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Use of chloral hydrate as a sedative for auditory brainstem response testing in a pediatric population

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ABSTRACT

Objective: Chloral hydrate (CH) is an oral sedative widely used to sedate infants and young children during auditory brainstem response (ABR) testing. The aim of this study was to record effectiveness, complications and safety of CH as a sedative for ABR.

Methods: From January of 2003 until December of 2007, 1903 children were tested for ABR, 568 of them being under the age of 6 months. CH (8%) was used for sedation at a dose of 40 mg/kg with a repeat dose, if necessary, for an adequate sedation, in 20–30 min. We recorded the effectiveness of CH as a sedative for ABR examination, as well as all complications related to the use of CH such as vomiting, rash, hyperactivity, respiratory distress and apnea. The statistical method used was the absolute and percentage frequency distribution of the occurrences.

Results: Sedation with CH was necessary to perform testing in 1591 (83.6%) of the examined children. However, in the population of the examined infants, only 341 (60%) were sedated with CH, because the remaining 227 (40%) fell asleep by themselves. Complications included hyperactivity in 152 children (8%), minor respiratory distress in 10 children (0.4%), vomiting in 217 children (11.4%), apnea in 4 children (0.2%) and rash in 10 children (0.4%). The complications of hyperactivity, vomiting and rash resolved without any medical treatment. The apnea cases were managed effectively by supplying ventilation to the children via a mask in the presence of an anesthesiologist.

Conclusions: The use of CH at a dose of 40 mg/kg up to 80 mg/kg is safe and effective when administered in a setting with adequate equipment and the presence of well trained personnel.

1. Introduction

Auditory brainstem responses (ABR) is an objective method of testing the auditory pathway and is especially useful in the detection of hearing loss in infants and young children that are not eligible for testing with puretone audiometry. Testing, however, must be performed with the child completely relaxed. In the case of infants, this may be obtained, after feeding with milk. In most other cases, mild sedation is required to reduce anxiety.

Chloral hydrate (CH) is a widely used oral sedative hypnotic drug which has been used for several decades in pediatrics for diagnostic procedures, such as ABR, computerized tomography or magnetic resonance imaging. CH is one of the oldest synthetic agents, considering that this substance was synthesized in 1832 [1]. It is administered orally or rectally and is rapidly absorbed from the gastrointestinal tract.

CH is metabolized to trichloroethanol which is the active metabolite and is responsible for the hypnotic action [2]. The half-life of CH is short (a few minutes) whereas for trichloroethanol it is 8–12 h. It should be noticed that in infants, the half-life is 3–4 times greater than in older children [2,3]. The mechanism of the sedative action of CH is still unknown. It is believed that its sedative effect on the central nervous system is mediated by gamma aminobutyric acid-A receptors (GABA), since the use of flumazenil (a GABA antagonist) in treating cases with CH overdose, has been proven successful [4].

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CH interacts with alcohol [5], anticoagulants [3], amitriptyline [1], flumazenil [4,6], furosemide [7], fluoxetine [8], as well as with other CNS suppressants [3] or stimulants [9]. The recommended dose for sedative action is 20–100 mg/kg, although for infants dose adjustment is required. Various side effects of CH have been reported [1,10] including vomiting, nausea, rash, hyperactivity, respiratory distress, apnea and arrhythmias, whereas some studies, based only on animal research, have reported that CH may have a carcinogenic effect [11,12].

In case of overdose, the first symptoms are ataxia and lethargy, further progressing to deep coma, which generally occurs within 1–2 h [3]. Deaths have been reported to occur after the ingestion of at least 5 g of CH [3]. The use of CH is not recommended in cases with a history of gastric ulcer, hepatic distress, breathing distress and porphyria [1].

In the audiology laboratory of our hospital, CH is being used for more than 2 decades, for the sedation of infants and young children examined by the ABR test. Although, CH is a widely used drug as a pediatric sedative, issues concerning its safety and efficacy continue to arise. Various relevant reports include only a limited number of subjects [e.g. 10,13]. The aim of this study was both to determine the effectiveness of CH in sedating, as well as to investigate the safety of its use in a large number of young children.

2. Methods

The subjects of this study were 1903 children, who were examined with ABR at our audiology laboratory from January 2003 to December 2007. Five hundred and sixty-eight of these children were under 6 months of age whereas the remaining 1335 were older, with maximum age 14 years.

According to our laboratory protocol, instructions were given to all parents to bring their children to the laboratory awake but drowsy and without having eaten for the last 3 h before the examination. In addition, the parents are asked to bring whatever food or drink consider appropriate, in order to mix it with CH. This commonly includes milk for infants and juice, milk, cream or yogurt for older children.

Special emphasis is given to their medical history. Children with severe pulmonary disease and recent upper respiratory tract infection had their appointments rescheduled until they met the criteria for sedation.

CH is given at a concentration of 8%. It is given at an initial dose of 40 mg/kg, with a repeat equal dose, if required, to obtain adequate sedation after 20–30 min. The maximum dose is 80 mg/kg (with the total dose not exceeding 1 g), which is consistent with the American Academy of Pediatrics (AAP) sedation guidelines [14]. For infants under 6 months of age, the maximum dose was 40 mg/kg, and this was only given in cases where the infant had not fallen asleep spontaneously within 10–20 min. CH was mixed with a banana-flavored liquid, in order to improve its bitter taste. In the rare cases where the infant did not cooperate or repeatedly vomited, the sedative was inserted into its stomach via a naso-gastric tube.

After CH ingestion, the children remained in a quiet and dark room with their parents until they were fully asleep. Subsequently, the children were transferred to the examination room and the ABR test was begun. During the whole course of the examination, the children were under the care of a qualified sedation nurse who observed them for any complications occurring due to CH intake, such as apnea, breathing distress, cyanosis, vomiting, hyperactivity, or cardiac rate changes.

Children with minor respiratory distress were connected to a pulse oximeter for observation of their blood saturation. Children presenting with cyanosis or apneas were immediately monitored with the guidelines suggested by AAP. The average time for the preparation and measurement of ABR was about 40–50 min. Following the end of the ABR examination the children remained in the audiology laboratory under the supervision of the sedation nurse until they recovered from sedation. Subsequently, instructions were given to the parents and then the children were sent home.

Table 1
Data of sedation with chloral hydrate.

	Children ≤ 6 months ($N = 568$)	Children > 6 months ($N = 1335$)
1st dose of CH	40 mg/kg	40 mg/kg
2nd dose CH if required	No	40 mg/kg (total dose not exceeding 1 g)
Time before 1st dose	15 ± 5 min	No delay
Time between 1st and 2nd dose	–	24 ± 7 min
Success rate of first dose	100%	72% (961/1335 children)
Total time of preparation and examination	34 ± 14 min	49 ± 22 min

The statistical method used for the results of the study was the absolute and percentage distribution of occurrences.

3. Results

Of the 1903 children examined by ABR, 1586 (83.3%) were sedated by CH, whereas 312 (16.4%) were quite relaxed to avoid sedation during testing and 5 (0.3%) couldn't be sedated with CH.

Considering the group of the 568 infants under the age of 6 months, CH sedation was needed in a smaller percentage (60%) of subjects (341 infants), whereas the remaining 227 (40%) fell asleep spontaneously. In the second group of the 1335 children over the age of 6 months, 1245 (93.2%) required sedation with CH, only 85 (6.4%) slept spontaneously and another 5 (0.4%) required sedation intravenously. Our data of CH administration are shown in Table 1.

It should be mentioned, that a naso-gastric tube for the administration of CH was used in 50 children (2.6%) over the age of 3.5 years who could not take the CH orally or those who were hyperactive or vomited. The final results, considering the sedating effect of CH, indicated a success rate of 99.7%. Complications were observed in 393 (20.6)% out of the 1903 children (Table 2).

4. Discussion

The development and clinical application of otoacoustic emissions marked the beginning of a new era in the field of screening for congenital hearing loss, because it allowed for an objective evaluation of hearing almost as soon as the babies were born [15,16]. A step further was the application of automated auditory brainstem responses, which is more time consuming, but it is generally reported to obtain a lower referral rate [17]. Combination of these two methods permits objective evaluation of both cochlear and retrocochlear hearing, and even newborns at risk for auditory neuropathy may be identified. Routine use of these methods in newborns, does not demand use of sedatives, but neverthless sedation is necessary in performing diagnostic ABR.

Table 2
Side effects of CH sedation used for ABR testing.

Side effect	Number of children	Percentage
Hyperactivity	152	8%
Vomiting	217	11.4%
Rash	10	0.5%
Minor breathing distress	10	0.5%
Apnea	4	0.2%