

Original Article

Pilot Study in Evaluating the Side Effects of Chloral Hydrate Sedation in Children

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Abstract

Retrospective review was done on 282 children under chloral hydrate sedation for computerized tomography of brain or thorax, electroencephalogram, echocardiogram or brainstem auditory evoked potential studies. The study period was from 1 April, 1997 to 31 March, 1999. Standardized sedation protocol and checklist for pre-sedation assessment, monitoring and discharge assessment were used. The overall risk of prolonged sedation was 8.9%. No statistically significant difference in prolonged sedation could be shown among the different age groups or among the different dosage groups. There was no desaturation, vomiting or paradoxical excitation. Our study suggested the incidence of complications arising from sedation by chloral hydrate might be lower than reported when the maximum dosage of chloral hydrate was limited to 100 mg/kg or two gram in selected patients. A larger prospective study may be necessary to reassess the need for routine intensive monitoring in all children undergoing sedation by chloral hydrate alone.

Key words

Chloral hydrate; Side effects

Introduction

Chloral hydrate has long been used for sedation in various procedures in children and considered to be safe, effective and well tolerated.¹⁻³ The guideline from American Academy of Pediatrics suggested the need for standardized documented monitoring for children undergoing sedation including chloral hydrate.⁴ Reported side effects from chloral hydrate included desaturation, vomiting, paradoxical excitation or prolonged sedation.⁵ There were even occasional deaths.² However recent literature suggested that chloral hydrate should be considered separately from other sedative agents.⁶ There was insufficient data on the incidence of adverse events when chloral hydrate was properly prescribed. This study aimed

at estimating the incidence when chloral hydrate was used in selected patients at appropriate dosages and as the sole sedative agent. We also tried to analyze factors that might be associated with an increased incidence of such adverse effects.

Methods

Retrospective review was done on patients who were admitted under Paediatric Department of Alice Ho Miu Ling Nethersole Hospital during a two year period from 1 April, 1997 to 31 March, 1999. Children who required chloral hydrate sedation for computerized tomography (CT) of brain or thorax, electroencephalogram (EEG), echocardiogram (ECHO) or brainstem auditory evoked potential study (BAEP) were included for analysis. Repeated doses of chloral hydrate were allowed.

Standardized sedation protocol and checklist for pre-sedation assessment, monitoring and discharge assessment were in place before the study and were used. (Appendix 1 & 2) All children were assessed by doctors before sedation and had the baseline vital signs monitored. Continuous SaO₂

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monitoring was routinely performed till the children were fully conscious. In case of desaturation, medical personnel would assess the child and determine if management of airway and/or oxygen supplementation was necessary. Blood pressure monitoring was optional. Monitoring of fluid input and output was routinely performed for children under two years of age. Such monitoring would be performed for children above two years of age if deemed necessary by the attending doctors or if the children developed vomiting during hospitalization. In case of vomiting or prolonged sedation, hydration status of the children would be assessed to determine if intravenous supplementation was necessary. Children would be considered as recovered from sedation if they satisfied the criteria for discharge from the hospital.² The criteria included stable cardiovascular function, patent airway, adequate hydration and normal conscious level. Normal conscious level referred to presence of intact protective reflexes (e.g. swallowing, coughing), ability to be easily aroused, ability to talk and sit up unaided (if age appropriate) and conscious state close to the child's normal level.

Desaturation was defined as SaO_2 below 90%. The lowest post sedation SaO_2 would be analysed. Paradoxical excitation would be determined subjectively by the accompanying parent or the nursing staff. Vomiting referred to those developed after administration of chloral hydrate. Vomiting or spitting during administration of chloral hydrate were not included. Both paradoxical excitation and vomiting depended on voluntary reporting from parents or observation by nursing staff. Prolonged sedation was defined as failure to recover 4 hours after the first dose of sedative. If the time to recovery were not recorded, the time to discharge would be taken as the equivalent.

Exclusion criteria included those who required sedation other than or in addition to chloral hydrate, who were given more than 100 mg/kg or two gram of chloral hydrate, who required oxygen supplementation before sedation, and those without record of both post sedation saturation and time to recovery/discharge.

Children were stratified into two groups: infants and those older than one year old. Dosages of chloral hydrate were stratified into three groups: ≤ 50 mg/kg, $>50-75$ mg/kg and $>75-100$ mg/kg. Dosages of chloral hydrate were analyzed in relation to the age groups and the type of investigations. Incidence of desaturation, prolonged sedation, vomiting and paradoxical excitation were analyzed in relation to the age groups and dosages of chloral hydrate using the Fisher's Exact test. Differences were considered to be statistically significant when $p \leq 0.05$.

Results

Three hundred and forty-four children were admitted for the specified investigations under sedation during the study period. Thirty children had sedation other than or in addition to chloral hydrate (three in BAEP group, one in ECHO group, two in EEG group, 24 in CT group). Among the remaining children, three received more than 100 mg/kg of chloral hydrate (two in BAEP group, one in CT group), three required oxygen before sedation and 26 did not have records of both post sedation saturation and time to recovery/discharge. Two hundred and eighty-two children were thus eligible for the study. There were 171 males and 111 females. One hundred and thirty-seven were infants and 145 were children older than 1 year old. Investigations included CT for 45 children, ECHO for 146, EEG for 21 and BAEP for 70. The dosage of chloral hydrate was ≤ 50 mg/kg in 226 children, $>50-75$ mg/kg in 45 and $>75-100$ mg/kg in 11.

The number of children requiring various dosages of chloral hydrate in relation to the two different age groups and in relation to the various investigations are shown in Table 1. Significantly higher dosages of chloral hydrate were more often required in children older than 1 year old ($p < 0.001$). There was also a significant difference in the dosage of chloral hydrate used in the various investigations ($p = 0.001$).

Two hundred and fifty-four children (90%) had post-sedation SaO_2 value available, 129 were infants and 125 were children older than 1 year old. The dosage of chloral hydrate was ≤ 50 mg/kg in 203 children, $>50-75$ mg/kg in 40 and $>75-100$ mg/kg in 11. The incidence of desaturation was 0/254 (0%). There were 269 children (94%) with record of time to recovery/discharge. One hundred and twenty-seven were infants and 142 were children older than 1 year old. The dosage of chloral hydrate was ≤ 50 mg/kg in 215 children, $>50-75$ mg/kg in 43 and $>75-100$ mg/kg in 11. The incidence of prolonged sedation in relation to age and dosage of chloral hydrate is shown in Table 2. Overall, 24/269 (8.9%) had prolonged sedation of more than 4 hours. However, no statistical significance could be shown among the different age groups or among the different dosage groups. None of the patients had vomiting or paradoxical excitation.

Discussion and Conclusion

Most reported studies on the use of sedative agents in children were done in those undergoing radiological

Table 1 Dosage of chloral hydrate in relation to age and procedures

		Dosage of chloral hydrate (mg/kg)			p-value
		<=50	>50-75	>75-100	
Age					<0.001
Infants	(n=137)	90.5%	8.8%	0.7%	
Children aged 1+	(n=145)	70.3%	22.8%	6.9%	
Procedure					0.001
CT	(n=45)	68.9%	31.1%	0%	
EEG	(n=21)	71.4%	19.1%	9.5%	
ECHO	(n=146)	82.2%	15.8%	2.1%	
BAEP	(n=70)	85.7%	5.7%	8.6%	

Table 2 Incidence of prolonged sedation in relation to age and dosage of chloral hydrate

Factor		Prolonged Sedation		p-value
		Yes	No	
Age				0.670
Infants	(n=127)	7.9%	92.1%	
Children aged 1+	(n=142)	9.9%	90.1%	
Dosage (mg/kg)				0.243
<= 50	(n=215)	7.9%	92.1%	
>50-75	(n=43)	11.6%	88.4%	
>75-100	(n=11)	18.2%	81.8%	

investigations.^{5,7-9} The dosages of chloral hydrate used in these studies were higher and additional sedative agents were often required. Lower dosages of chloral hydrate often sufficed for other investigations.¹⁰ Our study included cases given lower dosages of chloral hydrate for commonly performed investigations, including radiological imaging. This resembled more closely the clinical scenario encountered by the general paediatricians.

Our study showed that higher dosages of chloral hydrate were more often required for sedation in children older than 1 year of age. An earlier report showed similar finding though their children were divided into those above and below 48 months of age.⁵

A significant association between dosage and procedure is expected because of our standardized protocol. The finding that none of the children in the CT group required chloral hydrate dosage of >75-100 mg/kg might seem in contrary to the literature. This might be explained by one of the exclusion criteria. Twenty-four children in the CT group were excluded due to other sedative agents, leaving

only 45 children eligible for the study. Children undergoing sedation for CT imaging were required to have an intravenous line inserted according to the protocol of our radiology department. This might result in more liberal use of intravenous sedative agents rather than repeated or higher dosages of chloral hydrate.

The overall risk of prolonged sedation among our patients was 8.9%. There was no desaturation, vomiting or paradoxical excitation. This was different from that reported from the literature.^{5,7-10} Study by Greenberg et al suggested that up to 7% of children developed vomiting, 4% desaturation and 5% paradoxical excitation, though none were severe enough to require hospitalization.⁵ There was no prolonged sedation. In their study, children were routinely given 100 mg/kg of chloral hydrate with a total maximal dose of 2.5 gram. Vade et al used a dosage of 50-100 mg/kg (in infants) or 75-100 mg/kg (together with hydroxyzine and/or meperidine in children 1-4 years old).⁷ Mild hypoxia (SaO₂ <95%) was found in 5-9%, moderate to severe hypoxia (SaO₂ <90%) in 5-9%, prolonged sedation in 3-17%,

vomiting in 0-4% and agitation in 0.5-2% of their children. Incidence of desaturation was 3.6% in the study by Pereira.⁸ Other side effects were not reported. Dosage of chloral hydrate used was 50-120 mg/kg. In another small study by McCarver-May, 57% of the seven term infants had desaturation after 75 mg/kg of chloral hydrate.⁹ However all these infants also received concomitant pancuronium, morphine and phenobarbitone. Prolonged sedation, vomiting and agitation were not reported. Although underestimation of vomiting and paradoxical excitation was possible in our study because of voluntary reporting mechanism, the lower incidence of adverse events in our study might be related to the use of chloral hydrate as the sole sedative agents and inclusion of cases receiving lower dosages.

Difference in the definition of side effects might be another reason. Desaturation had not been defined in the AAP Guideline.⁴ Some studies defined desaturation as SaO₂ of less than 90%,^{8,9} others as less than 95%,^{5,7} while another study did not specify.¹⁰ We chose to define desaturation as SaO₂ of less than 90% because this was the level considered as of clinical significance.⁷ A more detailed analysis by comparing the pre-sedation SaO₂ data with the post-sedation SaO₂ data would be of interest. Sedation was defined prolonged if it lasted more than 2 hours after completion of investigation by Greenburg⁵ and as more than 2 hours after onset of satisfactory sedation by Vade.⁷ Prolonged sedation was not included for analysis in the other studies.⁸⁻¹⁰ We chose to define prolonged sedation as 4 hours after the first dose of sedative because the pharmacological properties of a drug would be related to the time of intake. Relation to the time after completion of investigation or onset of sedation might be less precise. Vomiting during administration of chloral hydrate might result in dosage taken lower than prescribed while vomiting after drug intake might result in airway obstruction in a sedated child. The latter would be of more relevance to the clinician. However timing of vomiting had not been clearly defined in previous studies.^{5,7}

The risks of prolonged sedation among our patients were not statistically different in the two age groups or in the various dosage groups in our study, though there was a trend that increased dosages were related to a higher percentage of prolonged sedation. This may be due to the small sample size of our study resulting in low power. A larger sample size of at least 160 in each study group may be able to demonstrate the statistical difference at the 0.8 power level. Our study also biased towards more prolonged sedation because the time to discharge was taken if the time to

recovery was not recorded. The longest duration of prolonged sedation in our study was 12 hours. This occurred in a two-year-old child in the ECHO group after receiving 75 mg/kg of chloral hydrate. Time to recovery was not recorded and time to discharge was taken.

In conclusion, this retrospective study suggested that the incidence of complications arising from sedation by chloral hydrate alone might be lower than previously reported. A larger prospective study may be necessary to refine the need for routine intensive monitoring in all children undergoing investigations by chloral hydrate alone.

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Appendix 1 Sedation Protocol for Paediatric PatientsGeneral instruction:

All patients should be sleep deprived. Advise to sleep 2 hours later and wake the child 2 hours earlier. Deprive sleep during travel to hospital and after admission. Take advantage of postprandial sleep in neonate (a bottle of milk to be given just before test). Sedation is then often not necessary.

CT scan:

1st line: Chloral hydrate (PO)

2nd line: Midazolam (IV) or Paraldehyde (PR)

3rd line: Ketamine (IV) + atropine (IV)

If still uncooperative, reschedule test

EEG:

1st line: No sedation. Attempt natural sleep as far as possible

2nd line: Chloral hydrate (PO)

3rd line: Phenergan (PO)

4th line: Atarax (PO)

Evoked potentials (including BAEP):

1st line: Chloral hydrate (PO)

2nd line: Midazolam (IV)

Echocardiogram:

Chloral hydrate (PO)

Consider no sedation in neonates

Dosage guide for chloral hydrate:

50 mg/kg/dose (75 mg/kg/dose for CT scan), if still not asleep after 15-30 min, top up with 25 mg/kg/dose (no top up for neonate; max 100 mg/kg or 2 gm)

Monitoring:

Baseline: conscious level/AR/RR/BP/SaO₂

During test: continuous monitoring of AR/SaO₂, intermittent recording or RR/BP if test prolonged

After test: continuous monitoring of AR/SaO₂ till conscious, intermittent measurement of AR/RR/BP/SaO₂ till discharge criteria met

Appendix 2 Sample Checklist

Assessment before procedure:

Diagnosis: _____

Current drugs: _____

Allergies: _____ Previous adverse reaction with sedation: _____

Concurrent illness: _____

Physical examination:

Current status: fit/not fit for sedation

Admission orders:

NPO _____ hr before procedure

AR/RR/BP/SaO₂ before sedation

Choral hydrate _____ mg 30 min before procedure (BW _____ kg)

Additional sedation _____

ARSaO₂ monitoring after sedation till conscious

BP after procedure and then Q ___ H

Signature: _____

Date/Time: _____

Assessment after procedure:

DAT when fully conscious

Adverse events during sedation: _____

- Discharge criteria fulfilled
- stable cardiovascular function and patent airway
 - adequate hydration
 - intact protective reflexes (e.g. swallowing, coughing)
 - easily arousable, can talk and sit up unaided (if age appropriate) and conscious state close to the child's normal level (if very young or handicapped)

Signature: _____

Date/Time: _____