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Original Article

Anaesthesia Section

# Comparison between Dexmedetomidine and Propofol for MRI Brain in Paediatric Patients- A Randomised Clinical Trial

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## ABSTRACT

**Introduction:** Dexmedetomidine is an $\alpha_2$ agonist that causes deep sedation after bolus, and can be given as infusion while performing Magnetic Resonance Imaging (MRI) brain in paediatric patients. There are reports of increased incidences of bradycardia and hypotension with prolonged recovery when it was used in high doses of 2-3 mcg/kg bolus. Lower dose of bolus may enhance the recovery profile and reduce the chances of bradycardia, while maintaining the efficacy of sedation.

**Aim:** To compare the induction of sedation, haemodynamics stability, success rate of the scan, efficacy of the drug and recovery profile of low dose dexmedetomidine and propofol infusion for MRI brain in paediatric patients.

**Materials and Methods:** This randomised clinical trial was conducted at Lokmanya Tilak Municipal General Hospital and Medical College, Sion Mumbai, Maharashtra, India, from November 2012 to April 2014. Total 70 American Society of Anaesthesiologist (ASA) grade I and II children aged 1-7 years posted for elective MRI brain were included in the study. Patients were divided into two groups i.e, dexmedetomidine group (n=35) and propofol group (n=35). Intranasal midazolam 0.2 mg/kg was given. Children in dexmedetomidine group were induced with 1 mcg/kg dexmedetomidine given over 10 minutes and maintained with dexmedetomidine at 1 mcg/kg/hr. Patients in propofol group received propofol bolus 2 mg/kg and infusion at 100 mcg/kg/min.

**Results:** The MRI scan was completed in 34 (97.1%) and 35 (100%) of children in dexmedetomidine and propofol group, respectively. Time for complete recovery was 68.9±31.5 and 40.1±23 minutes in the dexmedetomidine and propofol group, respectively. Time for induction was 12.4±3.53 and 6.46±1.9 minutes in the dexmedetomidine and propofol group, respectively. Bradycardia was observed in 8 (22.9%) patients in dexmedetomidine group. Haemodynamic parameters were with 20% of baseline in both the groups.

**Conclusion:** Propofol is a better anaesthetics in terms of recovery and induction time when used as an infussion for MRI brain in paediatric patients. Dexmedetomidine has a high incidence of bradycardia so requires a more vigilant monitoring.


**Keywords:** Haemodynamic parameters, Hypotension, Magnetic resonance imaging, Neonates, Recovery

## INTRODUCTION

Magnetic Resonance Imaging (MRI) brain in children is indicated for evaluation of convulsion, meningitis, encephalitis, hypoxic brain injury, trauma. Most of these children are very young sometimes even neonates. Neonates rarely require sedation, but from infancy the child's movements and anxiety towards strangers increases. For MRI brain the head is covered in a shield which makes it necessary for deep sedation before positioning. The high decibel noise created by MRI magnet, warrants deep sedation throughout the MRI study. Time taken for MRI brain is 25-40 mins. Any movement during scaning may lead to an entire sequence being repeated. Scan sequences may vary between 3-7 mins. All these factors make drugs that can be given as infusions ideal for MRI scanning in children. Previously, drugs like thiopentone and propofol have been compared for procedural sedation in MRI and Computed Tomography (CT) [1,2]. Though propofol showed early recovery, it was associated with more incidence of desaturation. A report in 2010 considered thiopentone inappropriate for sedation and dexmedetomidine convenient for sedation in patients without cardiac risk [3]. Dexmedetomidine is an $\alpha_2$ agonist that causes deep sedation after bolus and can be given as infusion. It creates a natural sleep like state [4]. Major advantage is the lack of respiratory depression and maintenance of a patent airway [5,6]. Reduction in cerebral metabolic rate and cerebral blood flow created by dexmedetomidine provides neuroprotection [7,8]. Raise in intracranial pressure is not observed with dexmedetomidine [9].

These merits make dexmedetomidine an ideal drug for paediatric MRI brain. Rapid recovery is mandatory in order to discharge the children on the same day. But dexmedetomidine has unpredictable success rate if used as sole agent [10]. Increased incidence of bradycardia and hypotension with prolonged recovery were observed when it was used in high doses like 2-3 mcg/kg bolus [11].

To restrict these limitation, in this study, a lower dose of 1 mcg/kg bolus followed by 1 mcg/kg/min infusion of dexmedetomidine was used. Similar doses have been compared with propofol earlier [12,13]. These studies show a longer recovery profile, lower incidences of desaturation, but higher bradycardia rate in the dexmedetomidine group. The propofol dose used, 3 mg/kg, may be responsible for higher incidences of desaturation. In another study, intravenous access was established after inhalational induction and intravenous midazolam was combined with dexmedetomidine. The combination of midazolam with dexmedetomidine may have prolonged the recovery in the dexmedetomidine group with increasing safety of MRI compatible anaesthesia machines, MRI scanning as a diagnostic tool in paediatric age group is increasing. In our institute 12-14 paediatric cases are done in routine hours with limited staff and securing an intravenous access in the holding area with intranasal premedication is time saving. Baseline sedation calms the child and helps parental separation. With a secure intravenous access, lower doses of propofol or dexmedetomidine are required for induction and maintainance of sedation. It was hypothesised that there would be lower incidence of respiratory depression, bradycardia and faster recovery in both the groups. A meta-analysis done in 2015 recomends higher quality Randomised Clinical Trial (RCT) of dexmedetomidine, with a focus on the recovery time [14]. This prospective RCT will add valued data to the present literature.

The primary aim of the study was to compare the recovery time of low dose dexmedetomidine and propofol for MRI brain in paediatric

patients. Induction time, success rate of the scan, efficacy of the drug and haemodynamic stability were the secondary outcomes.

## MATERIALS AND METHODS

This randomised clinical trial was conducted at Lokmanya Tilak Municipal General Hospital and Medical College, Sion Mumbai, Maharashtra, India, from November 2012 to April 2014. Institutional Ethics Committee approval was taken (IEC/30/12). This trial is registered under Clinical Trial Government with ID number NCT02776189.

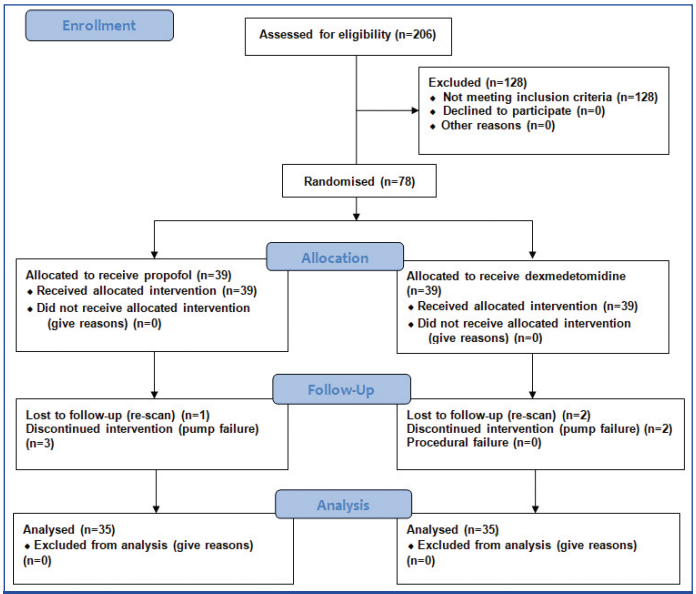
**Sample size calculation:** Sample size was calculated based on a published data [13]. The mean time for full recovery of dexmedetomidine was 44.2±18 minutes. The mean time for full recovery of propofol was 29.7 minutes. A total of 64 patients were required for a probability of 90% (β=0.9) that the study will detect a difference in mean at a two-sided 0.05 significance level (α=0.05). Taking a 10% attrition in follow-up, 70 patients were included in the study.

**Inclusion and Exclusion criteria:** All patients with American Society of Anaesthesiologist (ASA) grade I and II children aged 1-7 years posted for elective MRI brain were included in the study. Children with congenital heart disease, upper respiratory tract infection, patient on digoxin or β-blockers, children allergic to propofol or dexmedetomidine and children with body mass index >35 kg/m2 were excluded from the study.

Total 206 patients were evaluated for eligibility, 128 were eliminated {scans other than brain (n=100) and age criterion (n=28)}. Finally, 78 patients were enrolled, but eight were excluded from analysis due to infusion pump malfunction (n=5) and for being taken back for more MRI sequences within half an hour of their scan (n=3). Thus, the data of 70 children was analysed.

### Study Procedure

Computerised randomisation was used to allot children into two groups receiving either dexmedetomidine or propofol [Table/Fig-1]. Patients were evaluated on Outpatient Department (OPD) bases. On the day of MRI, nil by mouth status was confirmed and consent taken from parents. In the preanaesthesia room, weight and vitals of the children were recorded. They were given intranasal midazolam 0.2 mg/kg. After 15 minutes, intravenous line was secured. In the MRI console all children received intravenous glycopyrrolate 0.004 mg/kg.




**[Table/Fig-1]:** Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

- **Dexmedetomidine group:** Children in dexmedetomidine group were induced with bolus dose of 1 mcg/kg dexmedetomidine given over 10 minutes and maintained with dexmedetomidine infusion at 1 mcg/kg/hr.
- **Propofol group:** Patients in propofol group received propofol bolus of 2 mg/kg and infusion at 100 mcg/kg/min.

Oxygen was supplemented by face mask. After the child was sedated, position was given with a shoulder roll and head ring. Ear piece, cardioscope, respiration strap, pulse oximeter and head shield were then applied. The hands were immobilised with sand bags over a thick blanket.

**Primary parameters:**

1. Recovery time was the time in minutes from stoppage of infusion to full recovery, that is patients achieving a modified Aldrete score of 10 [15].
2. Time for spontaneous eye opening was the time in minutes from stoppage of infusion till the child opens the eye spontaneously.

**Secondary parameters:**

1. Time of induction was the time in minutes from start of either dexmedetomidine or propofol till child was sedated enough to allow positioning and the start of MRI scan.
2. Any additional drugs used at induction apart from the protocol were noted. Additional drug was intravenous ketamine 0.5 mg/kg.
3. Efficacy of the drugs was the percentage of patients sedated solely with dexmedetomidine or propofol and not requiring additional drugs. Number of procedural disruptions due to child awakening were recorded. Two or more awakening were taken as failure of sedation. Rescue drug was a combination of 0.5 mg/kg propofol and 0.01 mg/kg midazolam given if the patient moved during procedure.
4. Adverse events were defined as bradycardia, if heart rate <60 beats per minute, blood pressure >20% of preprocedure value and desaturation <96%. A follow-up was done after 24 hours.

## STATISTICAL ANALYSIS

All variables were analysed as continuous variable and expressed as the mean±SD. Significance was assessed at 5% level of significance. Student t-test (two tailed, dependent) was used to find the significance of study parameters on continuous scale within each group. The p-value <0.05 was considered statistically significant.

## RESULTS

The demographic data, weight, median age of children in each group and reason for scan is presented in [Table/Fig-2].

| Variables | Dexmedetomidine group (N=35) | Propofol group (N=35) |
|---|---|---|
| Age (years), mean (SD) | 3 (2.5) | 3 (4) |
| Weight (kg), mean (SD) | 12 (5.75) | 12 (5.4) |
| Female | 19 (54.3%) | 14 (40.0%) |
| **Reasons of scan** | | |
| Indications for MRI brain | 15 (42.8%) | 11 (31.4%) |
| Convulsion | 2 (5.71%) | 3 (8.57%) |
| Febrile convulsion | 5 (14.2%) | 3 (8.57%) |
| Spasticity | 8 (22.8%) | 7 (20%) |
| Learning disability | 0 | 2 (5.71%) |
| Microcephalus/hydrocephalus | 1 (2.85%) | 2 (5.71%) |
| Meningitis/encephalitis | 1 (2.85%) | 2 (5.71%) |
| Trauma | 1 (2.85%) | 2 (5.71%) |
| Brain screening for TB spine | 2 (5.71%) | 3 (8.57%) |

**[Table/Fig-2]:** Basic characteristics of children who were sedated with dexmedetomidine or of children who were sedated with propofol for MRI brain and the reason for scan.
Values are median (Inter-quartile ratio, IQR) for age, mean ( standard deviation) number (proportion)

The MRI scan was completed in 34 (97.1%) and 35 (100%) of children in dexmedetomidine and propofol group, respectively. One patient in dexmedetomidine group had preprocedure excessive cry, needed extra drug at induction and had three episodes of intraprocedural awakening and vomiting. The scan was postponed

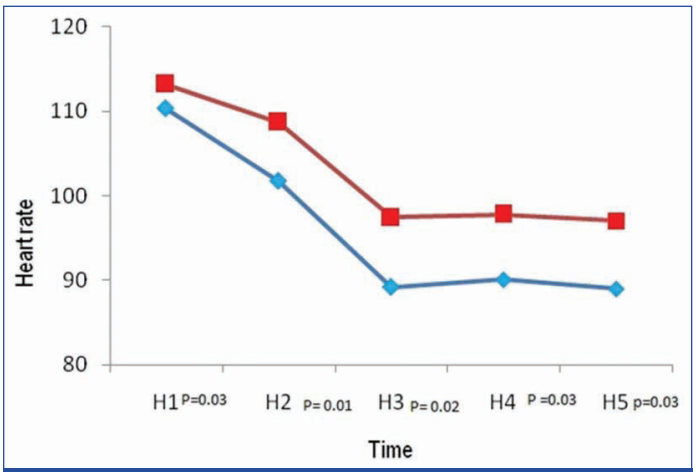
and patient observed till full recovery. This patient was included in analysis as the protocol dose of dexmedetomidine had been administrated. Efficacy of dexmedetomidine and propofol for sedating children for MRI brain scan without additional drugs was 82.9% and 68.6% group respectively. The difference in number of patients requiring additional drugs at induction between the two groups was clinically insignificant (p-value=0.16). One episode of intraprocedural awakening was seen in 3 (8.6%) and 4 (11.4%) patients in dexmedetomidine and propofol group respectively. The difference in episode of awakening between the two groups was clinically insignificant (p-value=0.43).

Time for induction, total MRI duration, time for spontaneous eye opening, time for full recovery and incidence of bradycardia are given in [Table/Fig-3]. The time for induction, spontaneous eye opening and complete recovery was significantly longer in dexmedetomidine group than in the propofol group.

| Parameters | Dexmedetomidine group (Mean±SD) | Propofol group (Mean±SD) | p-value |
|---|---|---|---|
| Time for induction (min) | 12.4±3.53 | 6.46±1.9 | <0.0001 |
| Duration of MRI scan (min) | 32.5±12.8 | 31.5±10.1 | 0.71 |
| Time for spontaneous eye opening (min) | 56.4±32.2 | 30.3±25.3 | <0.0001 |
| Efficacy of drug (n,%) | 29±82.9% | 24±68.6% | 0.16 |
| Time for recovery (min) | 68.9±31.5 | 40.1±23.0 | <0.0001 |
| Bradycardia incidence (n,%) | 8±22.9% | 0 | 0.011 |

**[Table/Fig-3]:** Comparative primary and secondary outcome data in both groups. p-value<0.05 was considered as statistically significant

Bradycardia was observed in 8 (22.9%) patients in dexmedetomidine group, among which 6 (17.1%) children had bradycardia in the recovery room. No patient in propofol group had bradycardia. No patient had desaturation, apnoea or abnormal breathing. The heart rate trends are shown in [Table/Fig-4]. The changes in systolic and diastolic pressures are shown in [Table/Fig-5,6]. There was no significant difference in both the groups regarding Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) changes. The SBP and DBP were within 20% of baseline in both the groups.

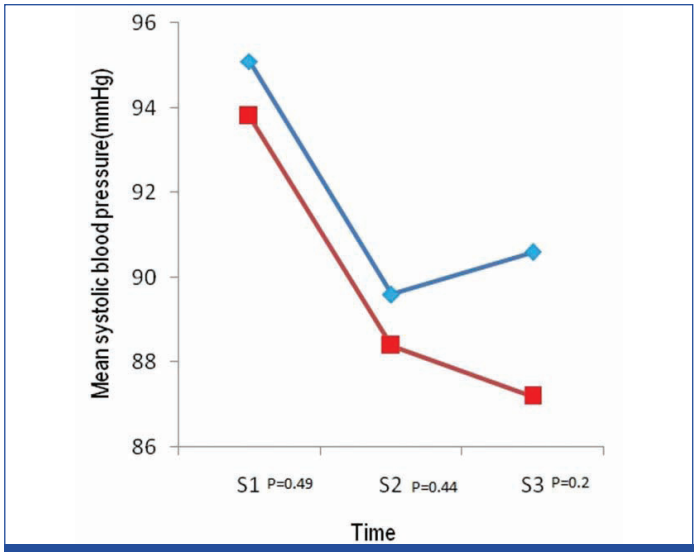



**[Table/Fig-4]:** Mean heart rate, at H1 (baseline), H2 (post sedation), H3 (post induction), at H4 (during procedure) and at H5 (post scan), of children sedated with dexmedetomidine (•) and propofol (•).

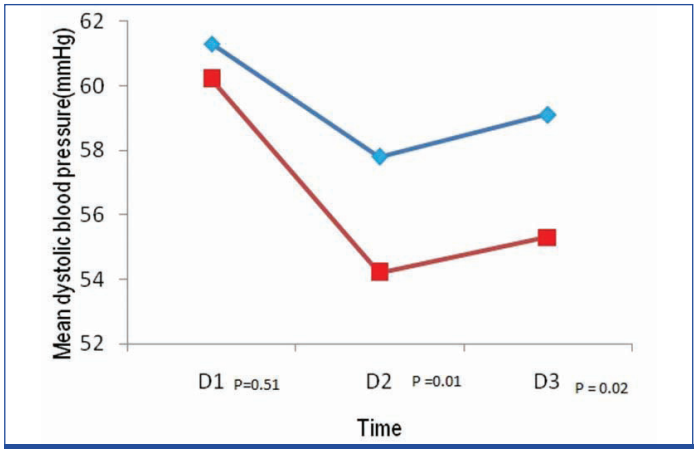
On follow-up after 24 hours, one child in dexmedetomidine group had fever and vomiting, one child in propofol group had rash. Parents of three children in dexmedetomidine group complained that the child was excessively drowsy for 2-3 hours.

## DISCUSSION

Time for spontaneous eye opening of children sedated with dexmedetomidine was longer as compared to propofol in this study. Time for recovery was when the children achieved a modified




**[Table/Fig-5]:** Mean systolic blood pressure, at S1 (aseling), at S2 (post sedation) and and S3 (post scan), of children sedated with dexmedetomidine (•) and propofol (•).




**[Table/Fig-6]:** Mean Dystolic blood pressure, at D1 (baseline), D2 (post sedation) and at D3 (post scan), children sedated with dexmedetomidine (•) and propofol (•).

Aldred score of 10 and could be discharged home. The time for complete recovery in the dexmedetomidine group was 28 minutes more than in the propofol group. Propofol had the advantage of early recovery. Parents of three patients in the dexmedetomidine complaint of excessive sleepiness even after discharge highlighting the clear headed recovery of propofol. Studies, show a lesser recovery period of dexmedetomidine of 35-40 minutes [12,13]. Though these studies have used the same bolus of 1 mcg/kg of dexmedetomidine as in the present study, these used a lower infusion rate of 0.5 mcg/kg/min for maintenance. These studies reported a higher failure rates with dexmedetomidine. Recent studies are in agreement with the present study results and give a mean recovery time of dexmedetomidine as 62-71 minutes [16,17]. The infusion dose in these studies is the same as in the present study. If the bolus dose and infusion rate is increased ,the recovery time of dexmedetomidine may reach 100 minutes [17]. Overall, this study like the previous studies confirm that dexmedetomidine when compared to propofol has a longer recovery period.

Time for induction of sedation in children with dexmedetomidine was 12.4±3.53 minutes as compared to 6.46±1.90 minutes when sedated with propofol in this study. Some studies have shown a longer induction time but these studies have induced children with sevoflurane and then started the study drug [12,14]. Though induction time has been reported, it becomes difficult to accept it as absolute induction time of dexmedetomidine. This study protocol was designed to cater to a high flow in paediatric MRI wherein 10-14 children are anaesthesised per day. Securing an intravenous line under premedication reduces intraprocedural uncertainties. As an advantage, the present protocol truly compares induction time of propofol and dexmedetomidine. Similar induction time

has been reported by studies where induction is purely by the dexmedetomidine or propofol drugs but all the studies including the present prove a shorter induction time of propofol when compared to dexmedetomidine [12,17].

Efficacy of dexmedetomidine and propofol for sedating children for MRI brain scan without additional drugs or as sole agents was 82.9% and 68.6% group, respectively, in this study. The efficacy of dexmedetomidine was higher than propofol though the difference was statistically insignificant. Contradictorily, previous study have reported this high success rate only with high doses of dexmedetomidine and higher additional drug requirement for sedation with dexmedetomidine in comparison with propofol [16]. When used as sole agent even in high doses of 2 mcg/kg/min, dexmedetomidine had an additional drug requirement of 29% [18]. The baseline intranasal sedation may be responsible for less additional drug requirement in this study.

The study highlightens a few facts. One being that MRI scan is possible in 99% of patients with low dose of dexmedetomidine with premedication and higher boluses of 2-3 mcg/kg are not required. Whether the children are premedicated and induced with dexmedetomidine or induced with sevoflurane and maintained with dexmedetomidine, the recovery time is approximately 68-70 mins. This probably reflects the elimination half-life of dexmedetomidine [19,20].

There were no events of desaturation in this study and none of the patients in either group needed airway manipulation. This may be due to the proper positioning given after induction of sedation with a small role under the shoulder. The other reason may be the low dose of propofol used for maintenance. Desaturation and airway manipulation has been reported when propofol is used in higher doses [1,2].

The present study recorded a 22.9% incidence of bradycardia in children sedated with dexmedetomidine, 17.1% children in the dexmedetomidine group had bradycardia in the recovery room. Total 16% occurrence of bradycardia has been reported in another study [11]. This study as well as the previous studies are not powered to measure the true incidence of bradycardia with dexmedetomidine [11,18]. The high incidence of bradycardia is a point to note as dexmedetomidine is still a drug for which prospective trials are limited in children.

A recent meta-analysis concludes propofol to be encouraged in paediatric patients undergoing MRI but at the same time admits limited number of studies included in this meta-analysis [21]. Thus, this study will add value to existing literature.

### Limitation(s)

The intraoperative end-tidal carbon dioxide and blood pressure could not be monitored due to lack of equipment. So, the blood pressure monitoring was done intermittently and not continually.

## CONCLUSION(S)

After premedication with intranasal midazolam sedation of children for MRI brain scan is possible with moderate doses of dexmedetomidine and propofol. Propofol is a better anaesthetics in terms of recovery and induction time. Dexmedetomidine has a high incidence of bradycardia so requires more vigilant monitoring.

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