May 2012

Effectiveness of premedication at the time of separation from parent and mask induction in paediatric patients coming for congenital heart disease surgery

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ORIGINAL ARTICLE

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ABSTRACT

Objective: To compare the effectiveness of oral midazolam and chloral hydrate on anxiety and sedation at various stages of pre-operative period in congenital heart surgery patients.

Study Design: Cross-sectional comparative study.

Place and Duration of Study: Operating rooms of The Aga Khan University Hospital, Karachi, from October 2009 to December 2010.

Methodology: Sixty-six patients between the ages of 6 months and 6 years received either chloral hydrate (Group C) or midazolam (Group M) pre-operatively. All congenital heart disease patients coming for cardiac surgeries were included while cases of emergency surgery and those patients in whom premedication was not given were excluded. Effect of premedication observed and documented by Anaesthesia Consultant. Documentation included demographics, level of anxiety and sedation at the time of separation from parent and at the time of mask application.

Results: Forty study subjects were male (61%) and 26 were females (39%). Eleven patients received oral midazolam while 55 received oral chloral hydrate. Sixteen patients were tearful and anxious (24%) while rests were calm and asleep. Thirty patients in group C (60%) were well sedated at the time of separation. Mask induction was satisfactory in 76% of chloral hydrate patients. Increase dose was suggested in 23 patients by anaesthetizing physician. Out of these 6 belonged to group M (54.5%) while 17 to low dose chloral hydrate group (30.9%) [< 40 mg/kg].

Conclusion: Chloral hydrate provides comparable anxiolysis but superior sedation and mask acceptance scores when compared with midazolam. Higher doses of chloral hydrate (50 mg/kg) were required to keep these patients calm and peaceful at the time of mask application for inhalation induction.

Key words: *Premedication. Midazolam. Chloral hydrate. Congenital cardiac defect.*

INTRODUCTION

Surgery in paediatric patients is associated with emotional, psychological and physiological changes during perioperative period. Some of these psychological changes may continue for several months postoperatively.[1] These changes become more pronounced in congenital heart surgery patients. Effective premedication is of utmost importance in these children to improve outcome. Instead of premedication some hospitals allow parental presence in the operating room during induction but studies do not show any benefit of this practice.[2]

Midazolam and chloral hydrate are commonly used for premedication at our institution but the timing, adequate dose and effectiveness of these agents needs to be addressed. Effective premedication is very important at several stages particularly at the time of separation from parent and mask induction. This is more important in congenital heart disease patients as crying and struggling at the time of separation and mask induction will increase oxygen consumption and further deterioration of saturation.

Midazolam is a most commonly used premedication for all kinds of surgeries.[3] Its safety in congenital heart disease patients and anxiolytic effect has been proved in several studies. It has been used in different doses ranging from 0.25 to 1.5 mg/kg and through different routes including oral, intramuscular (IM), intravenous (IV) sublingual, transmucosal, intranasal and rectal.[4-6] In addition, it has been used in all age groups to make patient cooperative at several stages of pre-operative period.[7] Due to its muscle relaxant properties, midazolam needs to be used cautiously in patients who are at risk of respiratory complications.[8]

Chloral hydrate is a sedative hypnotic drug and frequently used for procedures outside operating room.[9] It is metabolized in the liver to active metabolite 2,2, 2-trichloroethanol.[10] Chloral hydrate provides adequate sedation during procedure without significant side effects.[11] It is available in oral preparation and rectal suppositories. The maximum single dose is one gram and usually given in the doses of 25 - 75 mg/kg.

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Received January 28, 2011; accepted March 12, 2012.

Although premedication to relieve anxiety is important at the time of separation from parent but importance is usually not given to sedation at the time of mask application particularly in congenital heart disease (CHD) patients. Adequate sedation at the time of mask application will leads to smooth induction, prevention of tetralogy spells (tet spells) and drops in saturation. Present study was conducted to determine and compare the effectiveness of various doses of two premedication on anxiety and degree of sedation at various stages of pre-operative period in congenital heart disease patients.

METHODOLOGY

In this observational study conducted at the Aga Khan University Hospital, Karachi, from October 2009 to December 2010, 66 patients between the ages of 6 months and 6 years were given either chloral hydrate (Group C) or midazolam (Group M) pre-operatively. All congenital heart diseases patients coming for cardiac surgery were included while emergency surgery and those patients in whom premedication was not given or orders not written were excluded. Oral doses of these two drugs were categorized into low dose (M: < 0.4, C: < 40), intermediate dose (M: 0.4, C: 40) and high dose (M: > 0.5, C: > 50) in mg/kg. There were no ethical concerns regarding this study as this was an observational study.

A proforma was developed and filled by Consultant Anaesthetist. Documentation included demographics, type of surgery, premedication ordered and given, whether patient spit up or vomited after premedication and additional intramuscular or intravenous drugs needed to keep these children sedated at the time of separation. In addition, level of anxiety and sedation at the time of separation from parent and ease of mask application for inhalation induction was also documented. A four point scale was used to assess anxiolysis, sedation and mask acceptance.

Pre-medication orders were written by residents after consultation with primary anaesthetist. Initially low doses of both drugs were given but later conscious efforts were done to give higher doses of drugs.

All data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 17. Frequency and percentages were computed for categorical variables and analyzed by Chi-square test and Fisher exact test while quantitative variables were presented as median and interquartile (IQR) after normality checked and analyzed by Mann-Whitney test. Variables are age, weight, gender, sedation, anxiety and mask acceptance. P-values of less than 0.05 were considered significant.

RESULTS

Out of a total 66 paediatric patients, 40 were males (61%) and 26 were females (39%). Average weight of the patients was 11.09 ± 4.56 kg. Average age of patients was 33.48 ± 22.9 months. Demographic variable like age and gender were not significantly different between groups while median weight was significantly high in group M than group C [16.5 (IQR=8.8) vs. 10 (IQR=6.5) p=0.029]. Pre-operative medication was ordered and administered in 65 patients (98.5%) on the surgical floor. One patient was given pre-medication in the holding area when it was found that pre-operative order was not written. Eleven patients (17%) were given midazolam (M group) while 55 patients (83%) received chloral hydrate (C group).

Nine patients (13.6%) were tearful and 7 patients (10.6%) were anxious while rest were calm and asleep at the time of separation. At the time of mask induction, 26 patients (39.4%) were combative and started crying. Increase dose was suggested in 23 patients (34.8%) by anaesthetizing physician. Out of these, 6 belonged to group M while 17 belonged to low dose chloral hydrate group. Three patients vomited or spitted out pre-medication drug. Most of the patients (75%) had surgery in the morning. Seven patients required additional IV/IM premedication in the operating room or holding area.

Anxiety and mask acceptance of patients was not significant between groups while sedation (drowsy and asleep) was significantly higher in group C than group M (60% vs. 9.1%; p < 0.01) as shown in Table I.

In chloral hydrate group (Table II), mask acceptance was increased (76%) when the dose increased to 50 mg/kg. Thirty-three patients in group C were well sedated at the time of separation. Most of the anaesthetists suggested 50 mg/kg as the adequate dose. Four patients were still tearful even with high dose chloral hydrate.

Midazolam was given mainly to older children. Although 8 patients (73%) were free of anxiety but 10 patients (91%) were awake and alert, when sedation level was checked in midazolam group (Table III). Despite high anxiolytic scores, mask acceptance was low in these patients (37%).

Nine patients were tearful and combative at the time of separation from parent. Out of these two patients belonged to M group while 7 belonged to C group. Two

Table I: Comparison of anxiety and sedation between groups.

Variables	Group M n=11	Group C n=55	p-values
Anxiety			
Tearful and anxious	03 (27.3%)	13 (23.6%)	0.530
Calm and asleep	08 (72.7%)	42 (76.4%)	
Sedation			
Drowsy and asleep	01 (9.1%)	33 (60%)	0.002
Awake and alert	10 (90.9%)	22 (40%)	
Mask acceptance*			
Combative+crying+sobbing	05 (62.5%)	23 (45.1%)	0.450
Peaceful	03 (37.5%)	28 (54.9%)	

** Three patient in group M and four patients in group C are not included in analysis of mask acceptance due to IV Induction. Data are presented as number and (%).*

Table II: Effectiveness of chloral hydrate with respect to dosages (n=55).

Variables	Level	Chloral hydrate (Group C)			p-value
		50 mg/kg	40 mg/kg	< 40 mg/kg	
Anxiolysis	Tearful and anxious	04	05	04	0.315
	Calm and asleep	21	15	06	
Sedation	Drowsy and asleep	20	08	05	0.019*
	Awake and alert	05	12	05	
Mask acceptance†	Combative + crying + sobbing	08	13	02	0.029*
	Peaceful	15	06	07	

*Data is represented in frequency (n); * p<0.05 significant; Chi-square test applied; † Four patients are not included in mask acceptance due to IV Induction.*

Table III: Effectiveness of midazolam with respect to dosage (n=11).

Variables	Level	Midazolam (Group M)			p-value
		> 0.5 mg/kg	0.4 mg/kg	< 0.4 mg/kg	
Anxiolysis	Tearful and anxious	00	02	01	0.382
	Calm and asleep	02	02	04	
Sedation	Drowsy and asleep	00	00	01	0.517
	Awake and alert	02	04	04	
Mask Acceptance	Combative + Crying + Sobbing	02	02	01	0.449
	Peaceful	00	02	01	

** Three patients are not included in analysis of mask acceptance due to IV Induction. Data are represented in frequency (n). Chi-square test applied.*

of group C patients were given 50 mg/kg but one patient vomited out and the second patient received premedication in less than half hour. Both patients of M group received 0.4 mg/kg.

When we look at the suggestion by primary anaesthetist, it was notable that only 2 patients (18.2%) in M group and 25 patients (45%) in C group were considered as adequate dose. Doses higher than 40 mg/kg in C group were suggested in 11 patients (55%) by primary anaesthetist. None of these patients developed respiratory or cardio-vascular compromise during pre-operative period.

DISCUSSION

Effective premedication is of utmost importance in patients with CHD to avoid agitation and crying at the time of separation from parent and particularly at the time of mask induction. Although anxiolysis may be the main purpose of premedication in adult and older children but deep sedation is required in children between the ages of 6 months to 6 years particularly in CHD paediatric patients. Anxiety and agitation can trigger a Tetralogy of Fallot's spell in subjects (TOF).[6] Ideally premedication should provide quick sedation, easily administrable, palatable, of adequate duration to cover period of separation and mask induction. In addition, it should be able to maintain saturation in CHD patients who have already reduced saturation.

Both midazolam and chloral hydrate do not have any analgesic effect. Some centres still use intramuscular narcotic analgesics in addition to midazolam which is associated with pain and discomfort to patient along with dissatisfaction among parents.[12] Few centres still ask parents to accompany child to operating room,[13] but this practice is still controversial due to various reasons.

In the present practice of premedication to CHD paediatric patients, several combinations have been used. Chloral hydrate is commonly used in patients under 15 kg, while midazolam is used in older children. Lower than recommended doses of midazolam were used in most of the patients. Fear of desaturation due to higher doses of premedication is always present particularly in CHD patients who already have lower saturations.

Role of nursing staff is very important to follow written orders and give premedication in time.[14] In addition, if premedication was vomited out or spit up by patients then additional dose should be given by nurse or primary anaesthetist needs to be informed. In the present study all patients were visited pre-operative by a resident and premedication is ordered in all except one patient. In 4 patients pre-medication was not administered by staff nurse despite written orders. In addition, few patients did not receive premedication in time. This needs to be emphasized and early feedback along with counselling should be done.[15]

Effect of premedication is highly dependent on duration of fasting, amount of drug given, route of administration, time patient keeps oral premedication in mouth and presence of irritability. Hungry child usually require higher doses of sedation due to his irritability.[9] In this study clear fluids were allowed 2 hours prior to surgery.

Chloral hydrate was tolerated very well[16] and showed acceptable scores when higher doses were given to paediatric patients. Although there were few failures but it provided deep sedation without any serious side-effects.[17] Average time to deep sedation with chloral hydrate is about 25 minutes.[18] Most of our patients received premedication about half an hour before coming to operating room but few patients who received premedication in less than half an hour showed lower scores at both points.

Calm and quite child at the time of application of mask is of utmost importance in congenital heart disease patient and use of midazolam has been challenged in few studies.[19] Midazolam group patients were although less anxious but lower scores were noticed at the time of mask induction. Two patients who received more than 0.5 mg/kg were still combative and crying at the time of mask application. Sedation scores were also lower with midazolam and only one patient was asleep at the time of separation from parent. This poor mask acceptance and sedation scores can be corrected by using higher doses to deeply sedated patients as suggested (1.5 mg/kg) by Masue *et al*.[20]

Proforma

Effectiveness of premedication on anxiety and sedation level in paediatric patients coming for congenital heart surgery.

Age: _____ Sex: _____ Weight: _____ MR No: _____

Date: _____ Surgery: _____ Time of surgery: _____

A. Pre-operative visit by resident: ◎ Yes ◎ No
B. Premedication ordered: ◎ Yes ◎ No
C. Premedication given on floor: ◎ Yes ◎ No
D. Drug given but spitted or vomited out by patient: ◎ Yes ◎ No
E. Type of premedication given:
   1. Oral midazolam (dose in mg/kg) : ----------
   2. Oral chloral hydrate (dose in mg/kg) : ----------
   3. Others (mention dose and route): ----------
F. Timing of premedication (circle one):
   1. How many hrs before surgery ◎ > 1 hour ◎ 1 hour ◎ 1/2 hour
   2. In holding area: ----------
   3. Not given on floor: ----------
G. Accompanied by parent in the OR: ◎ Yes ◎ No
H. Anxiety level (4 point) at the time of separation from parent (√ one)
   1. Tearful / combative
   2. Anxious but easily reassured
   3. Calm
   4. Asleep
I. Sedation level (4 point) at the time of separation from parent (√ one)
   1. Alert/ active
   2. Awake/calm
   3. Drowsy but respond to verbal / tactile stimuli
   4. Asleep
J. Mask acceptance (4 point) at the time of induction (√ one)
   1. Combative / screaming
   2. Crying but easily reassured
   3. Occasionally sobbing/ mostly calm
   4. Peaceful
K. Corrective measure recommended / Done
   1. Adjustment in dose
   2. Change in premedication drug
   3. Floor nursing staff counselled or complaint form raised

Any other suggestion: ----------

CONCLUSION

Midazolam in the doses given at the study centre provides higher grades of anxiolysis but unable to provide adequate sedation and mask acceptance. Chloral hydrate on the other hand is comparable in terms of anxiolysis but superior in providing sedation and conditions at the time of mask application. Higher dose of chloral hydrate was required to keep these patients calm and peaceful at the time of mask application for inhalation induction.

REFERENCES

1. Kain ZN, Wang SM, Mayes LC, Caramico LA, Hofstadter MB. Distress during the induction of anaesthesia and postoperative behavioural outcomes. *Anesth Analg* 1999; **88**:1042-7.
2. Hannallah RS, Rosales JK. Experience with parents' presence during anaesthesia induction in children. *Can Anaesth Soc J* 1983; **30**:286-9.
3. Almenrader N, Passariello M, Coccetti B, Haiberger R, Pietropaoli P. Premedication in children: a comparison of oral midazolam and oral clonidine. *Paediatr Anaesth* 2007; **17**: 1143-9.
4. Layangool T, Sangtawesin C, Kirawittaya T, Prompan W, Attachoo A, Pechdamrongsakul A, *et al*. A comparison of oral chloral hydrate and sublingual midazolam sedation for echocardiogram in children. *J Med Assoc Thai* 2008; **91**:S45-S52.
5. Hosey MT, Asbury AJ, Bowman AW, Millar K, Martin K, Musiello T, *et al.* The effect of transmucosal 0.2 mg/kg midazolam premedication on dental anxiety, anaesthetic induction and psychological morbidity in children undergoing general anaesthesia for tooth extraction. *Br Dent J* 2009; **207**:E2; discussion 32-3.
6. Mohindra R, Beebe DS, Belani KG. Anaesthetic management of patients with congenital heart disease presenting for non-cardiac surgery. *Ann Card Anaesth* 2002; **5**:15-24.
7. Sun GC, Hsu MC, Chia YY, Chen PY, Shaw FZ. Effects of age and gender on intravenous midazolam premedication: a randomized double-blind study. *Br J Anaesth* 2008; **101**:632-9. Epub 2008 Sep 4.
8. von Ungern-Sternberg BS, Erb TO, Habre W, Sly PD, Hantos Z. The impact of oral premedication with midazolam on respiratory function in children. *Anesth Analg* 2009; **108**:1771-6.
9. Keidan I, Gozal D, Minuskin T, Weinberg M, Barkaly H, Augarten A. The effect of fasting practice on sedation with chloral hydrate. *Pediatr Emerg Care* 2004; **20**:805-7.
10. Solt K, Johansson JS. Binding of the active metabolite of chloral hydrate, 2,2,2-trichloroethanol, to serum albumin demonstrated using tryptophan fluorescence quenching. *Pharmacology* 2002; **64**:152-9.
11. da Costa LR, da Costa PS, Lima AR. A randomized double-blinded trial of chloral hydrate with or without hydroxyzine versus placebo for paediatric dental sedation. *Braz Dent J* 2007; **18**: 334-40.
12. Levine MF, Hartley EJ, Macpherson BA, Burrows FA, Lerman J. Oral midazolam premedication for children with congenital cyanotic heart disease undergoing cardiac surgery: a comparative study. *Can J Anaesth* 1993; **40**:934-8.
13. Kazak Z, Sezer GB, Yilmaz AA, Ates Y. Premedication with oral midazolam with or without parental presence. *Eur J Anaesthesiol* 2010; **27**:347-52.
14. Saunders S. The effective management and administration of premedication. *Nurs Times* 2004; **100**:40-3.
15. Duncan K, Pozehl B. Effects of individual performance feedback on nurses' adherence to pain management clinical guidelines. *Outcomes Manag Nurs Pract* 2001; **5**:57-62.
16. Hijazi OM, Haidar NA, Al-Eissa YA. Chloral hydrate. An effective agent for sedation in children with age and weight dependent response. *Saudi Med J* 2005; **26**:746-9.
17. Nicolson SC, Montenegro LM, Cohen MS, O'Neill D, Calfin D, Jones LA, *et al.* A comparison of the efficacy and safety of chloral hydrate versus inhaled anaesthesia for sedating infants and toddlers for transthoracic echocardiograms. *J Am Soc Echocardiogr* 2010; **23**:38-42.

18. Lipshitz M, Marino BL, Sanders ST. Chloral hydrate side effects in young children: causes and management. *Heart Lung* 1993; **22**:408-14.

19. Gharde P, Chauhan S, Kiran U. Evaluation of efficacy of intranasal midazolam, ketamine and their mixture as premedication and its relation with bispectral index in children with tetralogy of Fallot undergoing intracardiac repair. *Ann Card Anaesth* 2006; **9**:25-30.

20. Masue T, Shimonaka H, Fukao I, Kasuya S, Kasuya Y, Dohi S. Oral high-dose midazolam premedication for infants and children undergoing cardiovascular surgery. *Paediatr Anaesth* 2003; **13**:662-7.