Research Article

Premedicant in children: efficacy of oral Midazolam Vs. Triclofos

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Abstract

Hospital admission, anesthesia and surgery are stressful experiences for children which may lead to psychological trauma and personality changes. The increasing use of day care surgery, the avoidance of parental separation and the use of sedative premedication may reduce the stress of hospitalization in children and the risk of adverse psychological sequel. Search for an ideal premedicant drug for children is still on. **Aims and objectives:** To compare and evaluate the efficacy of midazolam and triclofos when given orally as premedicants in children. **Materials and methods:** In the present study 50 children were selected and were divided in two groups (midazolam group and triclofos group). Preoperative assessment was performed one day before the surgery by an observer.Evaluation of post-premedication sedation (thirty minutes post-premedication in the Midazolam group and sixty minutes post-premedication in the Triclofos group) was recorded. Level of sedation at the post premedication and level of sedation at the time of separation from parents was recorded. Behavior at the time of separation from parents and behavior during mask acceptance was recorded and analyzed. **Results:** On Post Premedicant it was observed that in midazolam group majority children (22) had sedation score of two whereas in triclofos group majority of the children (21) had sedation score four**.** Evaluation of the level of sedation at the time of separation from parents showed that majority of the children (22) in the Midazolam group had a sedation score of two whereas in triclofos group majority of the children (20) were having score four. The comparison of sedation scores between the two groups was done using the Fisher's exact probability test. The difference between the two groups was very highly significant statistically. While studying behavior at the time of separation from parents, it was observed that majority of the children in midazolam and triclofos were having score four (21 and 23 children respectively). In the Midazolam group, 14 children had a mask acceptance score of four and in the triclofos group, 20 children had a mask acceptance score of four. **Conclusion:** Even though the children are less sedated with oral midazolam as compared to triclofos, if produces an equally satisfactory separation from parents and satisfactory mask acceptance.

Key Word:oral Midazolam, Triclofos.

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INTRODUCTION

Hospital admission, anesthesia and surgery are stressful experiences for children which may lead to psychological trauma and personality changes. The increasing use of day case surgery, the avoidance of parental separation and the use of sedative premedication may reduce the stress of hospitalization in children and the risk of adverse psychological sequel.The ideal premedicant in children should be readily acceptable, have rapid and reliable onset with minimal side effects that would necessitate high levels of nursing supervision, provide for a rapid recovery and return to alertness postoperatively, thereby permitting early discharge from recovery area. Recent reports suggest that oral midazolam may fulfill many of these criteria.[1,2,3,4.] Moreover various routes of administration have been used in children for preanesthetic sedation; the oral route remains the least threatening method of drug administration.Midazolam is a potent imidazobenzodiazepine which possesses typical benzodiazepine properties namely, hypnotic and

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anxiolytic activity. Its short half life suggests that it should not prolong waking times. Midazolam has the advantage of a rapid onset and relatively short duration of action. Though the oral preparation of midazolam is commercially available now, the parental preparation is still being used by the oral route after mixing it in a vehicle to make it more palatable.[5,6] Moreover, the IV formulation by the oral route has been found to be more reliable and effective as compared to the commercially available oral formulation.[6] A dose of 0.25-0.5 mg/kg of midazolam orally has proven to be efficacious in children with fewer side-effects.[7]Triclofos is a monosodium salt of the phosphate ester Trichlorethanol (2,2,2-Trichloroethanol dihydrogen phosphate). Triclofos is rapidly absorbed from the GIT. Triclofos sodium is rapidly hydrolysed to trichloroethanol. Trichloroethanol is the active metabolite and passes into the cerebrospinal fluid, into breast milk, and across the placenta. The half-life of trichloroethanol in plasma is reported to range from about 4 to 12 hours but is considerably prolonged in the neonate. Tricloroethanol is excreted in the urine partly as glucuronide conjugate (urochloralic acid) and as trichloroacetic acid.[8] Triclofos has been used as a sedative for short procedures, but has not been widely studied as a premedicant. The oral solution is well-absorbed, proves effective within 30-40 min and produces hypnosis for 6-8 h in doses of 25-75 mg/kg.[9]Thus the present study was undertaken to study to compare and evaluate the effects of midazolam and triclofos when given orally as premedicants in children.

AIMS AND OBJECTIVES

To compare and evaluate the efficacy of midazolam and triclofos when given orally as premedicants in children.

MATERIALS AND METHODS

The present double blinded randomized control trial was conducted with objective to study the efficacy of oral midazolam against triclofos. Following inclusion and exclusion criteria was used to select the study subjects.

Inclusion criteria

- Children belonging to ASA physical status I or II
- Age: 1-8 years
- Either gender
- Scheduled for elective surgery
- Maximum body weight up to 20 kg

Exclusion criteria

- Children on anticonvulsant therapy and other sedative medications
- Those likely to have anticipated difficult airway
- Known sensitivity to benzodiazepines
- Coming for neurosurgical procedures
- Children with mental retardation
- Risk of pulmonary aspiration.

After the institutional Medical Ethics Committee approval and by using the above mentioned inclusion and exclusion criteria total 50 children were selected. An informed written consent was obtained from the parents of all the children.

Patients were randomly allocated into two groups.

1. Group M- Midazolam group
2. Group T- Triclofos group

Midazolam (0.5 mg. kg^{-1}) preparation was made by mixing preservative free midazolam (1 ml=5mg) in simple syrup base with orange flavor such that 1 ml=1 mg.

Preoperative assessment was performed one day before the surgery by an observer. The observer was an anesthesiology resident having at least two years experience and was blinded to drug administered. Nil per orders were according to the protocol of the department. Evaluation of post-premedication sedation (thirty minutes post-premedication in the Midazolam group and sixty minutes post-premedication in the Triclofos group) was recorded.

The following parameter was assessed to find the efficacy of premedication

1. Level of sedation post premedication (after an hour in the midazolam group and after half hour in the triclofos group).
2. Level of sedation at the time of separation from parents.
3. Behavior at the time of separation from parents.
4. Behavior during mask acceptance
5. The time from premedication to separation

The assessment was made by an observer who was blinded to the premedication the child received. Rescue medication was ketamine 3 $mg.kg^{-1}$ with glycopyrrolate ($10ug.kg^{-1}$) if the separation was unsatisfactory (i.e. 1 or 2).

The below table describes the various score used in the present study.

Score		Criteria
Sedation score	1	Agitated
	2	Awake
	3	Drowsy
	4	Asleep
Behavior at the time of separation from parents	1	Poor (crying, clinging)
	2	Fair (crying, not clinging)
	3	Good (whimpers, easily reassured)
	4	Excellent (easy separation)

Behavior during mask acceptance	1	Poor(terrified, crying)
	2	Fair (fear of mask, not reassured)
	3	Good(slight fears of mask, reassured)
	4	Excellent (unafraid, accept face mask)

STATISTICAL ANALYSIS

The result were analyzed using the unpaired t test, Fisher's exact probability test. For the purpose of statistical analysis, sedation score of 1 or 2 were clubbed together as awake and scores 3 or 4 were clubbed together as sedated and then analyzed. Because it was considered that children with score 1 or 2 to be awake and children who were drowsy and asleep to be sedated. Mask acceptance score of 1 or 2 were clubbed together as unsatisfactory and decided to compare with score of 3 or 4 clubbed as satisfactory and decided to compare with score of 3 or 4 clubbed as satisfactory.

RESULTS

Table 1: Demographic distribution of study subjects

Variable	Group M (n=25)	Group T (n=25)	Significance (p value)
Age years	3.52 ± 2.23	3.42 ± 2.10	P< 0.05 not significant
Weight in kg	12.34 ± 3.05	12.83 ± 5.85	P< 0.05 not significant
Male sex	18	14	P< 0.05 not significant
Female sex	7	11	

The mean age of children in midazolam group was 3.52±2.33 years whereas in the troclofos group was 3.42±2.12 years. The mean weight of children in the midazolam group was 12.34±3.05kg and that of the triclofol group was 12.83±5.85kg. There were total 18 male children in midazolam group whereas 14 in troclofos group. The agewise, weightwise and sexwise distribution of children in the midazolam and triclofol group was statistically not significant thus both the groups were comparable with each other.

Table 2: Comparison of sedation scores

Level of sedation		Group M (n=25)	Group T (n=25)	Significance (p value)
Post Premedicant	**1**	0	0	<0.001 Significant
	2	22	4	
	3	3	0	
	4	0	21	
At the time of separation from parents	**1**	0	0	<0.001 Significant
	2	22	4	
	3	3	1	
	4	0	20	

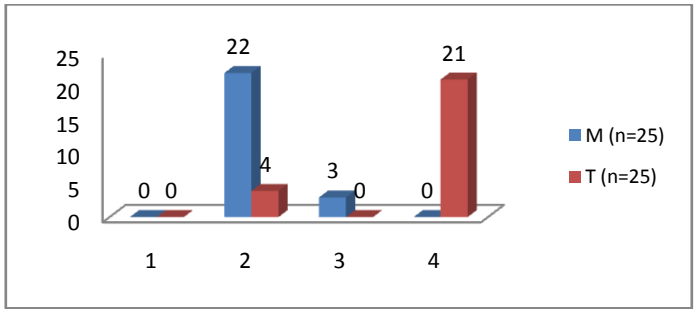

Figure 1: Post Premedicant Level of sedation

On Post Premedicant it was observed that in midazolam group majority children (22) had sedation score of two whereas in triclofos group majority of the children (21) had sedation score four. The comparison of sedation scores between the two groups was done using the Fisher's exact probability test and the difference was statistically significant.Evaluation of the level of sedation at the time of separation from parents was also done. And it was observed that majority of the children (22) in the Midazolam group had a sedation score of two whereas in triclofos group majority of the children (20) were having score four. The comparison of sedation scores between the two groups was done using the Fisher's exact probability test. The difference between the two groups was very highly significant statistically.

Table 3: Comparison of behavior/ separation score in the study groups

Separation score/ behavior score		Group M (n=25)	Group T (n=25)	Significance (p value)
Behavior at the time of separation from parents	1	0	0	P< 0.05 not significant
	2	0	0	
	3	4	2	
	4	21	23	
Behavior during mask acceptance	1	0	0	P< 0.05 not significant
	2	1	1	
	3	10	4	
	4	14	20	

While studying the behavior at the time of separation from parents, it was observed that majority of the children in midazolam and triclofos were having score four (21 and 23 children respectively). Since there were no children with unsatisfactory separation, children with

scores 3 and 4 were analyzed in both the groups and there was no statistically significant difference.In the Midazolam group, 14 children had a mask acceptance score of four and 10 had a score of three and only one child had score of two and there were no children with a score of 1. In the triclofol group, 20 children had a mask acceptance score of four whereas 4 children had a score of three and only one child had a score of two. Since the number of patients was equal in both the groups no statistical analysis done.

DISCUSSION

The present study was conducted to compare the efficacy of oral midazolam against triclofos as premedicant in children. For this purpose two groups were formed viz. midazolam group and triclofos group. The mean age of children in midazolam group was 3.52±2.33 years whereas in the troclofos group was 3.42±2.12 years. The mean weight of children in the midazolam group was 12.34±3.05kg and that of the triclofos group was 12.83±5.85kg. There were total 18 male children in midazolam group whereas 14 in troclofos group. The agewise, weightwise and sexwise distribution of children in the midazolam and triclofol group was statistically not significant thus both the groups were comparable with each other.In our study we have studied the sedation score, at appropriate time after premedication (i.e. 30 minutes after midazolam and 60 minutes after triclofos) and at separation. In this study the behavior of the children during separation from parents and mask acceptance was studied. This has been compared with triclofos which was the most common oral premedication at our institute and is available as commercial preparation. Triclofos was administered half one hour prior as compared to midazolam which was administered half an hour prior to the anticipated time of induction of anesthesia. We have chosen two different times in our study so as to assesses the sedation and separation scores at the peak effect of both the drug.[3,10]The mean duration from the administration of midazolam to separation was 36.32±4.67 minutes. We found that most of the children who had received oral midazolam were awake, calm, easily separable and readily accepted the mask in the operation theatre. This could be attributed to the fact that time interval from oral administration of midazolam to separation was limited to 30 – 45 minutes. This observation were comparable to the findings of McMillan et al,[3] The majority of children in the triclofos group were sedated, easily separable and readily accepted the mask. The mean duration from the administration of triclofos to separation was 65.60±3.74 minutes. None of the children in either of the group received any rescue medication.Thus both midazolam and triclofos are good agents for premedication in children. Children in the midazolam group were calm but awake whereas the children in the triclofos group were sleeping. The anesthesia resident who administered the drugs in the premedication room ensured that absolute silence was maintained.In the present study, for the purpose of statistical analysis we have clubbed the children as awake if they had sedation score of 1 or 2 and as sedate if they had sedation score of 3 or 4. In our study majority of children were awake in the midazolam group (22/25) as compared to triclofos where majority of the children were sedated (21/25) during post premedication and at separation. This observation was similar to the study conducted by Mitchell V et al.[11] It was also observed that very highly significant difference clinically and statistically ($p<0.0010$) in sedation score at post-premedication also sedation score at separation ($p<0.001$). In spite of this significant difference, no children in the midazolam group had unsatisfactory separation score. Four children had a score of three and 21 had a score of four in the midazolam group. In the triclofos group only 2 children had a score of three and 23 children had a score of four. Both were considered as satisfactory separation. We did not have any patients with unsatisfactory separation score in either group. So we compared only scores 3 versus score 4 and there was no statistical significance. As there was no unsatisfactory separation none of the children in either of our groups had to receive rescue medication.The mask acceptance was also satisfactory in both the groups. There were equal numbers of children with unsatisfactory and satisfactory mask acceptance in both the groups. Only one child in each group had unsatisfactory mask acceptance. So no statistical analysis was done. Since midazolam provides rapid anxiolysis and easy separation within 30 minutes. It may be conveniently used as a premedicant in children. This effect of midazolam as satisfactory premedicant could have been because the assessment was done during its peak effect. Hence it is better to prepare this formulation on a routine basis in pharmacies. As it has a shorter half-life it may be an ideal drug for use in children coming for short procedures and day stay anesthesia where in excessive sedation may be avoided.

CONCLUSION

Even though the children are less sedated with oral midazolam as compared to triclofos, it produces an equally satisfactory separation from parents and satisfactory mask acceptance.

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