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Procedural Sedation in Paediatric Practice

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Authors' contributions

This work was carried out in collaboration between all authors. Authors UKR and SB designed the study and wrote the protocol. Author TNG managed the literature searches and helped in analyses of the study. Authors SH and PK carried out the study and wrote the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Providing sedation techniques during the performance of diagnostic and therapeutic procedures on children decreases anxiety and discomfort. A number of drugs are available for the purpose. A retrospective record study in Paediatrics department of Burdwan Medical College & Hospital showed oral triclofos and per rectal diazepam were the two commonly used drugs for the purpose. However, intranasal midazolam is claimed to be a near ideal agent for procedural sedation. So, the above study was to compare efficacy and safety of intranasal midazolam over oral triclofos and per rectal diazepam.

Methods: Participants having ASA score I or II having age group 1 to 6 years requiring non-invasive or minimally invasive procedure were divided into three groups- one group received oral triclofos sodium, second group received per rectal diazepam and third group received intranasal midazolam spray prior to the procedure. Levels of sedation and recovery were scored using Ramsey sedation score and modified Aldrete scoring system respectively. Induction of sedation was defined as attainment of Ramsey sedation score of at least 3. Complete recovery was defined as a minimum score of 10 of modified Aldrete scoring system.

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Results: Both times of induction and recovery were significantly higher in triclofos group when compared to other two groups. Level of sedation attained was higher in per rectal diazepam group, although there was no case of over sedation. Adverse effects were comparable except for nasal irritation which was exclusively limited to midazolam group. Cost of therapy was higher with intranasal midazolam therapy than with per rectal diazepam therapy.
Conclusion: Per rectal diazepam appear to be a more ideal drug for procedural sedation over intranasal midazolam and oral triclofos.

Keywords: Procedural-sedation; midazolam; diazepam; triclofos.

ABBREVIATIONS

PSA= Procedural sedation and analgesia
ASA score= American Society of Anaesthesiologists Physical state classification score.

1. INTRODUCTION

Non-invasive and minimally invasive procedures performed on the paediatric population outside the operating room have increased with time over the last several decades [1-3]. They may experience a pronounced stress response to procedures that are either painful or require prolonged immobility [4]. Even for painless procedures like imaging studies, an apprehensive, crying and non-cooperative child is not an uncommon occurrence [5]. Providing sedation / anaesthesia techniques during the performance of diagnostic and therapeutic procedures on children decreases anxiety, discomfort and pain and may improve child well-being. It may contribute even to increase the success rate of procedures done by effective immobilisation of child [3,6].

Procedural sedation and analgesia (PSA) can be defined as the use of sedative, analgesic and / or dissociative drugs to provide anxiolysis, analgesia, sedation, and motor control during painful or unpleasant diagnostic and therapeutic procedures [2,7].

Anaesthesiologists possess specific expertise in the clinical management of patients receiving sedation and analgesia [8]. However, as there is a rising demand for PSA and anaesthesiologists are often unable to perform timely service, PSA is mostly provided by non-anaesthesiologists [9,10]. Accordingly, the American College of Emergency Physicians, the American Academy of Paediatrics and the American Society of Anaesthesiologists have all issued statements supporting the safe and appropriate use of sedative medications by non-anaesthesiologists to ameliorate this response [4,8,11-12].

A number of drugs are available to provide PSA for the purpose. However, several reports show that PSA is still often inadequate leading to procedural failure and avoidable procedural pain [7,13-16].

We performed a retrospective record study in the Paediatrics Department of Burdwan Medical College & Hospital to assess the drugs used for PSA in the last 6 months from July 2013 to December 2013. The study showed oral triclofos (40.54%) and per rectal diazepam (27.03%) were the two commonly used drugs for the purpose. Of the parenteral drugs, intravenous midazolam (18.92%) was commonly used. Intranasal midazolam was also occasionally used (3.15%).

Intranasal midazolam spray have been claimed to be a better agent for procedural sedation having significant sedative and anxiolytic properties with no significant effect on haemodynamics and respiratory physiology. The route has an additional advantage of having rapid and complete absorption of the drug due to high vascularity [5,17].

Hence, we conducted this study to compare the efficacy and safety of intranasal midazolam over oral triclofos and per rectal diazepam.

2. MATERIALS AND METHODS

Study was started only after obtaining clearance from institutional ethics committee (Memo no-BMC/CREC/13(2)/2013). It was an open label single centre observational prospective study. The study was carried out in the Department of Paediatrics of Burdwan Medical College & Hospital from March 2014 to May 2014. After getting written informed consent and getting each and every participant thoroughly examined by an anaesthesiologist, subjects were recruited for the study.

Participants having ASA score (American Society of Anaesthesiologists Physical state classification) I or II were included provided age

was ≥1 year but ≤6 years and the procedure was either painless (like, imaging studies) or involved minor trauma (like, venous catheter insertion, lumbar puncture etc.). Exclusion criteria were (i) Children in whom previous PSA was ineffective (ii) Children too stressed despite proper preparation (iii) Older children with serious behavioural disorders (iv) Children offering limited co-operation & / or with learning difficulties (v) Patients having abnormal airway including large tonsils and anatomical defects of upper and lower airways (vi) When it is expected that the chosen form of PSA will be ineffective for a specific child (vii) Evidence of sleep apnoea (viii) GERD or increased risk of choking (viii) Bulbar reflex defects (ix) Serious obesity (x) Emergencies and hence no empty stomach (xi) Children using opiates or sedatives (xii) Children using antiepileptic drugs and (xiii) Known allergies to sedatives.

Recruited subjects were divided into three groups- one group received oral triclofos sodium 70 mg/kg, second group received per rectal diazepam 0.5 mg/kg and third group received intranasal midazolam spray 0.5 mg/kg [2,18-19]. Minimum fasting period before the procedure was decided as per the recommendations of American Society of Anaesthesiologists [8]. Local anaesthetic was optional if the procedure involved was painful. Participant's pulse rate, blood pressure, respiration rate, oxygen saturation and level of sedation was recorded every 5 mins starting from the administration of the drug till complete recovery. Level of sedation was scored using Ramsey sedation score [20]. Recovery was noted as per modified Aldrete scoring system with a minimum score of 10 being defined as complete recovery [21]. Procedure was started only after induction of sedation. Induction of sedation was defined as attainment of Ramsey sedation score of at least 3 while score of 6 was considered over sedation. All the emergency equipments and drugs, including endotracheal tube, bag and mask ventilator, adrenaline, atropine, crystalloids etc., were made available before the introduction of the drug.

Sample size was calculated taking into considerations 80% power, 5% probability of Type I error to detect a difference of at least 2 mins. of time of induction of sedation by using one-way analysis of variance (ANOVA) statistical test assuming standard deviation for time of induction of sedation being 2 mins. It came out to be 15 in each of the 3 groups.

Statistical analysis was carried out using SPSS version 21. Qualitative variables were compared using chi-squared test of association while quantitative variables were compared using one-way analysis of variance.

3. RESULTS

Participants in each of the 3 groups were comparable in their baseline characteristics. Table 1 show the baseline characteristics of the study participants.

Between groups comparison was found to be significant in case of both time of induction and time of recovery. Post hoc analysis was done using Games-Howell test (as there was non-homogeneity of variance). It showed that both time of induction and time of recovery were significantly higher in triclofos group when compared to other two groups. Table 2 shows the times of induction and recovery among the three groups.

Table 1. Baseline characteristics of study participants

Categories		Triclofos (n=15)	Diazepam (n=15)	Midazolam (n=15)	*P*-value
Gender	Male	7	9	8	0.77
	Female	8	6	7	
Age (in months)		35.13 ± 17.9	38.2 ± 16.35	37.27 ± 17.79	0.89
Weight (in Kg)		11.83 ± 2.98	12.43 ± 2.62	12.07 ± 2.91	0.85
Pulse rate		104.67 ± 15.04	102.33 ± 16.61	103.8 ± 16.3	0.92
Systolic blood pressure		111.47 ± 10.6	110.27 ± 10.66	110 ± 10.09	0.92
Diastolic blood pressure		73.73 ± 8.24	72.67 ± 9.49	73.2 ± 8.78	0.95
Respiratory rate		15.87 ± 2.23	15.47 ± 2.64	16.27 ± 2.49	0.68

- *Values in Gender category are absolute numbers. Values in other categories are expressed in Mean ± Standard deviation.*
- *Units of systolic and diastolic blood pressures are mm of Hg.*
- *P-values are calculated by chi-squared test of association in gender category and by one-way analysis of variance in other categories.*

None of the patients in midazolam group or triclofos group attained Ramsey sedation score of >3. In contrast, majority of the patients in diazepam group attained Ramsey sedation score of >3. However, none of them showed over sedation.

Vital parameters, including pulse rate, blood pressure, respiration rate and oxygen saturation were maintained throughout the procedure in each of the group. None of the participant showed any serious adverse event. All the adverse events were mild and none required discontinuation of the procedure. Table 3 shows adverse effects in each of the three study groups. All the adverse events showed insignificant p-value when between groups comparison was made except nasal irritation ($P < 0.05$).

Table 4 shows the comparison of prices of oral solution of triclofos (500 mg / 5 ml, 30 ml), injectable diazepam (5 mg/ml, 2 ml) and intranasal midazolam spray (0.5 mg/puff, 50 md) as seen from http://www.cimsasia.com/ on 10/02/2015. Cost of therapy with oral triclofos and intranasal midazolam was considered using mean weight of each group. Cost of therapy with per rectal diazepam was taken 1 ampule for each patient as remaining drug in the ampule has to be discarded after use. Kruskal-Wallis H test showed significant *P*-value. Pairwise comparison showed that the cost of therapy with intranasal midazolam was significantly higher than with per rectal diazepam.

4. DISCUSSION

Medical procedures without sedation or anaesthesia may be quite distressing to the children and their parents. Younger children (< 8 years) show higher level of stress than older children [6,22]. The ASA guidelines for sedation by non-anaesthesiologists stress that a primary cause of morbidity associated with sedation/analgesia is drug-induced respiratory depression [8]. Another problem with procedural sedation is inadequate response which may even lead to cancellation of the procedure.

An ideal agent for PSA should be easily available, having quick onset of action and recovery with predictable depression of consciousness level and minimal cardio-respiratory depression. As none of the drugs meet all the criteria of an ideal agent, several studies have been performed to recognize the better available drug for PSA [5,18].

Table 2. Times of induction and recovery among the three groups

Efficacy variables	Triclofos (n=15)	Diazepam (n=15)	Midazolam (n=15)	*P*-value
Time of induction	57.93 ± 10.94	19.47 ± 2.95	19.33 ± 2.02	**< 0.001**
Time of recovery	102.13 ± 7.06	36.73 ± 3.63	38.73 ± 2.69	**< 0.001**

- *Times of induction and recovery are in minutes.*
- *Values are expressed in Mean ± Standard deviation.*
- *P-values are calculated by one-way analysis of variance*

Table 3. Adverse effects in each of the three study groups

Adverse effects	Triclofos (n=15)	Diazepam (n=15)	Midazolam (n=15)	*P*-value
Nausea/Vomiting	3	1	2	0.86
Agitation	2	1	1	1.00
Hypoxaemia	0	2	1	0.76
Nasal irritation	0	0	5	**0.007**
Recall	2	1	1	1.00

- *Values indicate the absolute numbers*
- *P-values are calculated by Fisher-Freeman-Halton exact test*

Table 4. Comparing cost of therapy in three treatment arms

Triclofos	Diazepam	Midazolam	*P*-value
14.32 (3.78)	10.69 (4.88)	63 (8.7)	**0.005**

- *Values are expressed in Median (Interquartile range)*
- *P-value is calculated by Kruskal-Wallis one way ANOVA*

Our retrospective study showed that oral triclofos and per rectal diazepam are the two most commonly used drug for PSA in the Paediatrics department of Burdwan Medical College & Hospital. Again, intranasal midazolam has been claimed to be a near ideal drug for PSA [5].

We considered the age group of 1 to 6 years. This is because sedation in infant and older children (>6 years) are associated with increased risk [7,23-24]. Participants having ASA score I or II only were included as ASA score III or IV require the presence of an anaesthesiologist.

Baseline characteristics of the participants were comparable in each of the three groups in our study. Times of induction and recovery of oral triclofos and per rectal diazepam obtained in our study was a bit higher than claimed by other authors [18,25]. Time of induction of intranasal midazolam was a bit higher while time of recovery was lower when compared to a review article [2]. Again, time of induction of intranasal midazolam was lower in comparison to a study conducted in Varanasi and Kolkata [5]. These variations may be ascribed to variation in study designs and different scales chosen to measure outcomes.

Our study showed that times of induction and recovery of intranasal midazolam and per rectal diazepam were significantly lower when compared to oral triclofos. However, levels of sedation were higher with per rectal diazepam although there was not a single case of over sedation. Adverse effects were similar in each of the three groups except nasal irritation which was exclusively limited to the group receiving intranasal midazolam. Again, cost of therapy was significantly higher with intranasal midazolam than with per rectal diazepam.

The study was not devoid of limitations. It was an observational study. Only either painless procedures or those involving minor pain were considered for the study. Study was performed with small sample size. However, it was a first study of this sort conducted in a rural based tertiary care hospital Burdwan Medical College & Hospital. In future, we are looking forward to carry out randomized controlled study with larger sample size.

5. CONCLUSION

The study shows although both intranasal midazolam and per rectal diazepam possess comparable efficacy, per rectal diazepam was cost effective time tested therapy devoid of any nasal irritation. Again, per rectal diazepam produced better depression of consciousness level to perform any procedure more securely. This is making per rectal diazepam more near to an ideal agent for PSA than intranasal midazolam and oral triclofos. Hence, per rectal diazepam should be preferred over intranasal midazolam and oral triclofos for procedural sedation in children. Further studies may be done with larger number of study subjects to support per rectal diazepam as a near ideal agent for PSA.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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