Chloral hydrate

An effective agent for sedation in children with age and weight dependent response

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ABSTRACT

Objective: Diagnostic and therapeutic procedures in children are made easier using sedation. However, there is no consensus about which drug should be used to achieve this. Furthermore, none of the drugs used for sedation are risk free. The aim of this work is to study sedation indications, effectiveness, and safety at our center.

Methods: A prospective observational study conducted at the Pediatric Day Care Unit, King Fahad National Guard Hospital, Riyadh, Saudi Arabia. The study covered 17.5 weeks in 2 periods: May 9th 1999 to June 13th 1999 and October 31st 2001 to February 11th 2002. Children ≤12 years were included. Collected data included demographics, indication, drug dosing and outcome. Data were reported as mean ± SD.

Results: We included 148 patients, age 38 ± 30 months. Adequate sedation was achieved in 79% after initial chloral hydrate (CH) dose of 56.9 ± 9.3 mg/kg, in 95% after adding 18.5 ± 6.4mg/kg CH and in 96% after adding second drug. Compared to nonrespondents, first CH dose respondents were younger and lower in weight. The CH side effects were few and mild.

Conclusion: Chloral hydrate is a safe and effective agent for sedation in children with an age and weight dependent response.

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A quiet cooperative child makes diagnostic and therapeutic procedures easy and doable. To achieve this, drugs that give sedation are needed. There is no consensus about which drug, route and dosing that should be used for sedation in children. Furthermore, none of these drugs are risk-free. This lead to reluctance in sedation utilization that still exists in some schools of medical practice.[1] Currently different regimens are used as either single or combined sedative agents.[2] The use of combined sedative drugs has declined because of the higher risk of side-effects.[3] Oral chloral hydrate (CH) was the most commonly used drug in many recent reports.[2,4-6] Rectal CH has been tried but was less effective.[7] Chloral hydrate showed a deeper and more prolonged sedation compared to oral midazolam.[8] However, this could be either an advantage or disadvantage based on the procedure that required the sedation. The literature reported variable success rate of sedation and incidence of adverse effects as well as different dose regimens of CH. At our Pediatric Day Care Unit, CH was the main drug used by most of our pediatricians to sedate patients for diagnostic procedures. The objectives of this study were to study indications, drugs used, doses required, effectiveness, nature of the response to the given drugs and safety of sedation at our Pediatric Day Care Unit.

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Methods. An observational prospective study conducted at the Pediatric Day Care Unit, King Fahad National Guard Hospital, Riyadh, Saudi Arabia. The study covered 17.5 weeks in 2 periods: May 9th 1999 to June 13th 1999 and October 31st 2001 to February 11th 2002. All children ≤12 years of age, admitted to the unit with no contraindication(s) to sedation were included. The exclusion criteria were gastric ulcer, hepatic impairment, respiratory or renal insufficiency, porphyria, hypersensitivity and administration of anticoagulants. The first CH, the need for second CH dose and the need for another drug was given as per physician judgment. The collected data covered age, gender, weight, diagnosis, procedure for which the patient needed the conscious sedation, amount and type of sedative drugs used and outcome of the sedation. Patients who failed to be sedated with first dose were given an extra dose or an extra drug after 30 minutes from the first dose if the drug dosing, and patient condition allowed. The maximum total dose of CH was 100mg/kg and not to exceed a total of 2 grams. The unit nurses monitored the patient's vital signs, pulse oximetry, cardiac rhythm, level of consciousness and side-effects of sedation. Sedation was considered successful if the patient was sedated enough to tolerate the procedure. Descriptive statistics and t-test were used for the statistical analysis using StatView software.

Results. One hundred and forty-eight patients were included in the study; 58% were males, with a mean age of 38.2 (SD ± 30.4) months and a mean weight of 13.9 (± 7.9) kg. Seventy-two percent of our subjects were ≤48 months of age. Seventy-three percent were ≤16 kg in weight. The most common procedures for which the sedation was given were CT scan and MRI (**Table 1**). Chloral hydrate was used as a first drug in all patients. After a first CH dose of 55.7 (± 9.3) mg/kg with a dose range of 32-80 mg/kg, 79% of the subjects were successfully sedated. The success rate increased to 95% after an additional CH dose of 18.5 (± 6.4) mg/kg given to 26 out of 31 initially inadequately sedated subjects of whom 23 responded (**Table 2**). Addition of other drugs after initially failing CH raised the success rate to 96%. The mean total CH dose for the 148 subjects included in the study was 58.5 ± 12.6mg/kg with a dose range of 35.3-97.7 mg/kg. The mean total CH dose given to the initially CH nonrespondents (26 subjects) was 71.6 (± 13.4) mg/kg. Compared to nonrespondents, respondents to the first dose of CH were younger and had lower weight with a *p* value of <0.0001 and <0.0001 (**Table 3**). Furthermore, does groups were not different in the first dose of CH (**Table 3**). Adverse effects were reported only in 4 subjects (2.7%).

Table 1 - Procedures carried out during the studied period.

Procedures	N of patients	(%)
Computed tomography scanning	45	(32)
Magnetic resonance imaging	41	(27.7)
Radioisotopic renography (DTPA, DMSA)	23	(15.1)
Auditory brain stem response	13	(8.7)
Ultrasonography	8	(5)
Echocardiography	7	(4.5)
Electroencephalogram	5	(3)
Others	6	(4)
Total	**148**	**(100)**

DTPA - diethylenetriaminepentaacetic acid,
DMSA - 2,3-dimercaptosuccinicacid.

Table 2 - Frequency and success rate of the various sedative agents used for nonrespondents to the first dose of chloral hydrate.

Drug used	N of patients	Dose (mg/kg)	Successful n	(%)
Chloral hydrate	26	18.5 ± 6.4	23	(88.5)
Midazolam	3	0.22 ± 0.1	1	(33.3)
DTP	1	1	1	(100)
Refusal	1		-	-
Total	**31**		**25**	**(80.6)**

Data reported as mean±SD
DTP - Demerol, Thorazine and Promethazine.

Table 3 - Differences between respondents and nonrespondents to the first dose of chloral hydrate (CH) in age, weight and amount of first and total CH dose.

Variable	Responders (N=117)	Nonresponders (N=31)	*p* value
Age (months)	31.6±27.5	58.7±31.8	<0.0001
Weight (kg)	12.1±4.9	17.4±6.1	<0.0001
First CH dose (mg/kg)	56.1±9.3	53.7±9.7	<0.2
Total CH dose (mg/kg)	**56.1±9.3**	**71.6±13.4**	**<0.0001**

Data reported as mean±SD

Three had vomiting shortly after the administration of CH and one had hyperactivity within one hour of CH dose.

Discussion. Chloral hydrate is still the most widely used sedative agent for sedation in children as reported in many previous studies.[2,4-6,9,10] In this study, there was a high success rate of sedation though it was slightly lower than some previous reports.[11-14] However, the CH doses used in those reports were higher with a mean of 87 mg/kg,[11] 78 mg/kg,[12] and 77 mg/kg[13] and a success rate of 94%, 98% and 98%. Alternatively, other studies reported lower success rate of 72% even when CH was combined with meperidine and hydroxyzine when used for dental procedures,[15] and a success rate of 70% and 91% in spite of relatively higher doses (70 ± 2 mg and 100 mg/kg) when used for MRI studies.[16,17] Previous reports showed higher success rate of sedation with CH in young children below a mean age of 36 months,[13] below 64 months,[14] and below 48 months.[17] In our study, also the respondents to the first dose of CH were of younger age as well as lower body weight compared to the non-responders while there was no difference between the 2 groups in the first dose of CH (**Table 3**). So the respondents did not respond because they were given a higher dose of CH but because they were of younger age, and lower weight compared to nonrespondents. Compared to the initial respondents, nonrespondents to the first dose of CH needed a higher total dose of CH of 71.6 ± 13.4 mg/kg to achieve a sedation success rate of 88% (*p* value <0.0001). Starting with CH dose of 56 mg/kg may give an initial low success rate and demand extra doses, especially in those who are ≥48 months of age. However, starting with CH dose of 71.6 mg/kg may lead to over sedation and more side-effects in the sensitive young group ≤48 months in age. Starting with age dependent dose may lead to better utilization of the resources without compromising the patient quality of care. In a retrospective study, there was no statistically significant difference in the duration of sedation among the different age or dosage groups.[18] The incidence of adverse effects in our patients was low and mild in severity, which was consistent with the previous reports that indicated the safety of CH in the absence of contraindications.[11,13,17-24] In a previous randomized double blind clinical trial, there was no significant difference in the adverse effects among those who received 70 mg/kg or 100 mg/kg of CH.[16] However, few single case reports showed significant side-effects, such as seizures, cardiac arrhythmias and significant respiratory depression with the usual sedative doses.[25-27] Furthermore, Hoffman et al[28] in a retrospective study found that CH was associated with high risk of complications including inadvertent deep sedation. However, inadvertent deep sedation did not significantly increase the risk of complications. Significant side-effects such as unsteadiness, injuries and hyperactivity were also previously reported after hospital discharge.[3,12] There is an existing concern about the side-effects of CH including carcinogenicity.[29] However, Steinberg[30] after the literature analyses concluded that the data did not suggest the need to ban CH as a medicine. However, possible modifications in its use are suggested. The American Academy of Pediatrics recommendations indicated that CH is effective with low acute toxicity in short-term oral use in the recommended doses, and carcinogenicity is of concern but the available information does not provide a basis to warrant selection of an alternative sedative agent.[31]

In conclusion, an intermediate dose of oral CH is safe and effective in our pediatric patients. Furthermore, the response to CH is age and weight dependent. We recommend starting with an age dependent dose when using CH for sedation. However, further studies are needed to support the validity of this evidence.

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