Original Article

Comparison of effects of dexmedetomidine with ketofol and ketofol alone on quality of sedation in pediatric patients undergoing magnetic resonance imaging: A prospective randomized controlled double-blind trial

ABSTRACT

Background and Aim: Patient movement during magnetic resonance imaging (MRI) is the most frequent cause of artifacts and poor scan quality. Children cannot lie still. Thus, anesthesia is required to keep the child calm and immobile. This randomized double-blinded clinical trial compares the clinical effects of the addition of dexmedetomidine as premedication with ketofol on the quality of sedation. We hypothesized that the addition of dexmedetomidine would improve the quality of sedation.

Methods: A total of 132 children aged 6 months to 10 years were randomized into groups DK (dexmedetomidine–ketofol) and K (ketofol). DK received an intravenous bolus of dexmedetomidine (0.5 mcg/kg) as premedication 10 minutes prior. Both the groups were induced with ketofol (0.5 mg/kg), and sedation was maintained with propfol infusion (100 mcg/kg/min). The primary objective was the quality of sedation as assessed by the University of Michigan Sedation Scale. Image quality, requirement of rescue propofol dose, recovery, and adverse events were also studied. Data are given as median [interquartile range (IQR)] or frequency.

Results: All 132 children completed MRI scans. The DK group showed significantly better quality of sedation, 71% versus 47% of children, a median difference of 1 (-0.569 to -0.0969), $P < .005$, a better quality of scan, a reduced number of additional doses of propofol, and a decreased total dose of propofol. Hemodynamic parameters and recovery times for the two groups were similar. There were no significant side effects in both groups.

Conclusion: The quality of sedation and the quality of the MRI scan are greatly improved by administering dexmedetomidine (0.5 mcg/kg) 10 minutes before to induction. Additionally, this technique decreases the need of propofol and gives better hemodynamic stability without delaying the recovery time.

Key words: Conscious sedation, dexmedetomidine, ketofol, magnetic resonance imaging, sedation

Introduction

A high-quality magnetic resonance imaging (MRI) scan, which is free from artifacts, requires the patients to remain

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immobile.[1,2] Pediatric patients are unable to lie still. Thus, sedation is frequently necessary to keep the child calm and still until the imaging is complete.[3] Many medications, including propofol, ketamine, and thiopentone, are frequently used for sedation in MRI rooms independently or in combination.

Ketofol, a combination of ketamine and propofol in the same syringe, is being utilized frequently for procedural sedation in the pediatric population. By enhancing safety and efficacy and allowing for a reduction in the quantity of propofol required to achieve sedation, the antagonistic hemodynamic and respiratory actions of each medication may boost the value of this pharmacological combination. They are frequently utilized for pediatric procedures such as cardiac catheterization, interventional radiology, oncological treatments, hematological procedures, and MRI sedation.[4-7]

Dexmedetomidine is a selective alpha-2 adrenergic agonist which has been used for MRI sedation as a sole agent as well as an adjuvant with other agents in pediatric patients. It has been found to decrease not only propofol requirement but also the need for airway support and provide better hemodynamic stability.[8,9]

The addition of dexmedetomidine with ketofol has never been compared in pediatric patients for MRI sedation. We hypothesized that a bolus of dexmedetomidine with ketofol induction would provide better sedation quality throughout the procedure and reduce propofol requirement during the maintenance of sedation. Comparing the impact of adding dexmedetomidine to ketofol on the quality of sedation was the primary goal of our study. The scan's quality, frequency of rescue doses of propofol needed to maintain sedation, the length of sedation, the time to recover, and any side effects were secondary outcomes.

Materials and Method

This prospective double-blinded randomized controlled trial was carried out in a tertiary care hospital. After approval from the institutional ethics committee and informed written consent from parents, a total of 132 children aged between 6 months and 10 years, belonging to the American Society of Anesthesiologists (ASA) physical status class I and II, and scheduled for MRI on an outpatient basis, were included in this study. We registered the study prospectively at the clinical trial registry of India (CTRI: www.ctri.nic.in).

Parents' refusal, patients with raised intracranial pressure, seizures, difficult airway, laryngomalacia, neck mass, congenital heart disease, gastroesophageal reflux disease, renal or hepatic dysfunction, any psychiatric disorder, allergy or contraindication to study drugs, patients requiring intubation, and an anticipated scan time less than 30 min and more than 1.5 hours were excluded from the study.

All children underwent preanesthesia checkups before the scan. They were kept fasting before procedure, according to pediatric fasting guidelines. The baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR), and oxygen saturation (SpO_2) were recorded upon arrival at the prescan room.

Enrolled children were randomly assigned in 1:1 ratio into two groups using a block randomization technique. An equal number of blocks of size 4 were used to divide all the patients into two groups (Group DK and Group K). A sealed opaque envelope was used for allocation concealment and opened just before shifting the child inside the MRI room. Parents and anesthesiologist fellows involved in patient recruitment, sedation, and data collection remained blinded till the study was completed.

Group DK (n = 66) received an infusion of dexmedetomidine at 0.5 mcg/kg over 10 minutes before induction by infusion pump.

For Group K (n = 66), a dummy syringe containing normal saline by infusion over 10 minutes was used before induction by infusion pump to maintain observer blindness.

After premedication, the child was taken into the MRI room, and SpO_2, ECG, and NIBP monitoring were attached. Injection Ketofol was prepared as a 1:1 mixture of 10 mg/ml of ketamine and 10 mg/mL propofol, drawn into a single 10 mL of syringe. Each milliliter of this solution contains 5 mg of ketamine and propofol. Induction of sedation was done with this solution of ketofol at a dose of 0.5 mg/kg. The sedation level was assessed by using the University of Michigan Sedation Scale (UMSS).[10]

UMSS = 2 to 3 was considered an optimum level of sedation for starting the scan. If this level was not achieved, an additional bolus of propofol (0.5 mg/kg) was given to achieve the target sedation score. A maintenance infusion of propofol was started via an MRI-compatible infusion pump immediately after the desired UMSS score at 100 mcg/kg/min. The child was then positioned on the scan table, a shoulder roll was placed to maintain patent airway, and oxygen at 2 liter/min was given to all the children via a face mask. After ensuring the patency of the airway and adequacy of respiration, the scan was allowed to start.

One anesthesia resident not involved in the study was inside the MRI room during the procedure. In case of child movement or signs of light anesthesia (tachycardia, tachypnea) a bolus dose of IV propofol (0.5 mg/kg) was given as rescue sedation, and if there was a sign of deep sedation or hemodynamic instability, the rate of infusion was decreased by 10% of the original rate. After completion of the scan, propofol infusion was stopped, and the child was shifted to the postanesthesia care unit (PACU). The number of rescue bolus doses of propofol administered during scanning was recorded.

A pediatric anesthesia fellow performed all these cases. Desaturation was defined as $SpO_2 < 95\%$.

The following parameters were measured during the procedure by a blinded observer.

1. Vitals parameters HR, SpO_2, NIBP, and RR were recorded every 5 minutes till the end of the procedure in the MRI suite and then in PACU.
2. Duration of MRI scan
3. Quality of sedation assessed by a blinded anesthesiologist
   Excellent sedation – When there was no patient movement during the scan, no rescue dose of propofol was required.
   Good sedation – When there was a minor movement of the patient, two or less than two rescue propofol doses were required
   Poor sedation When there was a significant patient movement, more than two rescue doses of propofol were required.
4. Quality of scan – Assessed by a single-blinded radiologist
   Excellent – No motion artifacts
   Good – Minor motion artifacts that do not require a repeat scan
   Poor – Major motion artifacts causing scan causing or a repeat of one or more scan sequences
5. Number of additional rescue propofol doses required
6. Total amount of propofol used during the procedure
7. Duration of sedation (time in minutes from the beginning of infusion of the drug to the point at which infusion was stopped)
8. Recovery time (time in minutes from the stoppage of infusion to the PACU recovery score over 8 out of 10)
9. The discharge time (when the child attains a modified Aldrete score ≥9) was also noted.
10. Side effects, including vomiting, respiratory depression, apnea, hypotension, hypertension, bradycardia, tachycardia, desaturation events, and allergic reaction, if any, were recorded.

Statistical analysis

The sample size was calculated assuming that 75% of children achieved a sedation score of 3 in the case group and 50% in the control group with 80% power and 5% type 1 error; the sample size was found to be 60 in each group. After an adjustment of 10% dropout, the sample size in each group is 66.

Data collected during the study were compiled using Microsoft Excel spreadsheets. The normality of data was tested with Kolmogorov–Smirnov one-sample test. Data were presented as median (IQR) (range) for ordinal variables, quantitative variables, and absolute numbers or percentages for categorical variables. Mann–Whitney u-test was used to analyze ordinal and continuous data. Chi-square test was used for categorical data.

Results

One 50 patients were screened for eligibility, of which parents of 14 children refused to participate and four did not meet the inclusion criteria [Figure 1]. A total of 132 children were recruited for the study and randomly allocated to two groups. The median age, weight, and sex ratio among the two groups were comparable. The distribution of patients according to the site and duration of MRI was comparable in both groups [Table 1].

The median difference in induction dose of ketofol used in the two groups was 0 ($P = 0.407$), and the difference in requirement of maintenance infusion of propofol was also insignificant. However, the need for rescue doses and the total dose of propofol in the K group was more than those of the DK group, that is, $P = 0.000$ and 0.048, respectively. Duration of sedation and recovery time remained comparable in the two groups [Table 2].

Quality of sedation was better in the DK group compared to the K group ($P = 0.005$), with 71% of patients having excellent sedation in the DK group versus only 47% of

Table 1: Demographic profile, site, and duration of MRI among the groups

Variables	Group DK ($n=66$)	Group K ($n=66$)	*P*
Age*	36 (12-63) (5-120)	24 (12-60) (5-120)	0.394
Sex **			
Male	46 (69.69%)	41 (62.12%)	0.463
Female	20 (30.30%)	25 (37.87%)	
Weight* (kg)	13 (8.85-18) (3.2-25)	13 (10.7-16.2) (7-33)	0.407
Site **			
Brain and spine	5	6	
Brain	58	60	
Abdomen and Pelvis	3	0	
Duration of MRI* (min)	40 (40-45) (35-55)	43 (40-45) (35-55)	0.073

*Values are expressed as median (IQR) (range). ** Values are expressed as frequency/percentage. DK: dexmedetomidine + ketofol; K: Ketofol; IQR: interquartile range

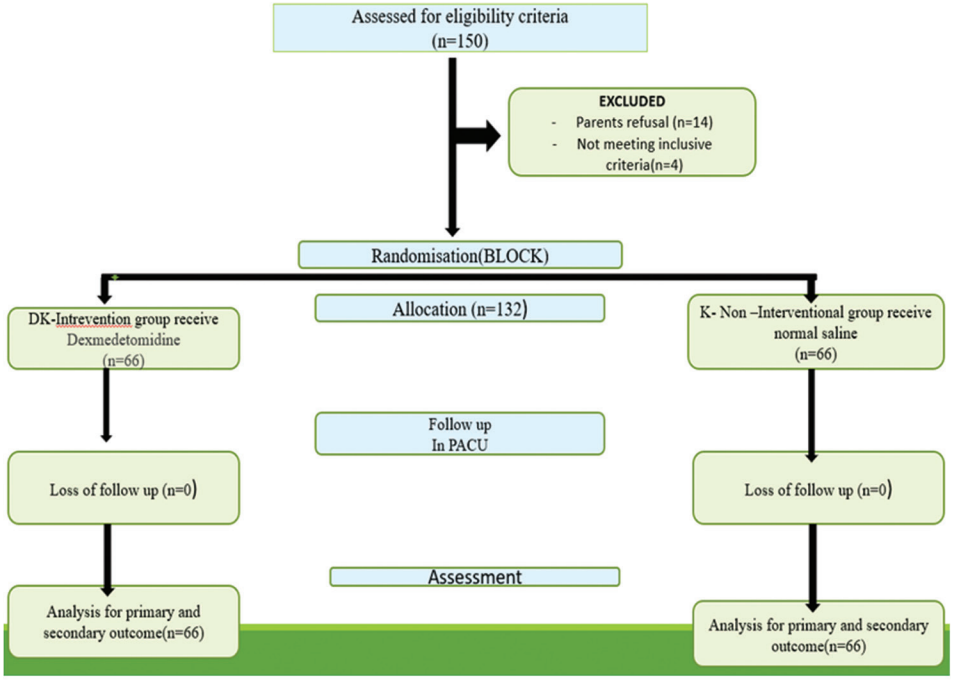

Figure 1: CONSORT diagram showing patients' enrolment flowchart

patients in the K group. The quality of MRI scan was also reported to be better in the DK group as against the K group ($P = 0.001$) [Table 3] [Figure 2].

Three patients in group DK developed bradycardia, requiring an injection of glycopyrrolate (10 mcg/kg). None of the patients in the K group had any such hemodynamic perturbations. However, hemodynamic parameters remained stable with no statistical difference in the two groups [Figure 3].

Discussion

The primary objective of our study was to compare the effect of the addition of dexmedetomidine to ketofol on the quality of sedation. In this study, we found that a single dose of dexmedetomidine (0.5 mcg/kg) given 10 minutes before induction significantly improved the quality of sedation in the DK group. It was observed that 71% of patients experienced excellent sedation in the DK group compared to only 47% in the K group. Dexmedetomidine, as a premedication, enhanced not only the quality of the sedation but also the quality of the scan. The number of rescue propofol doses needed and the total propofol given were also significantly less in the DK group.

As a common practice at our institution, we administer ketofol at induction, followed by propofol infusion for sedation in MRI. The rationale for using ketofol is to decrease the dose of propofol to maintain spontaneous respiration and avoid hypotension produced by a larger bolus dose of propofol.

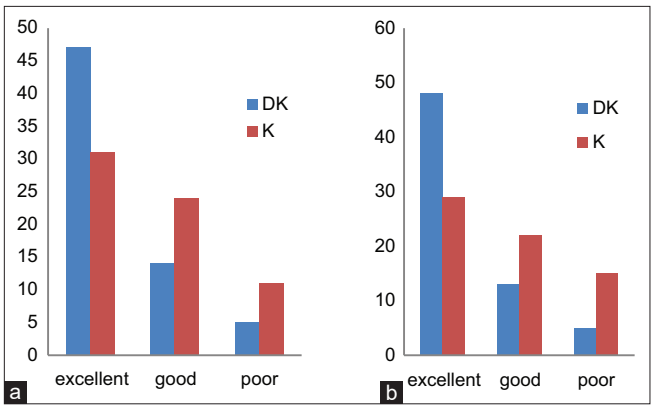

Figure 2: Distribution of quality of sedation (a) and quality of MRI Scan (b) between the two groups

Quality of sedation was categorized into excellent, good, and poor based on the additional propofol bolus required to maintain a UMSS of 2–3. It was found that 47 patients had excellent, 14 had good, and five had poor quality sedation in the DK group compared to 29 with excellent, 22 with good, and 15 with poor quality sedation in the K group. This was found to be statistically significant, with a *P* value of 0.005. Dexmedetomidine, used as a premedication, improved the sedation, which improved the quality of the scan, with only five patients requiring a repeat scan in the DK group as against 15 in the K group.

Koroglu *et al.*[11] compared dexmedetomidine and propofol for quality of sedation and quality of scans in 40 kids. They found that 63% of dexmedetomidine-treated and 66% of

Table 2: Comparison of induction, maintenance, rescue doses, total dose of propofol and duration of sedation, and recovery time given between the study groups

	DK (*n*=66)	K (*n*=66)	Median difference	95% CI	*P*
Induction dose (mg)	6.5 (4.42-9.0) (1.6-12.5)	6.5 (5.37-8.12) (3.5-16.5)	0	(-1.37 to 0.55)	0.407
Rescue dose of propofol (mg)	0 (0.0-5.25) (0.0-33.0)	10.50 (0.0-16.63) (0.0-50)	10.5	-10.862 to -4.305	0.000
Maintenance dose of propofol (mg)	81 (60-108) (19.20-172.50)	82.7 (70.25-105.75) (43.20-272.0)	1.75	(-20.6 to5.96)	0.277
Total dose of propofol (mg)	84 (60-110) (19.2-185)	92.5 (75-119.25) (43-321)	8.5	-30.01 to -0.168	0.048
Duration of sedation (min)	42 (41-46) (36-57)	44 (42-46) (36-56)	2	-1.925 to 0.865	0.085
Recovery Time (min)	27 (24-32) (19-39)	26.5 (25-29.5) (22-39)	-0.5	-0.852 to 0.034	0.055

Values are expressed as median (IQR) (range). Abbreviation: CI Confidence Interval

Table 3: Comparison of quality of sedation and quality of scan among the groups

	DK	K	Median difference (95% CI)	*P*
Quality of sedation*				
Excellent	47 (71.2%)	31 (47%)	1 (-0.569 to -0.0969)	0.005
Good	14 (21.2%)	24 (36.4%)		
Poor	5 (7.6%)	11 (16.4%)		
Median (IQR) Range	1 (1-2) (1-3)	2 (2-3) (1-3)		
Quality of scan*				
Excellent	48 (72.7%)	29 (43.93%)		0.001
Good	13 (19.6%)	22 (33.33%)		
Poor	5 (7.5%)	15 (22.7%)		
Median (IQR) Range	1 (1-2) (1-3)	2 (1-2) (1-3)	1 (-0.6849 to -0.1938)	

*Values are expressed as frequency/percentage

propofol-treated kids got excellent scans. The probable reason for equivocal scan quality in both groups could be the fact that the dose of dexmedetomidine that they used was 1 mcg/kg/min, followed by 0.5 mcg/k/h for the whole duration of the scan and 3 mg/kg dose of propofol at induction, followed by 100 mcg/kg/min in the other group. Drug doses used in both groups were significantly higher than we used in our study. Kamal *et al*.[12] investigations also showed no difference in the quality of scans produced by dexmedetomidine and propofol. The findings of Schmitz *et al*.[13] also contrast our results in that although there was a slight improvement in picture quality between the propofol mono group and the ketamine propofol group, this difference was not statistically significant.

Similarly, Sethi *et al*.[14] compared three doses of propofol infusion (100/75/50 mcg/kg/min) to assess the recovery time, quality of scans, and additional propofol requirement during the scan. They found no difference in the quality of the scan. The reason for this is that they gave midazolam 0.05 mg/kg i.v. to the child 30 min before the scan, and the induction dose of propofol and ketamine used for sedation was higher (1 mg/kg each) than what we used.

Our rationale for the lower dose of dexmedetomidine (0.5 mcg/kg) as a premedication was to improve sedation with minimal patient movement, reducing the need for additional propofol boluses to maintain an adequate level of sedation. Our study showed a propofol-sparing effect with low-dose dexmedetomidine (0.5 mcg/kg bolus given as premedication). The median difference in propofol requirement was 8.5, with total propofol given in the DK group of 84 (60–110) mg versus 92.5 (75–119.25) mg in the K group ($P = 0.048$). [Table 2].

Nagoshi *et al*.[9] and Schmitz *et al*.[13] had results similar to our study. Nagoshi *et al*.[9] found that the requirement of total propofol was significantly higher in group P compared to the D + P group, 215.0 (182.6–253.8) versus 147.6 (127.5–180.9), respectively, with a median Difference of -67.8, 95% CI = -80.6, -54.9; $P < .0001$. In the study conducted by Schmitz *et al.*,[13] median propofol requirement in propofol

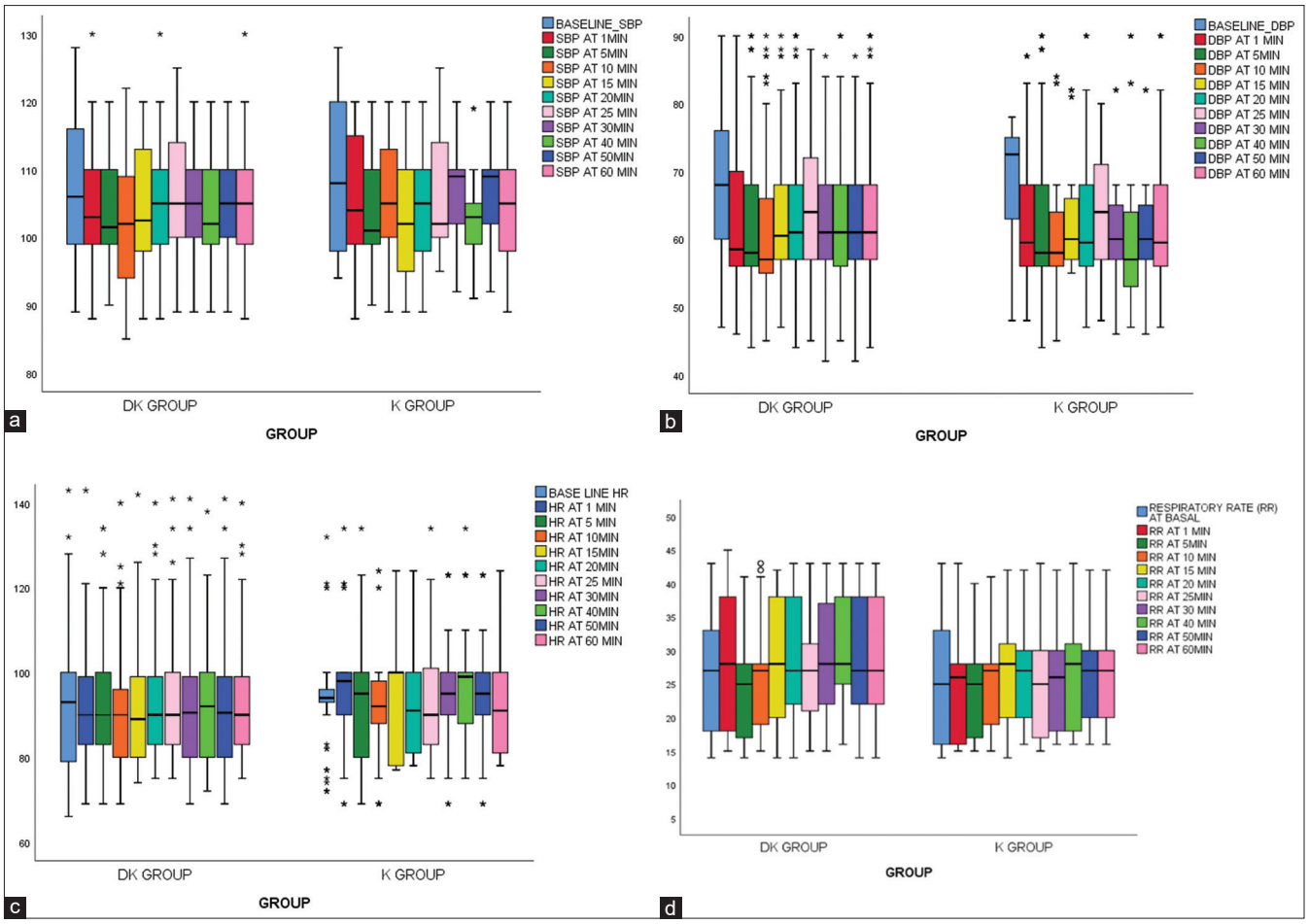

Figure 3: Graphical representation of SBP, DBP, HR, and RR at various time intervals among patients in the DK and K groups. (a) systolic blood pressure comparison at various time form interval between group, (b) diastolic blood pressure comparison at various time interval between group, (c) heart rate comparison at various time interval between group, (d) respiratory rate comparison at various time interval between group

mono group and ketamine propofol group was 165 (119-238) and 90 (69-135), respectively, with *P* value < .001.

In our study, hemodynamic variables, SBP, DBP, SPO2, and RR, remained comparable in both groups at baseline and at different intervals during the scan. This means both groups had stable vitals and did not show any specific difference. The maintenance of SBP and DBP at all points of time is because we used ketofol for the induction of sedation. Both ketamine and propofol counteract each other's side effects and maintain stable blood pressure.

In the study conducted by Sethi *et al*.,[14] a statistically significant difference was observed in the SBP at 20, 25, and 30 min between the groups; other hemodynamics, including DBP, HR, and SPO2, were comparable at various points of time between the groups with no significant variation seen within each group.

In contrast to our result, Abdellatif *et al*.[15] found that groups differ significantly in hemodynamics. The blood pressure and heart rate were the highest in the dexmedetomidine-ketamine group, while the hemodynamic condition was least affected by the dexmedetomidine-propofol group.

Also, Kamal *et al*.[12] observed that the mean HR was found to be lower in Group D as compared to Group P, the difference being significant up to 25-minute intervals ($P < 0.05$). The mean SBP decreased in both the groups from the baseline, the difference being highly significant up to 35 min in Group D and up to 30 min in Group P. This study also contradicts our findings. Koroglu *et al*.[11] found a highly significant decrease in HR from the baseline during sedation with dexmedetomidine as well as propofol ($P < 0.001$).

In groups DK and K, the median (IQR) MRI time was 40 (40-45) minutes and 43 (40-45) minutes, respectively. ($P = 0.073$). In a study conducted by Schmitz, where the median (IQR) duration of an MRI scan in the propofol-mono group and ketamine-propofol group was 57 (48-67) and 58 (48-70) min, respectively, there was no significant difference in the

duration of MRI between the two groups, and it was similar to our study.[13]

The recovery times in our study were 27 (24-32) and 26.5 (25-29.5) minutes for groups DK and K, respectively. ($P = 0.978$), indicating that the recovery times of the two groups were comparable. However, Schmitz *et al*.[13] found that recovery time is quicker in the ketamine-propofol group, 38 (22-65) versus 54 (37-77) minutes in the propofol group, $P = 0.001$.

Similarly, Sethi *et al*.[14] showed that the group receiving 50 mcg/kg/min of propofol had a shorter discharge time in comparison with the group which received 100 mcg/kg/min of propofol. These results are different from our findings.

Strength of study

Our study was double-blinded. Parents and anaesthesiologist fellows involved in patient recruitment, sedation, and data collection remained blinded, making our results more validated. A limited number of observers were chosen for evaluating the result measures to interindividual variation. Data were collected every 5 minutes to increase the reliability of picking all the patients who developed any significant adverse event.

Limitation of study

It is a single-center study including only ASA 1/2 patients. The scoring system used to assess the quality of sedation and scan is a subjective scale and is not validated.

Conclusion

Dexmedetomidine, given as premedication at a dose of 0.5 mcg/kg 10 minutes prior to induction, improves quality of sedation and quality of MRI scan. The other significant advantage of this technique is a decreased need for additional doses of propofol and better hemodynamic stability without delaying the recovery time.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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