VOLUME - 13, ISSUE - 07, JULY - 2024 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Paediatrics

COMPARISON OF SEDATIVE AND HEMODYNAMIC EFFECTS OF PROPOFOL AGAINST MIDAZOLAM-KETAMINE COMBINATION IN CHILDREN UNDERGOING MAGNETIC RESONANCE IMAGING.

Dr. Vaibhav Chadha	MBBS, PG Resident, Department of Paediatrics, N.C Medical College and Hospital, Israna, Panipat.
Dr. Amita Yadav	MBBS, PG Resident, Department of Paediatrics, N.C Medical College and Hospital, Israna, Panipat.
Dr. Alisha Chachra*	MBBS, M.D Anaesthesia, (GMCH, Chandigarh), PDCC Onco-Anaesthesia (AIIMS, RISHIKESH) *Corresponding Author
Dr. Shreya Jamwal	MBBS, PG Resident, Department of Paediatrics, N.C Medical College and Hospital, Israna, Panipat.

ABSTRACT **Introduction-** The need for magnetic resonance imaging (MRI) in children is increasing for accurate diagnosis. Sedation is required in the pediatric population as they cannot remain stationary for a sufficient length of time, needed for the completion of the procedure. **Methods-** In this prospective single-blinded randomized study, 100 children aged 1 month to 16 years who belong to the American Society of Anesthesiologist (ASA) status 1 and 2 admitted for MRI on a daycare basis were distributed into two groups. Group A(n=50) was sedated with Midazolam – Ketamine while group B (n=50) with Propofol. The effectiveness of sedation, hemodynamics and complications during the procedure and recovery period were recorded. **Results-** In our study, 80 patients were randomized into 2 groups (Group A and Group B). Group A received midazolam and ketamine combination and group B received propofol. 2 patients were excluded from group B because of the failure of induction. The quality of MRI evaluated in the study by us using a three-point scale -namely no movement, minor movement, and major movement. 45% patients in group A and 22.5% patients in group B had no movement during the examination No patient had major movement necessitating another scan. In our study, all patients in group A were administered Midazolam at a dose of 0.15mg/kg. The mean induction dose of propofol administered to the patients of group B was significantly higher than the dose of ketamine administered to group A (1.96 ± 0.41 mg/kg vs 1.69 ± 0.45 mg/kg; p-value0.01) **Conclusions-** Midazolam-Ketamine was found to be better than single-dose Propofol in children undergoing magnetic resonance imaging.

KEYWORDS : Midazolam-Ketamine was found to be better than single-dose Propofol in children undergoing magnetic resonance imaging.

INTRODUCTION

Nowadays the need for magnetic resonance imaging (MRI) in children is increasing for accurate diagnosis and appropriate medical treatment [1]. MRI does not involve exposure to ionizing radiation so it is preferred over other imaging techniques especially in children. It also provides extensive information about anatomic structures which is important in the diagnosis of numerous diseases but it is very sensitive to motion artifacts [2] and requires patient immobility for long hours So if any movement occurs during the imaging process for one sequence, the entire sequence needs to be repeated. [3–5]sedation is required in the paediatric population as they cannot remain immobile for a sufficient length of time for a sequence to be completed. Thus necessitating the need for sedation. [6] MRI tunnel and loud noise (as much as 90 dB) generated during the imaging process is anxiety-provoking. Hence, conscious sedation may be inadequate in controlling anxiety in children to allow timely and safe completion of an MRI study.

Most children suffering from Seizures who need MRI diagnostic procedures have neurological diseases, Epilepsy, vascular malformation, or oncological tumour growth or mental retardation they have a three-time higher risk of hypoxia under sedation[7]. These facts must be taken into account when sedation or anaesthesia for MRI in children is required. In the end, however, the main goals to be achieved are maximum patient safety, successful scanning, and paramount image quality.

Thus The main goals of the pediatric sedation/general anesthesia during Imaging procedures is to gain relief of anxiety, and control of excessive movement, so as to achieve an optimal imaging to understand the course of disease under the scope.[8] The American Academy of Pediatrics (AAP) defines the goals of pediatric sedation as follows:[9,10]

- To guard the patient's safety and welfare.
- To minimize physical discomfort and anxiety.
- Minimize psychological trauma and maximize the potential for amnesia.
- To control behavior and/or movement to allow for the safe completion of the procedure.
- To return the patient to a state in which safe discharge from medical supervision is possible.

An ideal sedative should have a shorter induction time, should not cause hemodynamic instability, and more rapid discharge from the emergency room.

Several aesthetic drugs such as intravenous dexmedetomidine, midazolam, fentanyl, propofol, Ketamine, and oral chloral hydrate have been used for sedation for paediatric MRI[11,12]

The complications of deep sedation include hypotension, bradycardia apnea, airway obstruction, aspiration, and raised intracranial pressure [13]. If any complication occurs during MRI it may pose a safety risk during MRI examination as the nature of MRI not allows easy access to patients [6,16].

There has been continuous debate about the use of appropriate drugs and dosage regimens for sedation during MRI in children. Different sedation methods are being employed by different medical fraternities based on their own experiences and preferences which has led a vast number of methods and loss of uniformity in procedures, leaving a great room for error.

The purpose of this study is to evaluate the sedative effects, hemodynamic, respiratory effects, and incidence of

complications of Propofol compared with Ketamine plus Midazolam in children undergoing MRI examination.

MATERIALS & METHOD

Aim

To compare the sedative and hemodynamic effects of Propofol compared with ketamine-midazolam combination in children undergoing Magnetic Resonance Imaging.

Primary Objective

To compare the sedative effect (induction dose, additional doses required, and recovery time) of midazolam plus ketamine versus propofol in children undergoing MRI using Ramsay sedation scale.

Secondary Objective

1) Hemodynamic monitoring during and after the procedure.

Study Site: N.C Medical college and hospital, Israna, Panipat.

Time Frame: The study was carried out at N.C Medical college and hospital, Israna, Panipat, over a period of 6 months from September 2023 to February 2024.

Study Design: "A prospective single-blinded randomized comparative study"

Inclusion Criteria

Patients between the ages 1 year and 14 years who belong to the American Society of Anaesthesiologist status 1 and 2 [4,3] admitted for MRI and required sedation at N.C Medical college and hospital, Israna, Panipat.

Exclusion Criteria

1) Hemodynamically unstable patient
2) Allergy to any of the drugs studied
3) ASA status III and above, that is a patient having significant disease with significant functional disability.

Sample-size Calculation

For a comparative study design based on a simple random sample, the sample size required was calculated according to the following formula.

Formula:

$$n = \{(Z_{1-\alpha/2} + Z_{1-\beta})^2(\sigma_1^2 + (\sigma_2^2/r)\} / (\mu_1-\mu_2)^2$$

Description

n = required sample size
α = probability of type I error (usually 0.05)
β = probability of type II error (usually 0.2)
Z = critical Z value for a given α or β
r = ratio
μ = mean value for given group
σ = standard deviation for given group.

Calculation

For comparative study design concerning the previous study, we have at 95 % confidence level and 80 % normal variate for power, with a mean (SD) 1.35 (0.65) and 1.09 (0.09) for group 1 and group 2 respectively, After putting these values in above formula we get the sample size for the study. So far our required sample size was as follows by using the above formula of sample size.

n ~ 40 (each group)
Therefore, our total required sample size for the study was -80.

Methodology

Data Collection And Tools

Data was collected in Microsoft Word and Microsoft Excel

This randomized prospective single-blinded study was conducted after the approval of our Scientific and Ethics committee at NC Medical college and hospital, Israna, Panipat. The study was planned on 80 Children of age between 1 year to 14 years who were scheduled to undergo Magnetic resonant imaging for the diagnostic purpose at our institute and satisfied the inclusion and exclusion criteria after obtaining informed written consent from the parents of the children.

The patients were shifted to the MRI induction room accompanied by parents after a period of fasting as per fasting guidelines proposed by the American Society of anaesthesiologists. [14] The intravenous line was secured and monitoring lines were attached which included non-invasive blood pressure (NIBP), and pulse oximetry for SpO2 monitoring. Baseline heart rate (HR), respiratory rate (RR), NIBP, and SpO2 values were recorded.

Group A – These patients received intravenous midazolam (1 mg/ml, 5 ml or 10ml at a bolus dose 0.15 mg/kg (maximum 4 mg) along with, ketamine (50 mg/ml, 2 ml) at bolus dose 1 mg/kg intravenously. Patient responses to verbal and tactile stimuli were evaluated 2min after the administration of the drug. Ketamine 0.5 mg/kg (maximum of 2 mg/kg) was added at 2-min intervals if adequate sedation was not achieved.

Group B- These patients received intravenous propofol (Propofol, 10 mg/ml, a bolus dose of 1 mg/kg. Patient responses to verbal and tactile stimuli were evaluated 2 min after the administration of propofol. Propofol 0.5 mg/kg was added at 2-min intervals if adequate sedation was not achieved.

The effectiveness of sedation during the procedure was evaluated according to the modified Ramsay sedation score (RSS) (Table 1).

The Ramsay Sedation Scale

Clinical Score	Patient Characteristics
1	Awake; agitated or restless or both
2	Awake; cooperative, oriented, and tranquil
3	Awake but responds to commands only
4	Asleep; brisk response to light glabellar tap or loud auditory stimulus
5	Asleep; sluggish response to light glabellar tap or loud auditory stimulus
6	Asleep; no response to glabellar tap or loud auditory stimulus

A score from 1–6 was assigned. according to the response of the patient to the stimuli. A score of 5 or above indicates adequate sedation [15]. RSS of 5 or above was aimed at for a comfortable procedure in our study. The imaging was initiated when the child was well sedated. Oxygen (2 l/min) by a nasal cannula/facemask was administered to all patients during the procedure. Recovery time was the time between the start of the scan and when the patient reaches a Ramsay score of 2.

Mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO2), and respiratory rate (RR) were monitored continuously and recorded at 5-min intervals during the study period. Additional doses of Ketamine and propofol according to the group respectively at the dose of 0.5mg/kg was also administered in between in case of inadequate sedation if needed. The observer who collected data was blinded to whether the patient has received midazolam plus ketamine or propofol during magnetic resonance imaging.

The quality of the MRI examination was evaluated using a three-point scale (1 = no motion; 2= minor movement;3= major movement necessitating another scan).

Statistical Method Used for Result Interpretation

- The continuous data is shown as Mean +/- Standard Deviation and categorical data are represented as absolute numbers and percentages.
- Nominal categorical data between the groups were compared using the Chi-square test or Fisher's exact test as appropriate and used correlation coefficient to observe

the linear relationship.

- All major data analysis packages, as well as spreadsheets, such as Microsoft Excel, used as per requirement. For all statistical tests, a p-value of less than 0.05 was taken to indicate a significant difference.

OBSERVATION AND RESULTS

In this prospective study, 80 patients belonging to ASA physical status I or II who were admitted for MRI on a daycare basis were taken for study.

After enrollment, group assignments were determined by a computer-generated number sequence and were contained in sequentially numbered opaque envelopes to ensure blinding.

A total of 80 patients were randomly allocated in 2 groups.

Group A - Patients who were admitted for MRI and received midazolam plus ketamine combination for sedation were included in group A.
Group B - Patients who were admitted for MRI and received propofol for sedation were included in group B.

So total analysis was done on 80 patients -40 from group A and 40 in group B

ASA Physical Status Distribution

In our study, out of 80 patients, 22 were interpreted as ASA status 1 and 58 patients belong to ASA status 2. In patients belonging to Group A, out of 40 patients 10 (25%) were ASA status 1, and 30 (75%) were ASA status 2. In patients belonging to Group B out of 40 patients, 12 (30 %) were ASA status 1 and 28 (70%) were ASA status 2.

ASA status distribution was comparable in both groups with no significant intergroup difference (p-0.63)

Table 1. Comparison Of Asa Status Between The Groups

ASA	Group				
	Group A (n = 50)		Group B (n = 48)		p-value
	Frequency	Percent	Frequency	Percent	0.63
ASA 1	10	(25%)	12	(30%)	
ASA 2	30	(75%)	28	(70%)	

Figure 4: Comparison Of Asa Status Distribution Between Two Groups

Distribution On The Basis Duration Of MRI

The average duration of MRI in group A was 40.19 ± 18.16 min while in group B was
36.96 ± 9.79 min.

The two groups were comparable in terms of the duration of the MRI procedure. (p-0.06)

Table 2: Comparison On Basis Of Duration Of Mri Between The Groups

	Group				
	Group A (n = 50)		Group B (n = 48)		p-value
	Ketamine		Propofol		
	Mean	SD	Mean	SD	0.06
RT (min)	40.19	18.16	36.96	9.79	

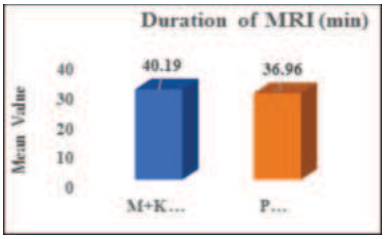

Figure 2: Comparison On Basis Of Duration Of Mri Between The Groups

Distribution Of Basis Of The Quality Of Mri Examination

The quality of the MRI examination was evaluated using a three-point scale (1 = no movement; 2= minor movement; 3= major movement necessitating another scan).

In this present study 27 (33.75) patients had no movement during the procedure. Out of which 18 patients belong to group A and 9 patients belong to group B .

53 patients had minor movement. Out of which 37 patients belong to group A and 16 patients belong to group B. No patient had major movement necessitating another scan.

Quality of MRI examination was comparable in both groups with no significant intergroup difference (p-0.55)

Comparison On Basis Of The Need For Additional Doses During The Examination

In our study, 32.5% of patients in group A required additional doses of ketamine while in group B 82.5 of patients required additional doses of propofol during the procedure.

The need for additional sedation was significantly higher in group B than group A. (P-Value<0.001)

Table 3: Comparison Of The Need For Additional Doses During The Examination

Additional	Group A (n=40)		Group B (n=40)		p-value
Doses	Frequency	Percent	Frequency	Percent	
Yes	13	32.5	33	82.5	< 0.001
No	27	67.25	7	17.5	

Recovery Time

Group A recovered with a recovery time of 47.86 ± 13.53 min and the recovery time of group B was 33.24 ± 3.94 min

The recovery time of Group A was significantly higher than that of group B (P=0.01).

Table 4: Comparison On Basis Of Recovery Time Between The Groups

	Group				
	Group A (n = 40)		Group B (n = 40)		p-value
	Ketamine+Midazolam		Propofol		
	Mean	SD	Mean	SD	0.01
RT (min)	47.86	13.53	33.24	3.94	

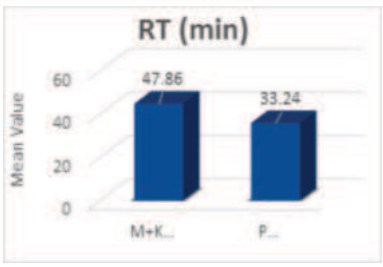

Figure 3: Comparison On Basis Of Recovery Time Between The Groups

Distribution Of Patients Based On Vital Parameters Between The Groups

Heart Rate

Mean heart rate values were found to be similar between the groups (P >0.05)

Table 5): Comparison On Basis Of Heart Rate Between The Groups

Statistics	Group		
	Ketamine + midazolam (n = 40)	Propofol (n = 40)	p-value

HR	0 mins	109.14 ± 17.84	108.71 ±16.01	0.34
	5 mins	110.44 ± 16.39	113.02 ±18.91	0.90
	10 mins	111.88 ± 17.87	108.29 ±16.12	0.38
	15 mins	117.34 ± 15.76	107.71 ±17.48	0.55
	20 mins	108.74 ± 17.32	106.77 ±16.77	0.37
	25 mins	109.5 ± 17.38	108.34 ±16.18	0.72
	30 mins	110.68 ± 16.42	107.77 ±14.28	0.56
	35 mins	109.3 ± 15.07	109.21 ±13.56	0.90
	40 mins	109.1 ± 13.91	108.9 ± 12.8	0.86

Respiratory Rate

In our study patients in both groups have been found to have a reduction in respiratory rate recorded in 5-minute intervals. Although the difference in respiratory rate reduction between the groups was not statistically significant (P >0.05).

Table 6): Comparison On Basis Of Respiratory Rate Between The Groups

Statistics		Group		
		Midazolam + ketamine (n = 40)	Propofol (n = 40)	p-value
RR	0 mins	24.56 ± 6.62	25.6 ± 5.93	0.28
	5 mins	24.21 ± 6.5	27.69 ± 5.78	0.49
	10 mins	27.42 ± 3.48	27.52 ± 5.7	0.14
	15 mins	27.45 ± 3.56	27.46 ± 5.9	0.16
	20 mins	26.13 ± 5.05	26.45 ± 6.1	0.25
	25 mins	22.05 ± 6.27	26.96 ± 5.86	0.26
	30 mins	24.43 ± 2.45	22.85 ± 5.63	0.41
	35 mins	23.01 ± 1.2	22.79 ± 5.7	0.26
	40 mins	25.44 ± 7.34	22.85 ± 5.65	0.35

Mean Arterial Pressure

In our study, although there was a decrease in mean arterial pressure in both groups, none of the patients had hypotension.

The difference in mean arterial pressure between 2 groups was not significant. (p>0.05)

Table 7): Comparison On Basis Of Mean Arterial Pressure Between The Groups

Statistics		Group		
		Midazolam + ketamine (n = 40)	Propofol (n = 48)	p-value
MAP	0 mins	63.66 ± 6.03	62.19 ± 6.52	0.32
	5 mins	61.5 ± 5.75	62.31 ± 7.22	0.26
	10 mins	64.8 ± 5.95	61.63 ± 7.17	0.27
	15 mins	64.72 ± 5.97	63.48 ± 7.09	0.31
	20 mins	66.2 ± 5.81	61.85 ± 6.75	0.28
	25 mins	65.54 ± 5.95	61.88 ± 7.04	0.13
	30 mins	63.1 ± 5.99	66.71 ± 7.08	0.20
	35 mins	62.04 ± 6.02	63.5 ± 6.78	0.21
	40 mins	65 ± 6.13	67.63 ± 6.71	0.25

Oxygen Saturation

In our study, both groups have been found to have reduction in oxygen saturations. Mean peripheral arterial oxygen saturations fluctuated between 96% and 98%.

Table 8): Comparison On Basis Of Peripheral Oxygen Saturation Between The Groups

Statistics		Group		
		M+K (n = 40)	Propofol (n = 40)	p-value
SPO2	0 mins	96± 1	98 ± 1	0.41
	5 mins	97± 2	96 ± 2	0.08
	10 mins	96 ± 2	96 ± 2	0.26
	15 mins	97± 2	95 ± 2	0.34
	20 mins	96± 2	96 ± 2	0.36
	25 mins	97± 1	96 ± 1	0.03
	30 mins	97± 1	97 ± 1	0.10
	35 mins	97± 1	97 ± 1	0.12
	40 mins	97± 2	97 ± 1	0.14

DISCUSSION

Our study aimed to compare the effects of midazolam-ketamine and propofol for sedative effect and hemodynamic parameters in children undergoing sedation for MRI.

In our study, 80 patients were randomized into 2 groups (Group A and Group B). Group A received midazolam and ketamine combination and group B received propofol. 2 patients were excluded from group B because of the failure of induction.

The quality of MRI evaluated in the study by us using a three-point scale -namely no movement, minor movement, and major movement. 45% patients in group A and 22.5% patients in group B had no movement during the examination No patient had major movement necessitating another scan.

In our study, all patients in group A were administered Midazolam at a dose of 0.15mg/kg. The mean induction dose of propofol administered to the patients of group B was significantly higher than the dose of ketamine administered to group A (1.96 ± 0.41 mg/kg vs 1.69 ± 0.45 mg/kg; p-value0.01)

Though MRI could be completed with both regimes. 32.5% of patients in group A and 82.5% patients in group B needed additional sedation during the procedure and the need of additional sedation was significantly higher in group B than group A (p-value<0.001)

To facilitate ambulatory radiological procedures in children, the anesthetic agent should facilitate rapid recovery. We observed that the recovery time of both groups following sedation for magnetic resonance imaging was 47.86 ± 13.53 min and 33.24 ± 3.94 min in group A and group B respectively. The difference between the groups was statistically significant (p-value=0.01). Hence the propofol group had a rapid awakening compared to another group.

Although we noticed a decrease in mean arterial pressure in both groups, none of our patients had hypotension while Christopher et al [16]in their study found more hypotension in the propofol group, but they used a high dose (250-300mcg/kg/min) of propofol infusion. In our study, we analyzed mean arterial pressure and the difference between 2 groups was not significant.

In our study, the difference in heart rate between both groups was not significant(P>0.05).

In our study both groups have been found to have a reduction in Respiratory rate and oxygen saturation however the difference in Respiratory rate reduction between the groups was not statistically significant (P >0.05).

Mean Peripheral arterial oxygen saturations fluctuated between 96% and 98% from the starting of the procedure to recovery. These findings are attributed to the predictable effects of the drugs. [17]

CONCLUSION

Midazolam-ketamine is found to be better than single-dose propofol in children undergoing magnetic resonance imaging. Although propofol has rapid awakening as the recovery time of midazolam ketamine is significantly higher than propofol. But propofol needs more induction dose and maintenance of sedation is a problem with single-dose propofol and patients might need additional doses during MRI. However, the results revealed no significant difference between the two groups in terms of quality of MRI and hemodynamic parameters. Further studies need to be done to substantiate our findings.

Limitations

- First, the drugs were used only for the MRI procedure.

Meaningfully, the dosages used in the study may be inadequate in interventional procedures.

- Secondly, Exclusion of patients with an ASA physical status III or higher mainly because the suitability of the regime in these children needs further evaluation.
- Lastly, we could not monitor sedation level during imaging, by bispectral index (BIS), because of the non-availability of MRI compatible Bispectral index monitor and we monitored sedation level during imaging by Ramsay sedation score which has subjective variations.

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