ORAL PREMEDICATIONS IN PAEDIATRIC DAY SURGERY

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ABSTRACT

The degree of sedation in 191 day-stay children after oral premedication were compared. One hundred and forty-six were 1-5 years old (Group 1) and were randomised to receive either chloral 40 mg/kg, midazolam 0.2 mg/kg, promethazine 1 mg/kg, trimeprazine 3 mg/kg or placebo. Forty-five were 5-12 years old and were randomised to receive either trimeprazine 3 mg/kg, midazolam 0.2 mg/kg or placebo (Group 2).

The children were assessed using four categories: asleep or drowsy, awake but calm, crying or anxious and oversedated or obstructed airway. They were assessed on leaving the ward, at separation from the parents, at induction, in the recovery room and one and two hours after returning to the ward.

In Group 1, it was found that chloral and trimeprazine gave the best degree of sedation but the sedative effect of trimeprazine lasted longer into the post operative period. In Group 2, it was found that the children did not require deep sedation and the anxiolysis obtained with midazolam was adequate.

Keywords: *outpatient children, chloral, trimeprazine, promethazine, midazolam*

SINGAPORE MED J 1996; Vol 37: 139-142

INTRODUCTION

A crying child coming into the operating theatre is not only distressing to the child, but also to the parents and the operating theatre staff. On the other hand, any premedication given to the child must not delay recovery and discharge in day surgery patients. This prospective controlled trial was therefore conducted to compare several commonly used premedicant drugs. Chloral, midazolam, trimeprazine, promethazine and placebo were used for children aged 1 to 5 years old; while midazolam, trimeprazine and placebo were used for children aged 5 -12 years old. The aim of this trial is to find out which of the above drugs gave the best preoperative sedation with the least postoperative drowsiness.

METHODS

A total of 191 children were studied after institutional approval was obtained. One hundred and forty-six were 1 to 5 years old (Group 1) and 45 were 5 to 12 years old (Group 2). These were all day surgery patients who did not require intramuscular premedication. The children were clerked by the ward doctors and any history of drug allergy obtained. They were then randomised to receive one of five premedication drugs for Group 1 and one of 3 drugs for Group 2. These drugs have been used in our hospital for pre-medication according to the anaesthetists' preference but no comparative trial has been done.

The premedication drugs were labelled A to E and the code held by the pharmacist. The five drugs for Group 1 were chloral hydrate, midazolam, promethazine, trimeprazine tartrate and placebo. The three drugs for Group 2 were midazolam, trimeprazine and placebo. The dose of chloral hydrate was 40 mg/kg (up to a maximum of 1 g), midazolam 0.2 mg/kg, promethazine 1 mg/kg and trimeprazine 3 mg/kg. These drugs were specially prepared by the hospital pharmacy to give a standard dose of 0.5 mL/kg. A new batch of drugs was prepared every week. They were also identically coloured using the colouring agents, Orange G. All the observers were therefore blinded to the identity of the given drug.

The premedication was given 1 to 2 hours before the scheduled operation. The child was then assessed at six stages using four categories as given in Table I.

Table I – Six stages of assessment and 4 categories of assessment.

Stage 1	by the ward staff when the child was leaving the ward for the operating theatre
Stage 2	by the operating theatre reception nurses when the child was separated from the parent
Stage 3	by the anaesthetist at the time of induction
Stage 4	by the recovery room nurses on discharge from the operating theatre to the ward
Stage 5	by the ward nurses 1 hour after arrival in the ward
Stage 6	by the ward nurses 2 hours after arrival in the ward

The four categories used were:

1. asleep or drowsy
2. awake but calm
3. crying or anxious
4. oversedated or obstructed airway

Other information recorded included the type of pain relief (parenteral opioid, regional block or local anaesthetic), type of operation, type of induction (intravenous or inhalational), and the interval between giving the oral premedication and the time of the induction. The anaesthetist was also asked to assess whether sedation was adequate at the time of induction.

The Pearson's X^2 test was used for analysis. The null hypothesis was that there was no difference in the degree of sedation for the different drugs at each of the 6 stages. A p value < 0.05 was considered significant.

RESULTS

Group 1

A total of 146 children were in Group 1. There were 34 children in the placebo group, 25 in the chloral group, 27 in the midazolam group, 31 in the trimeprazine group and 29 in the promethazine

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group.

Sixty-three percent of the children were given an inhalational induction and this proportion was consistent in all the five drug groups. 44.4% of the premedication was given 1 to 2 hours before induction and 37.5% more than 2 hours. Sedation was considered adequate in more than 50% of the children in the chloral and trimeprazine sub groups (Table II).

Table II – Degree of sedation at time of induction in Group 1 as assessed by the anaesthetist.

	Sedation adequate % of children	Sedation inadequate % of children
Placebo	32.0	64.0
Chloral	69.6	30.4
Midazolam	41.7	54.2
Trimeprazine	55.2	44.8
Promethazine	39.1	60.9

Eighty-six percent of the children were given regional blocks after induction and this proportion was consistent in all the five subgroups. There were no statistically significant differences between the various drug groups at $p<0.05$ for all the above data.

Table III gives the number of children, column percentages and statistical values for each drug group at the 6 different stages. None of the children was assessed to be oversedated and none had airway obstruction. For Stage 1, the responses of asleep/drowsy and awake but calm were grouped together for the X^2 analysis such that the number of cells with expected frequencies less than 5 would be less than 50% of the total cells. The 5 drugs did not give a statistically significant difference in outcome when the asleep/drowsy and the awake but calm outcomes were combined. The Pearson's X^2 analysis done for the 5 drugs comparing the outcome of asleep/drowsy and awake but calm gives a value of 17.89 with 4 degrees of freedom giving a p value of 0.0013. Therefore there is a significant difference in the 5 drugs when these 2 outcomes are compared. The column percentages show a larger percentage in the asleep/drowsy group for chloral and trimeprazine and more in the awake but calm group for placebo and midazolam.

At Stage 2, the 5 drugs produced significantly different outcomes. The column percentages showed a greater proportion of children were asleep/drowsy for chloral and trimeprazine while the promethazine group had a greater proportion of children who were crying/anxious.

At Stage 3, the 5 drugs again gave significantly different outcomes with a greater proportion of children asleep/drowsy after chloral and trimeprazine. A greater proportion of children were crying/anxious after placebo and promethazine.

At Stage 4, which was the recovery room, there was no significant difference in the outcome for the 5 drugs.

At Stages 5 and 6, the outcomes were significantly different for the 5 drugs. There was a greater proportion of children in the asleep/drowsy outcome for those who were given trimeprazine.

Group 2

A total of 45 children were in this group with 13 in the placebo group, 18 in the midazolam group and 14 in the trimeprazine group. Chloral and promethazine were omitted because the total dose needed would be excessively high.

In this group more than 60% of the children in each drug group were given an intravenous induction. Forty percent of the premedication was given 1-2 hours before induction and 48.9% more than 2 hours before induction. There were no statistically significant differences between the various drug groups at $p<0.05$

Table III – Data and statistical results for Group 1.

	Placebo	Chloral	Midazolam	Trimeprazine	Promethazine	Pearson's X^2	df	p value
Stage 1								
Asleep/drowsy	0(0.0)	5 (22.7)	1 (4.0)	9 (33.3)	3 (11.1)			
Awake but calm	31 (91.8)	15 (44.1)	22 (88.0)	16 (59.3)	19 (70.4)	2.46	4	0.6516*
Crying/anxious	3 (8.8)	2 (9.1)	2 (8.0)	2 (7.4)	5 (18.5)			
Stage 2								
Asleep/drowsy	3 (9.7)	10 (50.0)	2 (8.0)	9 (30.0)	3 (11.1)			
Awake but calm	17 (54.8)	3 (15.0)	15 (60.0)	12 (40.0)	11 (40.7)	22.64	8	0.0386
Crying/anxious	11 (35.5)	7 (35.0)	8 (32.0)	8 (30.0)	13 (48.1)			
Stage 3								
Asleep/drowsy	1 (2.9)	11 (44.0)	2 (7.4)	13 (41.9)	4 (13.8)			
Awake but calm	13 (38.2)	5 (20.0)	13 (48.1)	8 (25.8)	4 (13.8)	34.93	8	0.0000
Crying/anxious	20 (58.8)	9 (36.0)	12 (44.4)	10 (32.3)	21 (72.4)			
Stage 4								
Asleep/drowsy	3 (9.7)	1 (5.3)	0 (0.0)	5 (19.2)	3 (12.5)			
Awake but calm	15 (48.4)	6 (31.6)	7 (36.8)	8 (30.8)	12 (0.5)	9.20	8	0.3255
Crying/anxious	13 (41.9)	12 (63.2)	12 (63.2)	13 (50.0)	9 (37.5)			
Stage 5								
Asleep/drowsy	4 (11.8)	3 (12.0)	6 (23.1)	15 (48.4)	7 (24.1)			
Awake but calm	27 (79.4)	20 (80.0)	17 (65.4)	13 (41.9)	19 (65.5)	15.83	8	0.0449
Crying/anxious	3 (8.8)	2 (8.0)	3 (11.5)	3 (9.7)	3 (10.3)			
Stage 6								
Asleep/drowsy	2 (5.9)	3 (12.0)	6 (22.2)	18 (58.1)	9 (36.0)			
Awake but calm	30 (88.2)	21 (84.0)	21 (77.8)	12 (38.7)	16 (64.0)	29.64	8	0.0002
Crying/anxious	2 (5.9)	1 (4.0)	0 (0.0)	1 (3.2)	0 (0.0)			

Footnote: *the statistics for this stage was done with the asleep/drowsy and awake but calm groups were combined together so that the number of cells with expected frequencies less than 5 would not be more than half. Figures in brackets are column percentages.

for the above data. More than 70% of the children were given a regional block in each of the 3 drug groups.

Table IV gives the number of children, column percentages and statistical values for each drug group at the 6 different stages. None of the children were assessed to be oversedated and none had airway obstruction. For Stages 1 to 4, the responses of asleep/drowsy and awake but calm were grouped together for the X^2 analysis such that the number of cells with expected frequencies less than 5 would be less than 50% of the total cells. In Stage 1, the 3 drugs did not give a statistically significant difference in outcome when the asleep/drowsy and the awake but calm outcomes were combined.

At Stage 2, the outcomes were significantly different for the 3 drugs, with a greater proportion of children asleep/drowsy or awake but calm after trimeprazine and a greater proportion of children crying/anxious after placebo.

At Stage 3, there was no significant difference in the outcome when asleep/drowsy and awake but calm groups are combined. However, the column percentages showed that a greater proportion of children were asleep/drowsy after trimeprazine while a greater proportion of children were crying/anxious after placebo. The Pearson's X^2 analysis done for the 3 drugs comparing the outcomes asleep/drowsy and awake but calm gives a value of 6.74 with 2 degrees of freedom, giving a p value of 0.0345. There was therefore a significant difference in the 3 drugs when these 2 outcomes were compared.

At Stage 4, which was the post-operative period in the recovery room, there was no significant difference in the outcome. All 3 drugs had most of the children in the awake but calm outcome.

At Stages 5 and 6, there were significant differences in the outcome for the 3 drugs, with a greater proportion of children asleep/drowsy for those given trimeprazine.

DISCUSSION

When the children were leaving the ward, all the drug groups showed a large number of children who were awake but calm. This is because of the presence of the parents, since the oral premedication given would not have had adequate time to act. In the one to five age group, there were more children who were asleep or drowsy in the chloral and trimeprazine groups as compared to the other drug groups. There was no difference in the various drug groups for the older children.

The time of separation from the mother is probably the most frightening, especially for the younger children, and an effective premedication would be useful. Again, the chloral and trimeprazine groups gave better sedation both at the time of separation and at the time of induction. The midazolam groups in both the younger and older children showed a large number who were awake but calm at separation, although the dosage used in our study was in the lower range when compared to the study done by Parnis et al[1]. They found that 39 out of 49 children who received midazolam 0.25 mg/kg and 42 out of 49 who received 0.5 mg/kg were awake and calm at induction. We considered this awake but calm state satisfactory for the older children. This is in contrast to the placebo group in the older children where more were crying and anxious. However in the younger children, a greater degree of sedation is required since many in the midazolam group who were awake and calm at separation became tearful and anxious at induction.

At the early recovery stage, there was no statistically significant difference between the responses in the various drug groups for both the younger and older children. This probably reflects the fact that good pain relief was more important at this time, when the children were in the recovery room without their parents and just waking up from the anaesthesia.

When the children were back in the ward, they would be

Table IV - Data and statistical results for Group 2.

	Placebo	Midazolam	Trimeprazine	Pearson's X^2	df	p value
Stage 1						
Asleep/drowsy	0 (0.0)	1 (6.7)	1 (10.0)			
Awake but calm	10 (90.9)	14 (93.3)	9 (90.0)	2.34	2	0.3107*
Crying/anxious	1 (9.1)	0 (0.0)	0 (0.0)			
Stage 2						
Asleep/drowsy	1 (9.1)	0 (0.0)	5 (35.7)			
Awake but calm	6 (54.5)	15 (93.8)	9 (64.3)	8.47	2	0.0145*
Crying/anxious	4 (36.4)	1 (6.3)	0 (0.0)			
Stage 3						
Asleep/drowsy	2 (15.4)	1 (5.6)	6 (42.9)			
Awake but calm	7 (53.8)	16 (88.9)	7 (50.0)	4.83	2	0.0895*
Crying/anxious	4 (30.8)	1 (5.6)	1 (7.1)			
Stage 4						
Asleep/drowsy	1 (4.3)	0 (0.00)	2 (28.6)			
Awake but calm	6 (85.7)	15 (100.0)	4 (57.1)	3.26	2	0.1964*
Crying/anxious	0 (0.00)	0 (0.0)	1 (7.1)			
Stage 5						
Asleep/drowsy	0 (0.0)	2 (11.8)	6 (50.0)	11.10	2	0.0389
Awake but calm	13 (100.0)	15 (88.2)	6 (50.0)			
Stage 6						
Asleep/drowsy	1 (8.3)	0 (0.0)	4 (33.3)	7.54	2	0.0231
Awake but calm	11 (91.7)	17 (100.0)	8 (66.7)			

Footnote: *the statistics for this stage was done with the asleep/drowsy and awake but calm groups were combined together so that the number of cells with expected frequencies less than 5 would not be more than half. Figures in brackets are column percentages.

with their parents. The emphasis of the assessment at this stage would be to exclude prolonged sedation which would delay discharge. One to two hours after returning to the ward, the trimeprazine groups showed a greater number of children who were still drowsy. This was seen in both age groups. This was in agreement with the study done by Bramwell & Manford[2]. All the children were however discharged uneventfully six hours after the surgery.

In this study, a control group was used, as the study done by Beeby & Hughs showed that a certain percentage of children would be calm and quiet even without premedication[3]. In their study, 81% of the children aged 2-7 years had a satisfactory demeanour at induction as compared to 40% in our study, and 94% in the 7-9 age group as compared to 69% in our study. This may reflect a cultural difference in the two study population. In our study, it appears that the younger children definitely benefitted from some degree of sedative premedication. This was less conclusively seen in the older group.

Trimeprazine at 3 mg/kg gave good quality sedation but its effect lasted into the post surgical period. The additional advantages of trimeprazine include a decrease in gastric content and an increase in pH due to its cholinergic effect and a lower incidence of post-operative nausea and vomiting[4,5]. Chloral at 40mg/kg is perhaps more manageable in that it gave good preoperative sedation and little post-operative effect as seen in our study and that done by Anderson et al[6]. Unfortunately, the dose and volume needed in the bigger children would be too great. Midazolam, despite its low dose used in this study (0.2 mg/kg), showed a promising response in that it caused anxiolysis without much sedation in the older children. The problem with midazolam is that it comes in tablet form and a suspension has to be prepared specially by the pharmacist.

Several areas which have not been explored in this study include parental presence at induction and the use of EMLA (Eutectic Mixture of Local Anaesthetic) cream in the older children. The parents' presence at induction should help make the experience much less threatening for the younger children. However, at the time of the study, the operating room setup did not allow this as a routine practice. On the other hand, the older children should not have much anxiety on separation from parents. Their main fear would be that of pain and an unknown environment. Anderson et al[6] found that neither diazepam, alprazolam or midazolam reduced anxiety in children older than 4 years. Therefore the older child may actually not need any oral premedication. EMLA cream may be very useful in this group since it would allow a painless and rapid intravenous induction. EMLA cream has only been available to us recently.

CONCLUSION

From our study, we found that the younger children benefitted from some sedative premedication and that chloral and trimeprazine gave the best sedation at induction. However, the effect of trimeprazine extended longer into the post operative period. As for the older children, they may not need any premedication. If anxiolysis is required, midazolam 0.2 mg/kg would be useful.

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