P value significant if <0.05).

KEYWORDS

MRI, dexmedetomidine, rescue sedation

BACKGROUND:

The number of diagnostic and therapeutic procedures done outside the operating room has increased dramatically in recent years. In children, most of these procedures require sedation, analgesia or both to achieve the degree of cooperation or immobilization. While most of these procedures themselves pose little risk to the child, the administration of sedation or analgesia may add substantial risk. This may be particularly relevant for procedures, such as magnetic resonance imaging (MRI), as it calls for deep sedation.[1] Difficulty of access is the principal argument concerning the safety of deep sedation compared to general anesthesia. Although MRI equipment is expensive, this should not be a significant consideration when safety is of paramount importance. [2] Because procedural sedation is unable to guarantee patient compliance in these cases, a deeper level of sedation is often required. [3] American Academy of Pediatrics[4], defines Deep Sedation as a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after repeated verbal or painful stimulation (eg, purposefully pushing away the noxious stimuli). As per ***American Academy of Pediatrics*** [4] the goals of sedation in the pediatric patient for diagnostic and therapeutic procedures include:

1. Guard the patient's safety and welfare
2. Minimize physical discomfort and pain
3. Control anxiety, minimize psychological trauma, and maximize the potential for amnesia
4. Control behavior and/or movement to allow the safe completion of the procedure
5. Return the patient to a state in which safe discharge from medical supervision, as determined by recognized criteria, is possible

The success of sedation for MRI has typically been 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. [5] Therefore, appropriate drugs need to be selected, administered, and titrated to achieve these objectives. [6] Although many healthy young children have been managed by radiologists and nursing with oral or IV sedation [7], the efficiency of this technique is poor and the failure rate, particularly in children who are cognitively challenged, is substantial. Historically, chloral hydrate, fentanyl, midazolam,pentobarbital and propofol have been the drugs of choice in radiology departments. These drugs most commonly administered have half-lives which approach 24 h and have been associated with prolonged recovery times and sedation-related morbidity[8-15]Contraindications to sedation exist and include: [16,17]

1. Potential airway obstruction—for example, sleep apnoea
2. Respiratory centre abnormalities—for example, brain stem tumours respiratory centre desensitised to carbon dioxide—for example, conditions with chronically raised paco2
3. Renal or hepatic dysfunction leading to altered drug kinetics
4. Conditions in which a rise in paco2 would be detrimental—for example, raised intracranial pressure
5. Conditions with high risk of pulmonary aspiration of gastric contents.

OBJECTIVE: To compare the sedative effects of Dexmedetomidine in comparison to Propofol+Midazolam in children undergoing MRI.

PLACE OF STUDY: The study was carried out at the MRI Centre of a large tertiary care teaching hospital after obtaining clearance from the hospital institutional ethics committee. Children between the age groups 1 Month - 12 Yrs undergoing elective MRI under anaesthesia at a tertiary level hospital.

INCLUSION CRITERIA

1. Written and informed consent
2. 1 Month – 12 Yrs
3. ASA physical status I or II

EXCLUSION CRITERIA

1. Age <1 Month & > 12 Yrs
2. Congenital Heart Disease
3. A recent Upper Respiratory Tract Infection, Pneumonia or episode of Acute Severe Asthma in the proceeding 4 weeks
4. Recent use of Digoxin,Alpha 2 Agonist or Psychotropic medications
5. Allergies to the study drugs
6. Predicted difficult airway
7. Active, uncontrolled GERD
8. Recent use of study drugs in the last 30 days
9. Small duration scans < 50 minutes

STUDY DESIGN: A prospective, randomized, single blinded comparative study between two anaesthetic agents in a teaching hospital.

SAMPLE SIZE: A sample size of 30 patients in each group, as

calculated from the power of previous studies was taken, setting a significance level of P = 0.05, it was calculated that a group of 30 patients allowed the power of the study to be 95 %.

Group "P": Patients receiving Midazolam+Propofol combination
Group "D": Patients receiving Dexmedetomidine alone

RANDOMIZATION: Randomization was done using the sealed envelope technique; the subject/guardian picked a pre-sealed envelope before the procedure. The envelope was not opened in the presence of subjects/guardians. After opening the envelope secretly, the patient was allocated to either the "P" or the "D" group. The parents/guardians of the patient were not aware of the group allocation.

METHODOLOGY

1. Parents/Guardian were briefed and written informed consent obtained.
2. Intravenous access was obtained in the ward.
3. Pre-procedural Baseline Monitoring was done with HR,SpO_2,RR.
4. NPO Guidelines which were followed prior to MRI are:

Child > 3 Yrs – NPO for Solid & Milk X 08 Hrs
Child < 3 Yrs – NPO for Solids & Milk X 06 Hrs

Water & Clear liquids to allowed up to 2 Hrs before the procedure.

If the procedure was delayed IV fluids will administered in the Pre Anaesthesia Care Unit at the MRI Centre.

5. Drugs were administered on the scan table as follows:

a. Premedication:
   i. Inj Glycopyrolate 10 mcg/kg
   ii. Inj Midazolam 70 mcg/kg (only in Group P)

b. Group D-Dexmedetomidine
   i. Loading Dose - 1 mcg/kg over 10 min
   ii. Maintenance Infusion – 0.5 mcg/kg

c. Group P-Propofol
   i. Loading Dose – 2 mg/kg over 10 min
   ii. Maintenance Infusion – 50 mcg/kg/min

6. Procedure was started only after a Ramsay Sedation Scale 5 has been achieved. 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 loud noises or 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.
7. If a Ramsay score of 5 was not achieved after 25 min of study drug infusion IV, infusion rate was increased to a desired effect (maximum 0.7 mcg/kg/min in Group D or 80 mcg/min/kg in Group P).
8. **Rescue Sedation**
   a. If patient movements were observed during the imaging process, an additional supplementary bolus dose of midazolam 0.05 mg/kg in both the groups was administered, and the continuous infusion dose of the study drug was increased to 0.7 mcg/kg/min in Group D and to 150 mcg/kg/min in Group P.
9. Inadequate sedation was defined as difficulty in completing the procedure as a result of the child's movement during MRI examination.
10. Patients were allowed to breathe spontaneously without an artificial airway throughout the procedure. If the SpO2 level decreased below 93% for 30 s the imaging process was interrupted and the patient was taken out of the MRI tunnel. After airway patency was assessed, the neck was extended slightly and oxygen was administered via facemask, and the study drug infusion was discontinued temporarily.
11. The observer recorded the heart rate, respiratory rate, SpO2, every 5 min during the procedure. The observer also recorded all complications and side effects during or after the anesthetic.
12. The anesthetic was continued for upto 60 min and stopped. Care was taken to include patients with a scan duration approximating 60 minutes. This was for ease of the study. The smaller duration scans were excluded from this study.
13. The time intervals from the termination of the anesthetic until spontaneous eye opening, recovery of full responsiveness (based on a modified Aldrete score of 10/10) and discharge from PACU were recorded.

Table 1: Modified Aldrete Score

CATEGORY	SCORE	DESCRIPTION
Activity	2	Able to move 4 extremities voluntarily or on command
	1	Able to move 2 extremities voluntarily or on command
	0	Unable to move extremities voluntarily or on command
Respiratory	2	Able to breathe deeply and cough freely
	1	Dyspnoea or limited breathing
	0	Apnoeic
Circulation	2	Heart Rate +/-20% preanesthetic level
	1	Heart Rate +/-20%–49% preanesthetic level
	0	Heart Rate +/- 50% preanesthetic level
Consciousness	2	Fully awake
	1	Arousable on calling
	0	Not responsive
Oxygen saturation	2	Able to maintain saturation of 95% on room air
	1	Needs oxygen supplementation to maintain saturation of 95%
	0	Oxygen saturation +/-95% on supplemental oxygen

Statistical analysis:

- The information was collected using a structured questionnaire and information entered in computer software. Nominal data were presented as number (N) and percentage (%). Continuous variables (e.g. age, weight, heart rate, respiratory rate etc) were expressed as mean and standard deviation (SD).
- ***Chi-Square test*** was applied for comparison of nominal data.
- For continuous variable, ***Unpaired t test*** *was applied to compare between groups (Propofol Vs Dexmedetomidine).* ***Paired t test*** was applied to compare within group findings *(Pre-Vs Post).* Additional parametric as well as non-parametric analysis of the data was performed as deemed essential. p value of < 0.05 was considered as statistically significant. The analysis of the data was performed using Microsoft excel and SPSS. A total of 60 patients were included in the study and randomized into two groups viz Propofol (Group P) and Dexmedetomidine (Group D). No patient was excluded in the study. Final analysis of 60 patients was done. (Fig 1)

Fig 1: Flow diagram of patient distribution

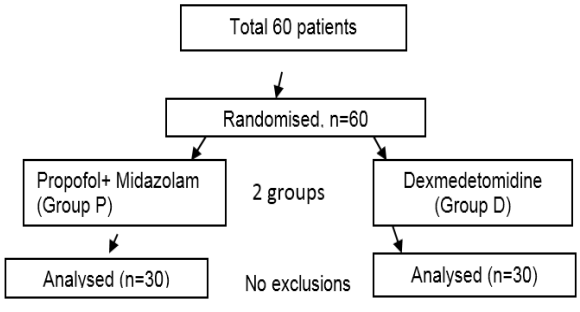

Table 2: Comparison of demographic variables between Group P & Group D. Un-paired t test is applied. P value is significant if < 0.05.

Parameter	Group P (n=30)		Group D (n=30)		Significance (P value)
	Mean	SD	Mean	SD	
Age	4.64	3.16	4.88	2.83	0.76
Weight	17.62	6.00	19.33	5.84	0.27

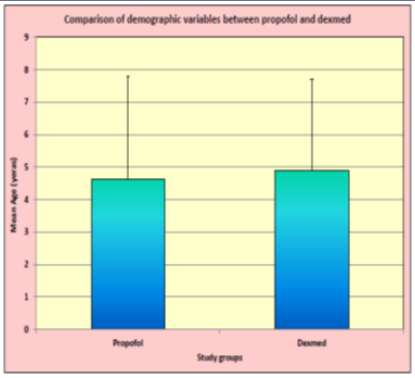

Fig 2 : No significant demographic difference between 2 groups

Table 3 : Comparison of induction and recovery between Group P & Group D. Un-paired t test is applied. P value is significant if < 0.05.

Parameter	Time points	Group P (n=30)		Group D (n=30)		Significance (P value)
		Mean	SD	Mean	SD	
Time to Ramsay sedation scale (min)	-	6.30	1.32	12.20	2.01	0.001
Time to Aldrete score(min)	-	13.73	1.89	21.10	1.84	0.001

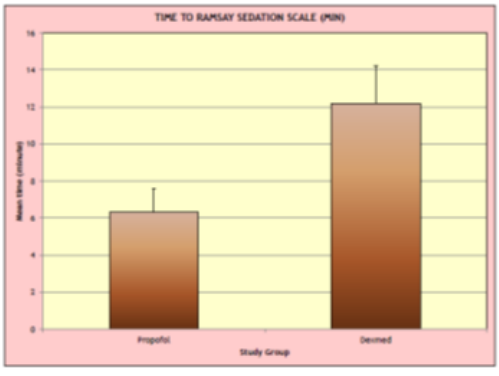

Fig 3 : The time to achieve a Ramsay Sedation Scale of 5 was significantly higher in the Group D as compared to Group P.

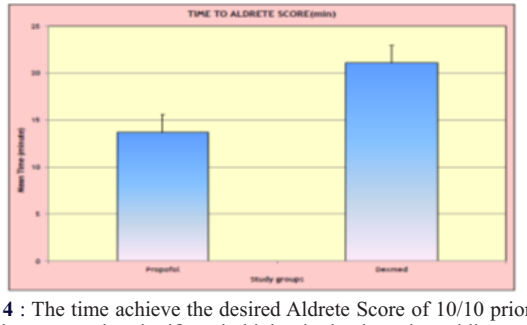

Fig 4 : The time achieve the desired Aldrete Score of 10/10 prior to discharge was also significantly higher in the dexmdetomidine group (Group D) as compared to the propofol+midazolam group (Group P).

Results :

Our results indicate that the patients' demographic were not statistically different between groups. **(Table 2) (Fig :2)** Both groups had adequate procedural sedation (RSS=5) for MRI scan and 100 % of the children in both the groups completed their scan without any interruption, interference or any complications. In a previous study [23], we noted that the onset of sedation time was 19 minutes for dexmedetomidine in MRI sedation. In this study, the faster onset of sedation time(Mean=12.20 minutes, SD=2.01 minutes) could be explained by the fact that we accepted the Ramsay score of 5 as the time to onset of sedation as opposed to the accepted Ramsay score in the previous study. [21] In our study, Propofol+Midazolam provided faster onset of sedation, recovery, and discharge times than dexmedetomidine.The time to Ramsay Sedation Scale =5 was significantly higher in Group D (Mean=12.20 minutes, SD=2.01 minutes) as compared to Group P (Mean = 6.30 min, SD =1.32 minutes), P value=0.001(P value significant if <0.05).**(Table 3) (Fig : 3)** The time to Aldrete Score 10/10 was also significantly higher in Group D(Mean = 21.10 minutes SD = 1.84 minutes) as compare to Group P (Mean = 13.73 minutes SD = 1.89 minutes),P value=0.001(P value significant if <0.05).**(Table 3) (Fig :4)** Previous studies indicate that infusion doses of Dexmedetomidine (0.2-0.7 mcg/kg/min) have provided effective procedural sedation (RSS=5) although with a minimal scan failure rates. [19,20,22] However no incidence of inadequate sedation was noted with Dexmedetomidine in our study as compared to previous studies. This could be explained by the fact we started with the loading dose of Dexmedetomidine (1mcg/kg/min) which was followed by higher doses of continuous infusion of 0.5 mcg/min/kg instead of a lower dose used in the previous few studies(starting does 0.2mcg/kg/min, titrated to effect) that too with or without a loading dose of Dexmedetomidine. Similarly propofol infusion (50-100 mcg/kg/min) with midazolam premedication (70 mcg/kg i.v. stat) was also found to have provided effective and adequate procedural sedation (RSS=5).[3,18,24] which corroborates with previous studies.The doses (of Propofol and Dexmedetomidine for infusion) used in our study were similar to these previous studies.[3,18,24] In both the groups there was no requirement of supplemental sedation or increasing the infusion rate. No other side effects or complications were attributed to either anaesthetic in this study.

Conclusion :

Both Dexmedetomidine alone (Group D) & the combination of Propofol+Midazolam (Group P) provided adequate conditions for MRI without failures in our study or any requirement of supplemental sedation.

- Combination of Propofol+Midazolam provided statistically significant rapid rates of anaesthetic induction when compared with Dexmedetomidine.
- Recovery to full responsiveness after Dexmedetomidine was statistically significantly prolonged.
- Although time required for induction and recovery are higher with Dexmedetomidine, the better therapeutic index of Dexmedetomidine gives it an advantage over combination of Propofol+Midazolam.

Limitation of the study :

There were minor limitations noted in the study. The MRI scans with a longer duration (approximately > 45 minutes) were chosen. Moreover the infusion was given for exact 60 minutes duration only after which it was stopped. This was done for the convenience of the analysis. This lead to exclusion of scan which were deemed to have smaller duration. This might have lead to a selection bias. Another limitation was that we did not monitor the blood pressure before, during or after the scan. Paediatric patients are more dependent on heart rate than on blood pressure to maintain cardiac output, hence monitoring of blood pressure would have been inconsequential. Moreover adding another parameter would have made the statistical analysis more complex.

Declaration by the author : Nil
Source of funding : Nil

REFERENCES

1. Malviya S, Voepel-Lewis T, Eldevik OP, Rockwell DT, Wong JH, Tait AR. Sedation and general anaesthesia in children undergoing MRI and CT: adverse events and outcomes. Br J Anaesth 2000;84:743–8
2. Lawson GR. Sedation of children for magnetic resonance imaging. Arch Dis Child 2000;82:150 –3.
3. Hasan RA, Shayevitz JR, Patel V. Deep sedation with propofol for children undergoing ambulatory magnetic resonance imaging of the brain: Experience from a paediatric intensive care unit. Pediatr Crit Care Med 2003;4:454–8.
4. American Academy of Paediatrics Committee on Drugs. Guidelines for monitoring and management of paediatric patients during and after sedation for diagnostic and therapeutic procedures. Paediatrics 2006:118:2587-2602.
5. Bluemke DA, Breiter SN. Sedation procedures in MR imaging: safety, effectiveness, and nursing effect on examinations. Radiology 2000;216:645–52
6. Dial S, Silver P, Bock K, Sagy M. Paediatric sedation for procedures titrated to desired degree of immobility results in unpredictable depth of sedation. Pediatr Emerg Care 2001;17:414 –20.
7. Sury MR, Hatch DJ, Delley T, Dicks-Mireaux C, Chong WK. Development of nursing-led sedation service for paediatric magnetic resonance imaging. Lancet 1999;953:1667–71.
8. Dalal PG et al. Sedation and Anaesthesia protocols used for magnetic resonance imaging studies in infants: provider and pharmacologic considerations. Anesth Analg 2006; 103: 863–868
9. Frush DP, Bisset GS 3rd, Hall SC. Paediatric sedation in radiology: the practice of safe sleep. AJR Am J Roentgenol 1996; 167:1381–1387.
10. Karian VE et al. Sedation for paediatric radiological procedures:analysis of potential

causes of sedation failure and paradoxical reactions. Pediatr Radiol 1999; 29: 869–873.
11. Mason KP et al. Sedatives used in paediatric imaging: comparison of IV pentobarbital with IV pentobarbital with midazolam added. AJR Am J Roentgenol 2001; 177: 427–430.
12. Ross AK et al. Moderate sedation for MRI in young children with autism. Pediatr Radiol 2005; 35: 867–871.
13. Chung T et al. The use of oral pentobarbital sodium (Nembutal) versus oral chloral hydrate in infants undergoing CT and MR imaging – a pilot study. Pediatr Radiol 2000; 30: 332–335.
14. Greenberg SB et al. High-dose chloral hydrate sedation for children undergoing MR imaging: safety and efficacy in relation to age. AJR Am J Roentgenol 1993; 161: 639–641.
15. Mason KP et al. Infant sedation for MR imaging and CT: oral versus intravenous pentobarbital. Radiology 2004; 233: 723–728.
16. Hollman GA, Elderbrook MK, Van Den Lagenberg B Results of a paediatric sedation program on head MRI scan success rates and procedure duration times. Clin Pediatr 1995;34:300–5
17. The Association of Anaesthetists of Great Britain & Ireland. MRI-Update-Safety in Magnetic Resonance Unit. The Association of Anaesthetists of Great Britain & Ireland,2010.http://www.aaagbi.org/publications/guidelines/docs/magnetic_resonance_unit.pdf
18. Frankville DD, Spear RM, Dyck JB, et al. The dose of propofol required to prevent children from moving during magnetic resonance imaging. Anesthesiology.1993;79 :953– 958
19. Nichols DP, Berkenbosch JW, Tobias JD, et al. Rescue sedation with dexemdetomidine for diagnostic imaging: a preliminary report. Paediatr Anaesth 2005;15:199–203
20. Berkenbosch JW, Wankum PC, Tobias JD, et al. Prospective evaluation of Dexmedetomidine for noninvasive procedural sedation in children. Pediatr Crit Care Med. 2005;6:435–439
21. Koroglu A, Demirbilek S, Teksan H, et al. Sedative, haemodynamic and respiratory effects of Dexmedetomidine in children undergoing magnetic resonance imaging examination: preliminary results. Br J Anaesth. 2005;94:821–824
22. Tobias JD, Berkenbosch JW, Russo P. Additional experience with dexmedetomidine in paediatric patients. South Med J2003;96:871–5.
23. Lubisch N, Roskos R, Berkenbosch JW, et al. Dexmedetomidine for procedural sedation in children with autism and other behavior disorders. Pediatr Neurol. 2009;41:88–94.
24. Usher GA, Kearney RA, Tsui BCH. Propofol total intravenous anaesthesia for MRI in children. Paediatr Anaesth 2005;15:23– 8.