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Original Research Article

EFFICACY AND SAFETY OF PAEDIATRIC SEDATION AND ANALGESIA FOR COMMON DIAGNOSTIC AND THERAPEUTIC PROCEDURES, ADMINISTERED BY PAEDIATRICIANS

Miryala Mahesh Nagendra[1], Usha Rani D[2], Varsha Suresh Ahirrao[3], Srinivasa K[4], Premalatha R[5], Rajesh K S[6]

[1]*Junior Resident, Department of paediatrics, MVJMC & RH, Bangalore, Karnataka, India.*
[2]*Assistant Professor, Department of Paediatrics, MVJMC & RH, Bangalore, Karnataka, India.*
[3]*Professor & Head of the Unit, Department of Paediatrics, MVJMC & RH, Bangalore, Karnataka, India.*
[4]*Professor & Head of the Unit, Department of Paediatrics, MVJMC & RH, Bangalore, Karnataka, India.*
[5]*Professor & Head of the Department, Department of Paediatrics, MVJMC & RH, Bangalore, Karnataka, India.*
[6]*Assistant Professor, Department of Paediatrics, MVJMC & RH, Bangalore, Karnataka, India.*

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Corresponding Author:
Dr. Usha Rani D,
Assistant Professor, Department of Paediatrics, MVJMC & RH, Bangalore, Karnataka, India.
Email: drusha83pd@gmail.com.

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ABSTRACT

Background: Increasing awareness regarding need of sedation and analgesia for various diagnostic paediatric procedures for better outcome and quality care has led to an increase in the use of paediatric sedation and analgesia (PSA) by paediatricians in their routine practice. Hence, this study was done to evaluate the paediatrician's choice of agents for sedation and analgesia for various common procedures and their efficacy and safety.

Materials and Methods: A prospective observational study was conducted over 2 years. 267 children of the age 6 months to 18 years, who were administered procedural sedation and/or analgesia by paediatricians, were included. Data regarding demographic details, indications for sedation and analgesia, medications used, procedural completion rates and safety of those medications was collected and analysed.

Results: The mean age of the study population was 5.27+/-4.00 years. EEG was the most common(34.1%) procedure done under PSA.Oral Trichlofos, IV Midazolam, IV Ketamine either alone or in combination were commonly used for PSA. Completion rate for procedures under PSA was 90.6% and ideal sedation was achieved in 91% of subjects. 3.7% of subjects had adverse events following PSA. They were desaturation and euphoria following Midazolam.

Conclusion: Skilled &trained paediatricians are effectively and safely administering sedation and analgesia for common paediatric procedures. Oral Trichlofos, IV Midazolam and IV Ketamine are preferred agents for procedural sedation and analgesia by paediatricians. Adverse events following PSA are transient and can be managed by paediatricians.

Keywords: Pediatric sedation, analgesia, paediatrician, adverse events.

INTRODUCTION

There has been significant increase in the utilization of invasive & non-invasive diagnostic and therapeutic procedures in the paediatric population. For smooth and successful conduction of procedures and better quality care to paediatric patients, sedatives and analgesics are routinely administered for various procedures. Now a day, with limited number of anaesthesiologists and associated higher cost, paediatric sedation and analgesia(PSA) is commonly administered by paediatricians.

Various procedures require different levels and duration of sedation. Inadequate sedation may cause unsuccessful procedures and pose detrimental effects on the patient. Sedation carries the risk of adverse events such as anaphylaxis, respiratory depression, hypotension and vomiting. Children are at higher risk of sedation related complications because of the physiological and anatomical unique

characteristics, making them more susceptible to respiratory depression and hypoxemia.[1]Therefore, adequate knowledge regarding administration of sedoanalgesics in paediatric population, physiological monitoring during the procedures, assessment of sedation levels and pain scale and preparedness for management of likely adverse events are essential for effective PSA.[2,3]Due to limited research on this topic, this study was done with an objective of determining safety and efficacy of pediatric sedation and analgesia by pediatricians for various diagnostic and therapeutic procedures.

MATERIALS AND METHODS

An observational prospective study was conducted from September 2022 to July 2024 in MVJ medical college and research hospital, located in rural Bangalore after obtaining institutional ethical committee approval. A written informed consent was obtained from the parents. All the children of ages 6 months to 18 years, receiving procedural sedation and/or analgesia by paediatricians, were included in the study. Intubated children and children requiring intubation during PSA, those with risk of difficult airway management and who had received sedation in previous 12 hours were excluded from the study.Sample size of 267 was estimated using the efficacy of Pediatric Procedural Sedation Outside the Operating Room at 99.3% from the study by Sirimontakan et al,[4]using the formula: Sample size (N) = Z1-α/22 p (100-p) / d2.

The medications were chosen and used by pediatricians, depending on whether only sedation and/or analgesia was required, nature of procedure-whether outpatient or inpatient based, expected duration of procedure and paediatricians' preference. Children were kept nil by mouth for 2hr prior to PSA in order to minimize the risk of aspiration associated with sedoanalgesics. After proper counselling, sedation and analgesia was administered by a paediatrician skilled in emergency management. Demographic details, underlying illness, indication for procedure, medications used along with the route and dose, outcome of sedation and analgesia and whether procedure successful or not and adverse events observed related to sedation and analgesia during and after procedure were noted in the proforma. The children were observed till they were completely recovered from sedation and anaesthetic effect of drugs.

Efficacy of the PSA was assessed in terms of completion rate of procedure and whether adequate sedation and analgesia was achieved during procedure.

For the estimation of level of sedation, Pediatric sedation state scale (PSSS)- a behavioural scalewas used. Ideal sedation achieved was considered when PSSS of 2-3 was achieved. 0-1 scale being over sedated and 4-5 scales being inadequate sedation.[5]

Wong Baker Faces pain rating scale was used for pain assessment. 0-1 is considered as the ideal state for analgesic procedures.[6]

Adverse events associated with PSA were studied.All the data regarding efficacy and adverse events associated with PSA practiced by paediatrician was entered in Microsoft excel data sheet and analysed using SPSS 22 version software.

RESULTS

The mean age of the population was 5.27 ± 4.00 years, majority being in the age group of 6 months to 5 yrs. Majority of the study participants were males 157 (58.8%). EEG and MRI brain were the common procedures done requiring PSA in children in our hospital followed by BERA and lumbar puncture. CNS diseases causing seizures were the commonest indications for doing procedures with PSA- EEG and MRI.

Out of 267 subjects, procedures were completed in 242 i.e. 90.6% of subjects. Ideal sedation was achieved in 91% of subjects. Among the subjects in whom procedure was completed, Ideal sedation scale of 2-3 was achieved in 99.1 %.The baseline characteristics are depicted in Table 1.

In 40 subjects, ketamine was given for analgesia for lumbar puncture, pleural tapping and bone marrow aspiration. 87.5% of those procedures were completed and 82.5% of them had adequate analgesia during the procedures.

For OPD procedures, oral Trichlofos was used as initial sedative at 50mg/kg/dose and repeat dose was given if required. Whenever adequate sedation was not achieved with oral Trichlofos, then patients were admitted, IV line was secured and either IV Midazolam at 0.1-0.2 mg/kg/dose (Maximum 6mg) or IV ketamine at 0.5-1mg/kg/dose (Maximum 2.5mg/kg) was given in 2 doses 15 minutes apart according to clinicians' preference. In case of failure here, third remaining IV sedative was used. In some of the inpatients with IV cannula in situ, IV midazolam or IV ketamine was used directly as initial sedative. Efficacy of different drugs used for PSA is represented in Table 2.

Completion rate for procedures performed under PSA was 100% for MRI hip, spine, pleural tapping and bone marrow aspiration. It was minimum for MRI Brain and BERA i.e. 86.3% and 87.8% respectively. Efficacy of various drugs used for PSA for different procedures is shown Table 3.

Adverse events following PSA was seen in only 10 patients out of 267 i.e.3.7% of subjects. In all those 10 patients, procedures were abandoned during that time. Adverse events noted were desaturation and euphoria. Adverse events following PSA along with details of drugs, diagnosis of subjects and procedure during which adverse events occurred is shown Table 4.

Table 1: Baseline characteristics of participants

Characteristics	Number (%)
Number of participants	267
Gender: male	157 (58.8%)
Mean age of participants	5.27 ± 4.00 years
Participants Completing procedures	242 (90.6%)
Participants achieving ideal sedation	243 (91%)
Indications of PSA	
EEG	91(34.1)
MRI	77 (28.8)
BERA	49 (18.4)
Lumbar puncture	46 (17.2)
Pleural tapping	2 (0.7)
Bone marrow aspiration	2 (0.7)
Adverse events	10 (3.7%)

Table 2: Efficacy of different drugs used for PSA

Sr. no	Drugs	No. of subjects N	No. of subjects with completed procedure n(%)	No. of subjects with ideal sedation achieved n(%)	p value
1	Trichlofos alone	24	21 (87.5%)	21(87.5%)	0.370
2	Midazolam alone	19	15(78.9%)	15(78.9%)	0.056
3	Ketamine alone	16	15(93.7%)	15(93.7%)	0.693
4	Trichlofos +Midazolam	46	42(91.3%)	43(93.5%)	0.520
5	Trichlofos +Ketamine	100	96(96%)	96(96%)	0.027*
6	Midazolam+Ketamine	24	22(91.7%)	22(91.7%)	0.906
7.	Trichlofos +Midazolam +Ketamine	38	31(81.6%)	31(81.6%)	0.028*
8.	Total	267	242(90.6%)	243(91%)	

*p value <0.05, statistically significant

Table 3: Efficacy of Various Drugs used in terms of Completion Rate and Ideal Sedation

Procedure	Drug/ drugs used	Total no. of subjects	No. of subjects with completed procedure n/N(%)	No. of subjects with ideal sedation achieved n/N (%)	p value
EEG	Total subjects	91	85(93.4%)	86(94.5%)	
	Trichlofos	84	13 (15.4%)	13 (15.4%)	0.721
	Trichlofos +Midazolam	12	9(75%)	10(83.3%)	0.577
	Trichlofos +Ketamine	58	56(96.5%)	56(96.5%)	0.256
	Midazolam +Ketamine	1	1(100%)	1(100%)	0.808
	Trichlofos+Midazolam+ Ketamine	1	0(0%)	0(0%)	<0.001*
	Ketamine alone	6	6(100%)	6(100%)	0.541
BERA	Total	49	43(87.7%)	42(85.7%)	
	Trichlofos	48	0(0%)	0(0%)	0.680
	Trichlofos +Midazolam	44	12(27.2%)	12(27.2%)	1.000
	Trichlofos +Ketamine	4	3(75%)	3(75%)	0.523
	Midazolam +Ketamine	30	27(90%)	26(86.6%)	0.811
	Trichlofos +Midazolam+ Ketamine	1	1(100%)	1(100%)	0.680
MRI Brain	Total subjects	73	63(86.3%)	64(87.6%)	
	Trichlofos	52	8(15.3%)	8(15.3%)	0.152
	Trichlofos +Midazolam	18	14(77.7%)	14(77.7%)	0.119
	Trichlofos +Ketamine	24	23(95.8%)	23(95.8%)	0.138
	Trichlofos +Midazolam +Ketamine	4	2(50%)	3(75%)	0.428
	Midazolam+Ketamine	5	5(100%)	5(100%)	0.385
	Midazolam alone	13	9(69.2%)	9(69.2%)	0.026*
	Ketamine alone	3	2(66.6%)	2(66.6%)	0.258
MRI Whole Spine	Total subjects	2	2(100%)	2(100%)	
	Trichlofos	1	0(0%)	0(100%)	-
	Trichlofos +Midazolam	1	1(100%)	1(100%)	-
	Midazolam	1	1(100%)	1(100%)	-
MRI Shoulder	Total subjects	1	0(0%)	0(0%)	-
	Midazolam +Ketamine	1	0(0%)	0(0%)	-
MRI Hip	Total subjects	1	1(100%)	1(100%)	-
	Trichlofos	1	0(0%)	0(0%)	-
	Trichlofos +Midazolam	1	1(100%)	1(100%)	-
Lumbar Puncture	Total subjects	46	44(95.6%)	44(95.6%)	
	Trichlofos	22	0(0%)	0(0%)	0.730
	Trichlofos +Midazolam	5	2(40%)	2(40%)	0.614
	Trichlofos +Ketamine	14	14(100%)	14(100%)	0.339

	Trichlofos +Midazolam+ Ketamine	3	2 (66.6%)	2(66.6%)	0.011*
	Midazolam + Ketamine	17	16(94.1%)	16(94.1%)	0.696
	Midazolam alone	5	5(100%)	5(100%)	0.614
	Ketamine alone	2	2(100%)	2(100%)	0.758
Pleural Tapping	Ketamine	2	2(100%)	2(100%)	-
Bone Marrow Aspiration	Ketamine	2	2(100%)	2(100%)	-

*p value <0.05, Statistically significant

EEG-Electroencephalography, BERA-Brain Stem Evoked Response Audiometry, MRI- Magnetic Resonance Imaging

Table 4: Adverse events following PSA

S.No.	Adverse event	Drugs	Procedure undergone	Diagnosis of the subject	Frequency
1.	Desaturation	Trichlofos	MRI Brain	Focal seizures-neurocysticercosis	1
		Trichlofos +Midazolam	BERA	Cerebral palsy (CP)	1
		Trichlofos +Ketamine	MRI brain	GDD-CP	1
		Midazolam +Ketamine	EEG	Myoclonic Seizures	1
		Trichlofos +Midazolam +Ketamine	Lumbar Puncture	Meningitis	1
2.	Euphoria	Midazolam	MRI Brain	Developmental Delay	1
		Midazolam	MRI Brain	GDD with Seizure disorder	1
		Midazolam	MRI Brain	Meningitis	1
		Trichlofos+ Midazolam	EEG	Developmental delay with seizures	1
		Trichlofos+ Midazolam	BERA	Isolated speech delay	1

GDD- Global Developmental Delay, CP- Cerebral Palsy

DISCUSSION

In our study, we observed that majority of the children requiring PSA were in the age group of 6 months to 2 years. The mean age of the subjects requiring PSA was observed to be 55 months in a similar study "Efficacy and Safety of Pediatric Procedural Sedation Outside the Operating Room." Done by Sirimontakan et al. On children from age group of 1 month to 20 years.[4] As older children do not require sedation for many procedures associated with mild discomfort like MRI/ EEG, they can be prepared before hands verbally by explaining them the details of procedure and what is expected. However, younger children do not understand and get scared easily. This can lead to incomplete or inadequate procedure or bodily harm. So, PSA is more commonly used in younger children than older.

In our study the commonest procedure done under PSA was EEG (34.1%), followed by MRI (27.3%), and BERA (18.4%).In the study conducted by Misra et al., the most common indications for PSA were incision and drainage(45%)and laceration repair(32.4%).[7]In the study conducted by Was fy et al., the main procedures done under PSA were dental procedures, MRI and CT.[8]We have not included the procedures done in minor OT like incision and drainage, as PSA is given by anaesthetist in minor OT in our hospital. As, apart from common infections, CNS diseases like seizures, developmental delay, meningitis are the most common illnesses among children attending our hospital, MRI Brain and EEG are the common investigations done here which require PSA.

Benzodiazepines, ketamine, propofol, ketamine with propofol, nitrous oxide, and etomidate are all well-studied agents used in Pediatric Procedural Sedation (PPS).[9] In our hospital, oral Trichlofos, IV midazolam and IV Ketamine are commonly preferred for Pediatric procedural sedation by pediatricians. These drugs, either alone or in combination, were used for PSA in our study.

Similar study on "Pediatric procedural sedation and analgesia in the emergency department: surveying current European practice" has described the pediatric procedural sedation and analgesia practice patterns in European emergency department. They reported that 82% of pediatric cases were sedated by general pediatricians. Midazolam (100%) and ketamine (91%) were used for most children for procedural sedation and analgesia, whereas propofol (67%), nitrous oxide(56%), intranasal fentanyl (47%), and chloral hydrate(42%) were used less frequent.[10]

In a similar study done in Thailand by Sirimontakan et al. on "Efficacy and safety of pediatric procedural

sedation outside the operating room", the common sedative medications used for PSA were fentanyl(68.8%), midazolam(65.6%), ketamine(55.4%), propofol(46.7%), chloral hydrate (6.8%), dexmedetomidine(2.9%), morphine(0.2%), and etomidate (0.2%).[4]A study conducted in Brazil by Sukys et al. in a pediatric emergency unit found that midazolam was the sedative of choice in 80% of rapid intubation sequences.[11]

Oral Trichlofos, Midazolam and ketamine are the most commonly used drugs used for PSA in India.[12, 13]Orally administered Trichlofos is a commonly used sedative-hypnotic medication for OPD based procedures requiring milder sedation.Midazolam has rapid action onset, short action duration, anterograde amnesia, and a wide variety of administration routes.[11]Ketamine is a dissociative anaesthetic agent that acts on the N-methyl-d-aspartate-glutamate receptor, disconnecting the limbic and thalamocortical systems, dissociating the central nervous system from external stimuli. The cataleptic state allows potent analgesia, sedation, and amnesia, while maintaining airway patency, protective stimuli, and cardiovascular stability. It is widely used in painful short-term procedures or in those in which amnesia is desired.[14]

Dexmedetomidine (DEX) is an alpha-2 adrenergic agonist with an action that is not mediated by GABA, which promotes sedation without decreasing the respiratory drive. In the emergency department, it is mainly used for imaging studies.However, it has not been approved by the Food and Drug Administration for pediatric use yet,due to lack of data demonstrating its safety profile. [15]So, it is still not used commonly for PSA in our hospital.

Overall, efficacy of procedural sedation administered by paediatrician was good. 90.6% of the procedures could be completed under PSA. Ideal sedation scale of 2-3 was achieved in 99.1 % of the subjects in whom procedures were completed. Ideal sedation was achieved in 91% of all the subjects. Failure of completion of procedures was because of either inadequate sedation or deep sedation with adverse events or inability to maintain the sedation till the completion of procedure despite the stipulated sedoanalgesic doses. The success rate of the procedure under PSA, along with patient characteristics and skills of the personnel administering PSA, also dependsupon nature of procedure (duration of the procedure, level of pain, discomfort in the procedure).

In a similar study done by Sirimontakan etal., the success rate of the procedure under PSA was 99.3%. Better completion rate in above study could be because those PSA were administered by intensivists and had the benefit of expanding sedation services in intensive care units.[4]

In a study on Safe and Efficacious Use of Procedural Sedation and Analgesia by Non-anaesthesiologists in a Pediatric Emergency Department by Pitetti et al., Procedural sedation and analgesia was successfully provided in 1177 (98.6%) of 1194 sedation events.[16]In the similar study conducted by Misra et al. in children less than 2 years of age where PSA was administered by emergency physicians, only around 10 out of 173 subjects (5.8%) had inadequate sedation.[7]Similar to our study, in the above studies also the PSA was effectively administered by non-anaesthesiologists including pediatricians.

In our study, for analgesic procedures, ketamine was preferred either alone or with other sedative. The overall completion rate of procedures was 87.5%with 82.5% subjects achieving the ideal (0-1) pain scale.Misra et. al studyreported that midazolam combining with ketamine as the most commonly used combination for analgesia with 94.2% efficacy.[7]

Success rate of lumbar puncture and EEG under PSAwas 95.7% and 93.4% respectively. Completion rate for MRI Brain and BERA was relatively low,87.8% and 86.3% respectively. It could be becauseof non-maintenance of sedation throughout these prolonged procedures and also due to the unfavourable patient characteristics associated with primary illnesses requiring the diagnostic procedures.

In general, for most of the OPD procedures, oral Trichlofos (50mg/kg/dose) was used as initial sedative as it can be given orally, cheap and easily available. However, its success rate was low i.e.87.5%. In the study by Kaplan et al., on Trichlofos sodium for pediatric sedation in non-painful neurodiagnostic studies, ideal sedation depth obtained using the University of Michigan Sedation Scale (UMSS) score was similar to our study.[17]The reasons for low success with oral Trichlofos may bedue to its variable efficacy. This can be attributed to lack of co-operation from children either by non-acceptance of full dose due to spitting or not swallowing completely.[18]

The success rate of using intravenous midazolam alone was 78.9 % and the success rate of IV midazolam improved to more than 91% after addition of Trichlofos and Ketamine. We observed that success rate of ketamine, used either alone or in combination with Midazolam/Trichlofos was good(93.7%, 96% and 91.7% respectively). A systematic review by Samuel Oh et al. involving 25 clinical trials concluded that the use of ketamine can provide safe, effective and timely sedation in pediatric patients.[19] It was inferred in a retrospective cohort study by Mark A Gilger and colleagues that the combination of midazolam and ketamine provide safe and effective sedation for pediatric patients undergoing endoscopy.[20]

For painful procedures, adequate analgesia is needed. Only sedation without analgesia for painful procedures was found to be associated with significant failure rate of the procedure along with significant distress to the patient. Ketamine alone or in combination with other drugs for lumbar

puncture, was effective in 94.4% subjects. Completion rate for lumbar puncture without adequate analgesia was very poor i.e. only 40%. Similarly, a double-blind randomized placebo controlled trial of oral midazolam vs oral midazolam plus oral ketamine for children undergoing laceration repair, conducted by Barkan et al, showed the failure rate of 27% in the midazolam group compared to 6% in the combination group.[21]

Adverse events following PSA were not common and when present were only transient and easily manageable. It was seen in only 10 patients out of 267 i.e.3.7% of subjects. Adverse events noted were desaturation and euphoria. 5 patients receiving IV midazolam either alone or with Trichlofos had euphoria.5 patients had respiratory depression with desaturation and was commonly seen with combination of sedatives. All the children who had these adverse effects had either chronic or acute neurocognitive issues in form of cerebral palsy, global/isolated developmental delay, seizure disorder, neurocysticercosis & meningitis. Even though the overall incidence of adverse events in our study was comparable to Sirimontakan et al. study i.e. 3.7%, the severity of adverse events was mild.In the Misra et al. study one subject had apnoea and bradycardia needing ventilatory support.[4,7]

Similar to our study where we observed euphoria following IV midazolam, the study by Wenzel etal. on"Central nervous side effects of midazolam during transesophageal echocardiography" reported that 6 of 104 subjects had aggressiveness, euphoria, depression following midazolam requiring IV infusion of Flumazenil for reversal of symptoms in some of them.[22]

CONCLUSION

Procedural sedation and analgesia is being administered successfully and safely by skilled pediatricians for various procedures associated with discomfort, anxiety or pain. Oral Trichlofos, IV midazolam and IV Ketamine are the preferred agents for procedural sedation and analgesia. Although Oral Trichlofos is preferred oral sedative for various OPD based diagnostic procedures, alone at the advised dose range (50 mg/kg/dose) itis not effective in achieving adequate sedation for most of the procedures. IV ketamine either alone or in combination with other sedatives, is better sedative and analgesic for successful completion of many of the common diagnostic and therapeutic procedures. The adverse events are transient and easily manageable.

Limitations of the study

- As this was an observational study determining practice of PSA by paediatricians uniform guidelines were not followed while choosing sedatives and analgesics during the study.
- Uniform guidelines for various procedures were not followed
- Various other factors like time taken for achievement of sedation, duration of study procedure and recovery time from sedoanalgesia were not considered.

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