The use of chloral hydrate in pediatric electroencephalography

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ABSTRACT

Objective: Sleep is a known activator of epileptiform discharges on electroencephalography. Chloral hydrate is used frequently for electroencephalography sedation. Our objectives were to study the value and limitations of chloral hydrate.

Methods: One hundred and fifty nine consecutive pediatric electroencephalograms were included prospectively. One electroencephalography technologist collected chloral hydrate related data. Electroencephalogram requisitions and recordings were reviewed separately by one certified electroencephalographer.

Results: The children's ages ranged between 8 days to 19 years (mean=5.7 years). Natural sleep was recorded in 11% and only 2% were sleep deprived. Sedation was given to 45% mostly using chloral hydrate (96%). Children with chronic neurological abnormalities were more likely to receive chloral hydrate (odds ratio=9.8, 95% confidence interval=4.5-21). Chloral hydrate was effective in inducing sleep in 97%, however, 34% of the children woke up spontaneously before the test was completed, particularly those with chronic neurological abnormalities (p=0.0003). A second dose was necessary in 13%. Recording an initial period of wakefulness followed by sleep onset was more likely achieved in natural sleep electroencephalograms when compared to the sedated group (82% vs 10%, p<0.0001). These electroencephalograms were more likely to contain epileptiform discharges (p<0.001).

Conclusion: Although chloral hydrate was effective in sleep induction, the sleep onset was frequently missed and the hypnotic effects were not sustained, particularly in children with chronic neurological abnormalities.

Keywords: Sedation, sleep, electroencephalogram, child, pediatric, use, chloral hydrate.

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Sleep is one of the well-known procedures of activating focal and generalized epileptiform discharges on electroencephalography (EEG).[1,2] When the clinical suspicion of epilepsy is high and the awake EEG is normal, sleep EEG usually provides additional diagnostic information.[1] Falling asleep normally is always superior to drug induced sleep as spike activation may occur mainly in the lighter stages of sleep.[2] Sleep deprivation is therefore used to achieve this goal.

Occasionally, achieving natural sleep is difficult and drugs need to be used. In fact, sedation is frequently used in young and uncooperative children and several sedative hypnotic agents have been used.[3-5] Benzodiazepines and barbiturates should not be utilized because of their antiepileptic properties and induction of faster EEG frequencies.[5,6]

Chloral hydrate (CH) is used frequently for EEG sedation.[3,4,7] It improves the EEG quality because of decreased muscle and movement artifacts and

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improved organization of normal sleep features.[8] However, CH may result in significant reduction of epileptiform activities and therefore may alter EEG interpretation.[7] In fact, some authors suggested that it might have an antiepileptic property.[9] Other studies in children found it ineffective as an antiepileptic drug.[10] The reduction in epileptiform activities is more likely related to recording deeper stages of sleep in well sedated children. The use of sedation is also not without complications. Serious cardiac and respiratory effects and excessive sedation have been associated with sedating agents, even when normal doses are used.[3] Several cases of childhood poisoning and cardiorespiratory arrest following CH aspiration were reported.[11,12]

For all these reasons, the use of CH should not be routine. The objectives of this study were to examine the value of CH for EEG sedation and assess its efficacy in sleep induction, and effects on EEG abnormalities. We hypothesized that CH may not be universally effective and may result in attenuation of epileptiform activities as a result of recording deeper sleep stages.

Table 1 - Summary of important items included in the data collection sheet.

1.	**EEG Type**
	a. Awake recorded (no sedation)
	b. Natural sleep record (no sedation or sleep deprivation)
	c. Sleep deprived EEG (no sedation)
	d. Sedated for EEG
2.	**Time of the day when the EEG was done**
3.	**Duration of night sleep**
4.	**Time from the last night sleep or nap**
5.	**Time from the last meal**
6.	**Sedation**
	a. Drug used
	b. Dose given (body weight)
	c. How long before EEG was it given
	d. Need for repeated doses
7.	**Sleep**
	a. Was the child awake throughout the record
	b. Was the child asleep throughout the record
	c. Was the child awake initially then fell asleep
	d. Was the child asleep then awoken spontaneously

Methods. Consecutive pediatric EEGs performed at the Neurophysiology Unit of King Abdulaziz University Hospital (KAUH) were included prospectively. All EEGs were recorded between March 19 and July 18, 2000. King Abdulaziz University Hospital is a multispecialty adult and pediatric hospital providing primary care to the Jeddah area, as well as secondary and tertiary care for a regional population of western Saudi Arabia. King Abdulaziz University Hospital is the main teaching center of western Saudi Arabia in collaboration with King Faisal Specialist Hospital & Research Centre. The pediatric neurology group is a major referral center for the western region, particularly the Jeddah area. One certified electroencephalographer (EEGer) reports all pediatric EEGs at KAUH.

A data collection sheet regarding the use of sedation was designed as shown in Table 1. One EEG technologist (co-author Marilou Aquino) completed these forms during the EEG recording sessions. All EEG requisitions and recordings were reviewed sparately by one EEGer. He examined the requisitions to identify the referral source, EEG number, child's age, EEG indication, history of epilepsy, and current antiepileptic drugs. Based on the description of the child's events and the underlying clinical scenario, the most likely diagnosis responsible for requesting the EEG was coded as follow: 1) Established epilepsy, 2) Probable seizure or seizures of new onset, 3) Non epileptic paroxysmal events (e.g. migraine, syncope, breath holding spells), 4) Acute central nervous system (CNS) disorders (e.g. toxic, metabolic, infectious, or hypoxic encephalopathy), and 5) Non epileptic chronic CNS disorders (e.g. mental retardation, autism, attention disorder). The same EEGer evaluated the EEG recordings to identify epileptiform or background abnormalities, and sleep staging. The EEG abnormalities were coded as follow: 1) Focal epileptiform discharges, 2) Multifocal epileptiform discharges, 3) Generalized epileptiform discharges, 4) Focal background disturbance, and 5) Diffuse background disturbance. Statistical analyses were performed using Epi Info, version 6.[13,14] Categorical variables were examined in 2x2 tables using Chi-square statistics. The magnitude of significant associations is presented as p values, odds ratios (OR), and the 95% confidence interval for the OR.

Results. During the study period, 159 EEGs were included. The children's ages ranged between 8 days to 19 years (mean 5.7 years, standard deviation 4.6). The first EEG was studied in 109 (69%) of the cases and 31% were repeat EEGs. Seventy-six children

Table 2 - Some EEG variables in the non sedated and sedated EEG.

EEG related variables	No sedation Number/Total (%)	Sedation Number/Total (%)	P value
Source			
1. In-patient ward	12/88 (13.5%)	41/71 (58%)	<0.0001
2. Out-patient department	72/88 (82%)	29/71 (41%)	<0.0001
3. Intensive care units	4/88 (4.5%)	1/71 (1.5%)	NS*
Requesting physician			
1. General practitioner	6/88 (7%)	1/71 (1.5%)	NS
2. Pediatric neurologist	31/88(35%)	22/71 (31%)	NS
3. General pediatrician	36/88(41%)	33/71 (46%)	NS
4. Other pediatric subspecialist	15/88(17%)	15/71 (21%)	NS
Indication			
1. Established epilepsy	40/88 (45%)	36/71 (51%)	NS
2. Probable seizures	29/88 (33%)	27/71 (38%)	NS
3. Non epileptic paroxysmal events	14/88 (16%)	0/71 (0%)	0.001
4. Acute CNS disorders	3/88 (3.5%)	3/71 (4%)	NS
5. Chronic CNS disorders	2/88 (2.5%)	5/71 (7%)	NS
Abnormal EEG result	30/88 (34%)	54/71 (76%)	<0.0001
a. Focal epileptiform discharges	10/30 (33%)	13/54 (24%)	NS
b. Multifocal epileptiform discharges	2/30 (6.5%)	2/54 (4%)	NS
c. Generalized epileptiform discharges	13/30 (43%)	7/54 (13%)	0.004
d. Focal background disturbance	1/30 (3%)	5/54 (9%)	NS
e. Diffuse background disturbance	4/30 (13%)	27/54 (50%)	0.002

NS = Not Significant (p>0.05)

(48%) had established epilepsy and 46% were receiving antiepileptic drugs. Chronic neurological abnormalities (e.g. cerebral palsy, developmental, or chromosomal abnormalities) were documented in 46%. Natural sleep was recorded in 17 (11%) EEGs. Only 2% were sleep deprived. Sedation was given in 71 (45%) and CH was used in 96% of these cases. Two children had diazepam, 2 had promethazine, 1 had midazolam, and 1 child had chlorpromazine for EEG sedation. Most children (85%) had a CH dose ranging between 25-75 mg/kg, which was given less than one hour before the test in 91%. No side effects were noted. Children less than 2 years of age were 12 times more likely to receive CH when compared to older children (95% confidence interval (CI) 5-30, p<0.0001). As well, children with chronic neurological abnormalities (e.g. cerebral palsy) were 9.8 times more likely to receive CH when compared to neurologicaly normal children (95% CI 4.5-21, p<0.0001). The use of antiepileptic drugs and the number of EEG (first or repeat) did not correlate with the use of CH or acheivement of sleep.

Chloral hydrate was effective in inducing sleep in 97%. Stage 1 sleep was recorded in 19%, stage 2 in 60%, and stage 3 in 21% of the EEGs. Stage 1 sleep was more likely recorded in the natural sleep EEGs when compared to the sedated group (62% versus 19%, p=0.004). Recording an initial period of wakefulness followed by sleep onset was even more likely achieved in the natural sleep group (82% versus 10%, p<0.0001). These EEGs were much more likely to contain epileptiform discharges when compared to the continous sleep recordings (91% versus 27%, p=0.0007). Twenty four (34%) of the children who received CH woke up spontaneously before the test was completed, particularily those with chronic neurological abnormalities (p=0.0003). This was not related to the CH dose, however, a second dose was given in 13%.

Table 2 shows a summary of the EEG sources, indications, and results in the two groups with and without sedation. Eighty four (53%) EEGs were reported as abnormal. Sleep EEGs were more likely to be abnormal (odds ratio (OR) 5.3, 95% CI 2.5-11). Sedation also correlated with abnormal EEG results, however, generalized epileptiform discharges were more likely noted in the non sedated EEGs (Table 2). The only sleep factor (as listed in Table 1) that correlated with achieving sleep during the EEG, independent of CH use, was the duration of the preceeding noctornal sleep. Children who slept less

than 4 hours were more likely to sleep when compared to those who slept more than 4 hours at night (86% versus 39%, p=0.0002).

Discussion. The study results confirm several observations regarding the value of CH in EEG sedation. Chloral hydrate was safe and very effective in sleep induction. This is similar to the findings of Rumm et al, who found CH effective in 86% of children on first attempt with no side effects.[15] A recent study compared the hypnotic effects of CH with other sedatives and found no statistically significant differences in the effect on sleep induction or sleep activation effects.[16] This means that CH is not only safe, but also as effective as other agents. However, children with neurological disorders had a much greater failure rate when compared to neurologicaly normal children (27% versus 4%).[15] We did not encounter this high failure rate, however, one third of our children woke up spontaneously before the test was completed, particularily those with chronic neurological abnormalities. This was not dose related, however, a second CH dose (i.e. higher total dose) may be necessary in some of these children.

In our study, sedation was not given routinely as 55% of the children were not sedated for EEG. Children with chronic neurological abnormalities and young infants were more likely to receive CH. This suggests that physicians used CH rather selectively, particularly in out-patients who were less likely to receive CH. Very few children received inappropriate sedatives such as benzodiazepines reflecting increased physician's awareness about this issue.

Overall, sleep EEGs were more likely to be abnormal and the use of CH correlated with abnormal EEG results. However, lighter stages of sleep were more likely recorded in the natural sleep EEGs. Recording an initial period of wakefulness followed by sleep onset was even more likely achieved in the natural sleep group. These EEGs were much more likely to contain epileptiform discharges when compared to continous sleep recordings. This is one of the limitations of drug induced deep sleep as spike activation may occur mainly in the lighter stages of sleep.[2] Sleep deprivation is a good solution to this problem, but was used very infrequently in our sample. In fact, the children who slept less than 4 hours the night prior to EEG were more likely to sleep regardless of whether CH was given or not. This highlights the effectiveness sleep deprivation in achieving sleep, which was non-intentional in this group.

We conclude that chloral hydrate is a safe and effective agent for sleep induction. However, the sleep onset was frequently missed which may alter the EEG interpretation. The sedative effect was not sustained in many children, particularly those with chronic neurological abnormalities. Sleep deprivation is underutilized and needs to be used more frequently.

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