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RESEARCH ARTICLE

COMPARISON OF ORAL MIDAZOLAM VERSUS ORAL TRICLOFOS FOR SEDATION OF CHILDREN POSTED FOR COMPUTED TOMOGRAPHY SCAN - A RANDOMIZED CONTROLLED, DOUBLE BLIND CLINICAL STUDY

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Abstract

Background: To maintain immobility of children for good quality computed tomography (CT) scans, sedation may be used. Present study was planned to compare the efficacy of oral triclofos and oral midazolam in children undergoing CT.

Methodology: The prospective, comparative, randomized Indian study was conducted in Department of Anaesthesia at a J.J. Hospital and Grant Medical college. Study population was paediatric subjects between 2 years and 5 years (both inclusive) with ASA-I, exhibiting fearful or refractory behaviour at previous CT Scans. Oral triclofos 100 mg/kg was given to one group (100 patients) and oral midazolam 0.75 mg/kg in other group (100 patients) in preoperative room with facility of oxygen and multipolar monitor. Standardized scoring systems (Ramsay Sedation Scale, Aldrete Recovery Score) were used for evaluation. Vascular parameters, time of sedation onset and duration of recovery were also assessed.

Results: Mean age and gender distribution were comparable between study groups ($p>0.05$). On comparing heart rate, systolic and diastolic BP between the Midazolam and Triclofos groups at all time-points, no significant difference was found ($p>0.05$). Mean sedation score and recovery score in the Midazolam group were found to be significantly higher compared to Triclofos group ($p<0.05$). Mean onset of sedation was found to be significantly quicker in the Midazolam group ($p<0.05$). In addition, the mean duration of sedation and duration of CT scans were significantly lower in the Midazolam group ($p<0.05$).

Conclusion: Midazolam was found to have a better sedative profile compared to Triclofos in paediatric patients undergoing CT.

Introduction:-

When children undergo computed tomography (CT) scans it is particularly crucial that they remain immobile during the procedure so that good quality scans are obtained. However, this may be a challenge because of emotional as well as psychological disturbance in children because of unfamiliar hospital environment, fear of the radio-imaging procedure, and separation from parents during procedure. To avoid these drawbacks and to obtain good quality CT

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scans, sedation as well as anaesthesia may be used.[1] Sedation remains the most crucial and sometimes challenging part of a diagnostic procedure in children.[2] Numerous drugs administered alone or in combination (propofol, midazolam, chloral hydrate, nitrous oxide as well as ketamine) have been recommended in children to attain satisfactory sedation as well as analgesia.[3] Yet no drug is absolutely safe or completely reliable according to available evidence and clinical experience.[4] In some available literature, this has been called as 'brutacaine' and is said to give rise to fear of hospitals as well as medical procedures amongst the young.[5]

The ideal sedative for the paediatric population must be one that has a rapid onset of action, a short yet adequate duration of action, lesser side effects, no effect on hemodynamic parameters or respiration, broad safety margin, and rapid smooth recovery.[6] Midazolam, a water-soluble benzodiazepine, with appealing pharmacodynamics for brief, out-patient procedures is increasingly used and recommended for pediatric sedation.[7] It is short-acting having sedative, anxiolytic, amnesic as well as muscle relaxant properties. It can also be administered to the paediatric patient by various routes like oral and intra-nasal.[8] Oral triclofos is another sedative agent which has been utilized in the pediatric population. It is a stabilized form of chloral hydrate but is a relatively older sedative-hypnotic drug. The oral solution is absorbed well, proves effective within a period of 30-40 minutes and creates hypnosis for 6-8 hours in doses of 25-75 mg/kg.[9]

On an extensive literature search, it was found that there is a dearth of scientific evidence which has compared oral midazolam and oral triclofos (stable chloral hydrate) for sedation in children undergoing CT scan. In addition, the available evidence gives varied findings. In a study by Gupta et al., oral midazolam and oral triclofos showed equal effectiveness as well as safety in pediatric population.[10] However, a similar study by Chaudhary et al. found that midazolam is a better pre-medicant in paediatric patients as compared to triclofos.[11] Hence, the present study was planned to compare the efficacy and safety of triclofos and midazolam in children undergoing CTat a tertiary care teaching hospital.

Methodology:-

The prospective, comparative, randomized Indian study was conducted in Department of Anaesthesia at a J.J. Hospital and Grant Medical college located in Mumbai city of Maharashtra state. Data was collected between September 2018 to August 2020 and eligible children were screened for study inclusion during this period. Study was initiated only after institutional ethics committee permission. The study population was composed of paediatric subjects between the age of 2 years and 5 years (both inclusive) with ASA-I, who exhibited fearful or refractory behaviour at previous CT-Scans, at thehospital. Children allergic to sedative agents, or having hepatic, respiratory, cardiac, endocrine, or metabolic impairment, or who had received a sedative hypnotic agent within the past 48 hours were excluded from study.

Study procedure and drug administration

After careful pre-anaesthetic examination, written informed consent was obtained from parents. Randomization was done in blocks of 10 using computer generated sequence. Group allocation was kept in serially numbered opaque envelops. Faculty member not involved in the study prepared and administered the drug. Clear mango juice without pulp with colour like triclofos was added to injection midazolam and the volume equalized in both groups was 1 ml/kg. Investigator observing the patients was blinded to the drug administered. Patients were kept nil orally for six hours. Study drug was administered in equal volumes as per group allocated. Oral triclofos 100 mg/kg was given in children in Group-I (100 patients) and oral midazolam 0.75 mg/kg in Group-II (100 patients) in preoperative room with facility of providing oxygen and multipolar monitor.

Parameters Evaluated

Following parameters were monitored for all the enrolled paediatric patients:

1. Sedation score
2. Pulse and heart rate, blood pressure
3. Respiration and oxygen saturation
4. Time of sedation onset and duration to recovery

Standardized scoring systems like Ramsay Sedation Scale (RSS) and Aldrete Recovery Score were used for evaluation of study groups.

Ramsay Sedation Scale (RSS):
Various scientific publications have endorsed RSS as sedation scale of choice, which have excellent inter-rater reliability and validity, and was one the most frequently used sedation scale system according to a survey.[12]The level of sedation is graded by RSS in the form of 6-point score as mentioned in table 1:

Table 1:- Ramsay Sedation Score[12]

Ramsay Sedation Scale	
Score	Definition
1	Anxious and agitated or restless or both
2	Cooperative, oriented, and tranquil
3	Responds to commands only
4	Brisk response to a light glabellar tap or loud auditory stimulus
5	Sluggish response to a light glabellar tap or loud auditory stimulus
6	No response to a light glabellar tap or loud auditory stimulus

Paediatric subjects were taken for CT scan after they achieved Ramsay Score >4 or at one hour regardless of level of sedation. Patients who were inadequately sedated were supplemented with intravenous (iv) midazolam at the dose of 0.05 mg/kg repeated after five minutes if still inadequate (up to 0.1 mg/kg).

Continuous monitoring of pulse oximetry and intermittent assessment of respiratory rate (RR), heart rate (HR) and blood pressure (BP) to evaluate for cardio-respiratory depression was done. Recovery was assessed with the help of Aldrete Recovery Score (Table 2).[13] Study was terminated once recovery criteria was fulfilled.

Table 2:- Aldrete Recovery Score[13].

Parameter	Description of patient	Score
Activity level	Moves all extremities voluntarily/on command	2
	Moves 2 extremities	1
	Cannot move extremities	0
Respirations	Breathes deeply and coughs freely	2
	Is dyspneic, with shallow, limited breathing	1
	Is apneic	0
Circulation (blood pressure)	Is 20 mm Hg > preanesthetic level	2
	Is 20 to 50 mm Hg > preanesthetic level	1
	Is 50 mm Hg > preanesthetic level	0
Consciousness	Is fully awake	2
	Is arousable on calling	1
	Is not responding	0
Oxygen saturation as determined by pulse oximetry	Has level >90% when breathing room air	2
	Requires supplemental oxygen to maintain level >90%	1
	Has level <90% with oxygen supplementation	0

Maximum total score is 10; a score of ≥9 is required for discharge.

Onset of sedation was defined as time from drug administration to time at which Ramsay Score >4 is achieved, and **duration of sedation** is defined as time from onset of sedation to time at which recovery is achieved. **Recovery from sedation** was based on assessment of Aldrete scores for all the children (Aldrete Score > 8). **Recovery time from completion of scan** to time to achieve Aldrete Score > 8 was also noted.

Statistical Analysis

After data collection, data entry was done in Microsoft Excel.Data analysis was done with the help of statistical software Graphpad InStat.v3.0Quantitative data was presented with the help of Mean and Standard deviation.Comparison of continuous data (onset time of sedation, recovery time etc.) was done between the two study groups using unpaired t testDescriptive data was used to represent proportions and other relevant parameters. P value <0.05 was considered to be statistically significant.

Results:-

Demographic details

A total of 200 patients were enrolled in the study, 100 in Midazolam group and 100 in Triclofos group. The mean age and gender distribution were found to be comparable statistically between study groups (p>0.05). The demographic details have been mentioned below in table 3.

Table 3:- Demographic details of patients in study.

Parameters assessed	Midazolam group (n=100)	Triclofos group (n=100)	P value
Age details			
Mean age in years	3.44 + 1.01	3.32 + 0.99	0.23*
Median age (range) in years	3 (2-5)	3 (2-5)	-
Age distribution			
Children aged 2 years	20	33	0.14$
Children aged 3 years	35	33	
Children aged 4 years	26	23	
Children aged 5 years	19	11	
Gender distribution			
Number of males	55	49	0.47$
Number of females	45	51	

P>0.05 considered not significant by Unpaired t test* or Chi-square test$

Diagnostic modalities

Majority of patients in the Midazolam group were subjected to either HRCT thorax (37%) or CT brain (34%). In the Triclofos group, majority of children were indicated for CT brain (37%) or HRCT thorax (30%). The details of diagnostic modalities prescribed are noted in table 4.

Table 4:- Diagnostic modalities in the study groups.

	Midazolam group (n=100)	Triclofos group (n=100)

CT Abdomen + Pelvis	10	13
CT Brain	34	37
CT Brain + Orbit	4	7
CT Neck + Abdomen + Thorax	11	13
HRCT Thorax	37	30
CT Abdomen + Pelvis + HRCT	1	0
CT Brain + Abdomen	1	0
CT Knee	1	0
CT IVP	1	0

Heart rate, Systolic BP and diastolic BP assessment

No significant difference was found between study groups for the vascular parameters at any time-point ($p>0.05$). No significant change in heart rate, systolic BP and diastolic BP, in either of the study groups was found on intra-group analysis ($p>0.05$).

Sedation and Recovery score

The mean sedation score and the recovery score in the Midazolam group were found to be significantly higher ($p<0.05$). (Table 5)

Table 5.:- Sedation score and recovery score of patients in study groups.

Parameters assessed	Midazolam group (n=100)	Triclofos group (n=100)	P value
Mean sedation score	4.93 + 0.66	3.58 + 0.91	**<0.01***
Mean recovery score	8.58 + 0.74	4.95 + 0.84	**<0.01***

P < 0.05 considered significant by unpaired t test

Onset and Duration of Sedation, Duration of scan

The mean onset of sedation was found to be significantly quicker in the Midazolam group ($p<0.05$). In addition, the mean duration of sedation and duration of CT scans were significantly lower in the Midazolam group ($p<0.05$). (Table 6)

Table 6:- Onset and duration of sedation of patients in study.

Parameters assessed	Midazolam group (n=100)	Triclofos group (n=100)	P value
Mean onset of sedation (mins)	15.38 + 2.47	35.33 + 3.11	**<0.01***
Mean duration of sedation (mins)	22.54 + 2.17	75 + 12.47	**<0.01***
Duration of scan (mins)	4.81 + 0.56	5.6 + 1.19	**<0.01***

Discussion:-

The alien environment, the separation from parents during the procedure and fear of hospitals leads to the emotional and physical reaction of the paediatric patient.[14]Oral midazolam and oral triclofos have been used as sedative agents during CT scans but have not been compared for their effectiveness especially in Indian population. In present study, it was noted that alterations of both Midazolam and Triclofos on vascular parameters and SPO2 were insignificant, and were found to be equally safe on these parameters. These were similar findings to other identical studies by Ankesh Gupta et al, KolathuRadhika et al., Stephen et al and Chaudhary et al. [11,15,16,17]

RSS indicates the extent of sedation. Higher the sedation score, better is the extent of sedation. The maximum Aldrete recovery score possible is 10, and higher the score the better is the recovery of the patients. Based on the findings, Midazolam had significantly better extent of sedation as well as had significantly better recovery. In addition, sedation onset was significantly quicker in Midazolam group, along with significantly quicker recovery and also lower CT scan durations. The main reason behind the longer duration of CT scan in the triclofos group was the requirement of additional top-up in this group as the paediatric patient was moving during the CT scan procedure.In the study by KolathuRadhika et al., after premedication, 93.33% children of midazolam group were adequately sedated (sedation score 4) compared to 60% in the triclofos group.[17] In the study by Gupta et al., onset and duration of sedation were significantly lower in the Midazolam group versus triclofos ($p<0.05$).[15] In addition, the recovery time was significantly shorter with Midazolam versus triclofos ($p<0.05$).95% children compliant with Midazolam versus 65% to triclofos. In the study by Chaudhary et al., after 60 minutes of medication, 60% patients on Midazolam achieved excellent sedation compared to 50% in Triclofos group.[11] In the study by Fallah et al., quicker onset of sedation with Midazolam was found versus triclofos ($p<0.05$).[18] However, in the study by Agostino et al., a slightly different finding was noted as compared to other similar studies.[31] Adequate sedation was achieved in 100% patients on Chloral hydrate, compared to 50% in Midazolam group.

The study had a few limitations. It was a single-centre study done in a limited number of enrolled patients. In addition, a short follow-up was done due to which long term effects of the sedative agents was not assessed. Future studies can be conducted at multiple centres and also the patients may be followed up for longer period post radiological assessment which can add to our study findings.

Conclusion:-

Midazolam was found to have a better sedative profile in paediatric patients aged between 2-5 years undergoing computed tomography with adequate safety profile.Both the sedatives were equivalent based on the effect on vascular parameters and oxygen saturation after sedative administration.

References:-

1. Wachtel RE, Dexter F, Dow AJ. Growth rates in pediatric diagnostic imaging and sedation. Anesth Analg. 2009;108:1616-21.
2. Algren JT, Algren CL. Sedation and analgesia for minor pediatric procedures. PediatrEmerg Care 1996;12:435–41.
3. Singh R, Kumar N, Vajifdar H. Midazolam as a sole sedative for computed tomography imaging in pediatric patients. PedAnes 2009;19:899-904.
4. Yaster M, Nichols DG, Deshpande JK et al. Midazolam-fentanyl intravenous sedation in children: case report of respiratory arrest. Pediatrics 1990;86:463–6.
5. McGlone RG, Ranasinghe S, Durham S. An Alternative to ‘‘Brutacaine’’: a comparison of low dose ketamine with intranasal midazolam in children before suturing. J AccidEmerg Med 1998;15:231–6.
6. Temme JB, Anderson JC, Matecko S. Sedation of children for CT and MRI scanning. RadiolTechnol 1990;61:283–5.
7. Reves JG, Fragen RJ, Winik HR, et al. Midazolam: Pharmacology and uses. Anesthesiology 1985;62:310–24.
8. Klein EJ, Brown JC, Kobayashi A, Osincup D, Seidel K. A randomized clinical trial comparing oral, aerosolized intranasal, and aerosolized buccal midazolam. Ann Emerg Med. 2011;58:323-9.
9. Jackson EA, Rabbette PS, Dezateux C, Hatch DJ, Stocks J. The effect of triclofos sodium sedation on respiratory rate, oxygen saturation, and heart rate in infants and young children. PediatrPulmonol. 1991;10:40–5.
10. Gupta A, Pandey M, Choudhry L, Jain A, Pemde H. Oral midazolam versus oral triclofos for sedation of children for computed tomography scan - a randomized clinical trial. JSAN 2015;2:41-5.

11. Chaudhary S, Jindal R, Girotra G, Salhotra R, Rautela RS, Sethi AK. Is midazolam superior to triclofos and hydroxyzine as premedicant in children? J Anaesthesiol Clin Pharmacol. 2014;30(1):53–8.
12. Sessler CN, Grap MJ, Ramsay MA. Evaluating and monitoring analgesia and sedation in the intensive care unit. Crit Care. 2008;12(3):S2.
13. Aldrete JA. Modifications to the postanesthesia score for use in ambulatory surgery. J PerianesthNurs. 1998;13(3):148–55.
14. Beeby DG, Hughes JO. Behaviour of unsedated children in the anaesthetic room. Br J Anaesth. 1980;52:279–81.
15. Gupta A, Gunjan, Shekhar S, Gupta S, Gupta A. Comparison of Oral Triclofos and Oral Midazolam as Premedication in Children undergoing Elective Surgery. Anesth Essays Res. 2019;13(2):366-9.
16. Stephen MC, Mathew J, Varghese AM, Kurien M, Mathew GA. A Randomized Controlled Trial Comparing Intranasal Midazolam and Chloral Hydrate for Procedural Sedation in Children. Otolaryngol Head Neck Surg. 2015;153(6):1042-50.
17. Radhika KP, Sreejit MS, Ramadas KT. Efficacy of midazolam as oral premedication in children in comparison to triclofos sodium. Indian J Anaesth. 2016;60(6):415–9.
18. Fallah R, Nakhaei MHA, Behdad S, Moghaddam RN, Shamzadeh A. Oral Chloral Hydrate vs. Intranasal Midazolam for Sedation During Computerized Tomography. Indian Pediatrics. 2013;50:233-5.