CERASUS JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Sedation with chloral hydrate and melatonin in childhood electroencephalography

Betul Diler Durgut[1]
Emine Tekin[1]

1. *Division of Pediatric Neurology, Giresun University Faculty of Medicine, Giresun, Türkiye*

Received: 09 August 2024
Accepted: 24 September 2024
Published: 15 February 2025

Corresponding Author: Betül DILER DURGUT, M.D.
Division of Pediatric Neurology,
Giresun University Faculty of Medicine, Giresun, Turkey
Email: betuldlr@hotmail.com

Abstract

Objective: Recording an electroencephalography (EEG) in children is challenging due to their restlessness during the procedure and inability to follow the required instructions. Sleep deprivation and the use of sedative agents are necessary to perform the recording. This study aims to evaluate the need for sedation in patients and to compare the effectiveness and side effects of sedation with chloral hydrate and melatonin.

Methods: Patients who underwent EEG recording between December 2023 and March 2024 were retrospectively evaluated. The chloral hydrate and melatonin groups were formed for the patients requiring sedation. According to the protocol applied in our clinic, chloral hydrate was administered orally at a dose range of 30-50 mg/kg (max 1500 mg), while melatonin was given orally at a dose of 1-3 mg. The sociodemographic information of the patients was recorded from hospital charts, sleeping rates and EEG recording duration were compared.

Results: Of the 471 patients EEG performed, 240 (51%) were female and 231 (49%) were male. The mean age was 9.1±5.1 years, with a median age of 9.5 years. Sleep deprivation was appropriately carried out in 434 patients (92.3%), while 37 patients did not achieve sleep deprivation. Among the 76 patients who received sedation, chloral hydrate was used in 45 (59.2%) and melatonin in 31 (40.8%). Sleeping ratios were 82.2% and 80.6% in the chloral hydrate and melatonin groups respectively; there was no statistically significant difference in sleeping rates (p: 0.86). No serious drug-related side effects were observed in either group. Rare gastric complaints, such as gastric discomfort and nausea/vomiting were noted in the chloral hydrate group.

Conclusion: Melatonin and chloral hydrate provided similar rates of sedation. This study showed that either drug can be chosen for the sedation in pediatric EEG recordings.

Keywords: Children; chloral hydrate; electroencephalography; melatonin; sedation

You may cite this article as: Diler Durgut B, Tekin E. Sedation with chloral hydrate and melatonin in childhood electroencephalography. *Cerasus J Med.* 2025;2(1):15-20. doi: 10.70058/cjm.1529462

Introduction

Electroencephalography (EEG) is a valuable method used for the diagnosis and classification of epilepsy, determining the treatment and prognosis.

An ideal EEG recording should include both wakefulness and sleep states in a patient. Sleep EEG is preferred in children because it facilitates compliance, reduces EEG artifacts, and increases the likelihood of diagnosis. In younger children, restlessness during the recording and inability to follow instructions can decrease the success rate of EEG recordings.

Sleep deprivation (decreasing the sleep and keeping the patient awake till the EEG recording for a time appropriate for their age) is used as an activation method because it facilitates falling asleep during the recording and increases the likelihood of detecting interictal discharges [1]. Sedation is required in children who cannot undergo EEG recording despite sleep deprivation. Clinics use different drugs for sedation based on their experience, such as chloral hydrate, melatonin, and hydroxyzine [2-4].

In childhood, both awake and sleep EEG recordings are performed. Sleep deprivation is accepted as an activation method as it increases discharges in EEG. Despite sleep deprivation, patients who have difficulty falling asleep, such as those with autism spectrum disorder, attention deficit hyperactivity disorder, mental retardation, cerebral palsy, and those failing to attain sleep spontaneously may require sedation. Chloral hydrate has been used for many years for sedation purposes. However, chloral hydrate requires close monitoring due to its side effects and long recovery time. To optimize time and resources, alternative agents are necessary to induce sleep effectively. Melatonin is an alternative agent to chloral hydrate because it is considered safe and the recovery time is shorter.

Chloral hydrate is a sedative-hypnotic agent that has been extensively used for inducing sleep during EEG recordings for many years. It can be administered orally or rectally. It is rapidly metabolized by alcohol dehydrogenase in the liver and erythrocytes to its active metabolite, trichloroethanol. This active metabolite crosses the blood-brain barrier and exhibits hypnotic properties. Chloral hydrate has been associated with serious side effects such as oxygen desaturation, delayed apnea, and respiratory arrest [5]. Due to these potential complications, close monitoring of patients is necessary.

Melatonin is a hormone produced in the pineal gland that acts on the suprachiasmatic nucleus of the hypothalamus to induce sleep. It is advantageous due to its low incidence of side effects.

The International League Against Epilepsy (ILAE) recommends partial sleep deprivation for EEG recordings in children aged 12 years and older, as well as in adults. For children under 12 years old, ILAE suggests administering melatonin or conducting sleep deprivation. The recommended dose of melatonin is 1-3 mg given 30-60 minutes before the EEG. In cases where melatonin is not available or partial sleep deprivation is inadequate, chloral hydrate is recommended. Partial sleep deprivation in children under 6 years old involves reducing sleep by 1-3 hours, or by an amount estimated to be necessary for falling asleep at the time of the EEG. For children aged 6-12 years, this includes delaying bedtime by 3 hours and waking up 2 hours earlier than usual, and staying awake until the time of recording. In children aged 12 and older, this involves going to bed 2 hours later (no later than midnight) and waking up at 4:00 AM, remaining awake until the EEG. For adults, it is defined as sleeping between 24:00 and 04:00 before the recording. [6]

In this study, we aimed to determine the need for sedation in our patients and to compare the effectiveness of chloral hydrate and melatonin for sleep induction. The secondary aim of this study is to investigate the side effects associated with the use of chloral hydrate and melatonin during childhood electroencephalography.

Methods

EEG recording

In our clinic, EEG recordings are requested from the pediatric neurology outpatient department. All patients and their families are routinely informed about the importance of sleep deprivation when EEG appointments were scheduled.

Patients with conditions such as autism spectrum disorder, attention deficit hyperactivity disorder, intellectual disability, cerebral palsy for whom EEG recording may be challenging due to anticipated difficulties or inability to sleep despite appropriate sleep deprivation, are sedated for the procedure. Written consent is obtained from families for both EEG recording and sedation. Chloral hydrate or melatonin is preferred for sedation in these cases.

EEG recording is conducted according to the international

10-20 system, which involves the placement of electrodes to capture 18-channels of recordings.

Drugs for sedation

Chloral Hydrate: In our clinic, chloral hydrate is administered orally at a dose range of 30-50 mg/kg (max 1500 mg).

Melatonin: In our clinic, melatonin is administered orally at a dose of 1 mg for patients weighing less than 15 kg, and 3 mg for patients weighing 15 kg or more.

Data Collection:

Patients who underwent EEG recordings in the EEG laboratory between December 2023 and March 2024 were included in the study. Patient data were accessed through hospital charts retrospectively. Information collected included age, gender, sleep deprivation status, need for sedation, and EEG duration. Patients who received sedation were divided into two groups: those administered chloral hydrate and melatonin. Sleeping rates and EEG durations were compared between these groups.

Statistics:

Statistical analyses of the study were performed using the trial version of SPSS 22.0 (SPSS Inc., Chicago, IL) package software. Kolmogorov-Smirnov test was employed to examine whether the quantitative variables were suitable for the normal distribution. Independent groups were compared with the Mann-Whitney U/ Kruskal-Wallis H test in terms of variables that were not normally distributed. The relationship between qualitative variables was examined using chi-square analysis. The descriptive statistics of the quantitative variables that conformed to the normal distribution were shown as mean ±standard deviation, and the descriptive statistics of the quantitative variables that were not normally distributed were shown as median (min-max) or mean ±standard deviation. Descriptive statistics for qualitative variables were expressed as frequency (%). Statistical significance was considered $p< 0.05$.

Ethics Committee Approval:

Ethics committee approval was obtained from local Clinical Research Ethics Committee (Date/Number: 17.07.2024/01)

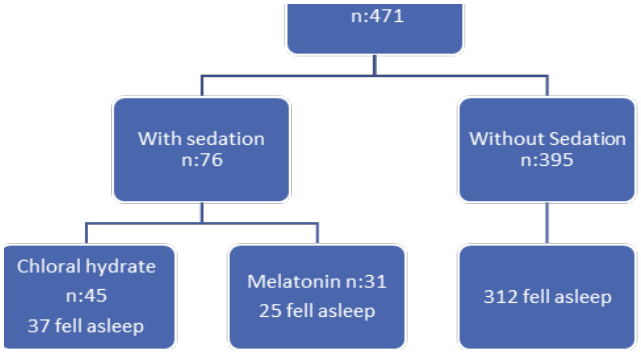

Figure 1: Flow chart of the patients' with EEG recordings

Results

In a three-month period, 471 patients who underwent EEG recordings were included in the study. Of these patients, 240 (51%) were female and 231 (49%) were male. The average age was 9.1 ±5.1 years, with a median age of 9.5 years. Sleep deprivation was appropriately conducted in 434 patients (92.3 %), while 37 patients failed sleep deprivation. Among the 395 patients who did not require sedation, 312 (76%) fell asleep, whereas 62 (81.6 %) of the 76 patients who received sedation,

Table 1: Characteristics of patients undergoing sedation

	Chloral Hydrate n(%) n:45	Melatonin n(%) n:31	p
Age (year± SD)	8.07 ± 4.49	6.87 ± 4.31	0.19
Sex Boy n(%) Girl n(%)	 28(62) 17(38)	 19(61) 12(39)	1.00
Sedation rate	37 (82.2)	25(80.6)	0.86
Sleep EEG duration (m)	23.35	23,8	0.50

m:minute

fell asleep. Patients requiring sedation, 45 (59.2 %) were in chloral hydrate and 31 (40.8 %) were in the melatonin group. (Figure 1-flow chart)

Children who received chloral hydrate, 82.2% fell asleep, compared to 80.6% in the melatonin group; however, there was no statistically significant difference between the groups (p=0.86) (Table 1). The mean EEG recording duration was 32±11.3 minutes, with a median of 35 minutes. No serious drug-related side effects were observed in either group. Rare gastric complaints, such as gastric discomfort and nausea/vomiting, were noted in the chloral hydrate group, observed in 3 patients."

Discussion

In our study, no significant difference was found in sedation efficacy between melatonin and chloral hydrate groups during EEG recordings (P= 0.86). This study demonstrated that chloral hydrate and melatonin, both used for sedation, showed no superiority in inducing sleep over each other. Sedation was required for 76 out of 471 patients, which corresponds to 16.1% of the patients. Side effects were observed only in the chloral hydrate group, with mild gastric discomfort noted in 3 patients.

In the literature, there are studies comparing sleep induction using chloral hydrate and melatonin. Some studies have found chloral hydrate to be more successful than melatonin in inducing sleep, while others have not observed a significant difference [5, 7].

Dirani et al. compared their old and new protocols for EEG recordings in patients aged 6 months to 17.7 years. The old protocol involved the use of chloral hydrate, with a second dose given when necessary. In the new protocol, melatonin, hydroxyzine, and chloral hydrate were sequentially added until sleep was achieved. As a result, the sleep induction rate with melatonin (44.6%) was significantly lower compared to chloral hydrate (95.2%) [5]. In the study, despite using higher doses of melatonin (2.5 mg for children under 5 years old, 5 mg for those 5 years and older), the sleep induction rate with melatonin was notably lower compared to our findings. Unlike our study their patients were kept up late and awakened at the usual morning hour. Our sleep deprivation involved delaying bedtime and waking up earlier then the usual time. We speculated that this difference might account for this disparity. Additionally, in our study, we did not use sequential medications for sedation purposes.

Unlike Dirani et al., Fazli et al. did not find a significant difference in the rates of sedation induction. In their study, which included children aged 6 months to 5 years, they compared 25 mg/kg of chloral hydrate with a dose of 0.4 mg/kg of melatonin [7]. The success rates were found to be similar in the melatonin and chloral hydrate groups, at 92% and 95%, respectively (p=0.5). In contrast, in our study, these rates were 80.6% and 82.2%, respectively (p=0.8). Our study group consisted of patients aged 4 to 14.2 years. The lower sedation induction rate in our study may be attributed to the difference in patient age groups. As a result, Fazli et al. found melatonin advantageous due to its shorter recovery time and absence of side effects.

Ashrafi et al. randomized 248 uncooperative patients aged 1 month to 6 years for EEG recordings. They compared chloral hydrate and melatonin groups and found similar sleep onset latency. However, the sleep and sedation duration were significantly shorter in the melatonin group compared to the chloral hydrate. Re-dosing was required for 6 patients in the chloral hydrate group and 20 patients in the melatonin group. Both groups experienced few side effects. They recorded the shorter sleep duration and sedation period-drowsiness as two advantages of melatonin over chloral hydrate [8].

In another study, 174 children aged 0-4 years were given melatonin 1 hour before EEG recording, with 3 mg for those weighing less than 15 kg and 6 mg for those weighing 15 kg or more. All children were encouraged to remain sleep-deprived before their sleep EEG. For children over 3 years old, they were kept awake until midnight, then allowed to sleep from 00:00 to 04:00, and were not permitted to sleep until they arrived at the hospital for EEG. The control group was retrospectively composed of patients who received chloral hydrate. The study concluded that melatonin sedation was effective and safe; however, it was found to be less successful in children with developmental and behavioral issues [9].

In the study by Holsakul et al., patients aged between 1 and 5 years, as well as older patients who did not cooperate for EEG recordings, were included. The patients were randomly divided into three groups: the melatonin group (Group A), the melatonin and sleep deprivation combination group (Group B), and the chloral hydrate and sleep deprivation combination control group (Group C). Sleep deprivation was defined as going to sleep 2 hours later than usual, waking up at the usual wake-up time, and not napping during the day. The dose of melatonin used was 3 mg. If the patient

did not fall asleep, the dose was repeated after 1 hour. If sleep still did not occur, chloral hydrate at 25 mg/kg was administered 1 hour after the second dose, with an additional dose of 50 mg/kg if necessary, followed by another 25 mg/kg if needed. In Groups A, B, and C, 5, 3, and 1 patient required a repeat dose, respectively. Unlike our study, this study examined sleep onset latency, defined as the time from drug administration to the onset of stage 2 sleep. Melatonin alone was found to be as effective at inducing sleep as when combined with sleep deprivation. However, the efficacy of melatonin was lower compared to chloral hydrate in combination with sleep deprivation, particularly in terms of sleep onset, latency, and sleep efficiency [10]. These findings are consistent with those of a previous study by Ibekwe et al. in 2017 [9].

In a meta-analysis comparing melatonin with Triclofos (a prodrug pharmacologically converted to an active metabolite similar to chloral hydrate) for EEG recordings, chloral hydrate showed a success rate of 90% and melatonin 76% (p=0.054). Although this meta-analysis did not find a significant difference between the groups, it was noted that the chloral hydrate group had longer sleep durations, fewer requirements for a second dose, and more frequent side effects compared to melatonin, suggesting melatonin as a viable alternative for initiation of sleep. Despite weak evidence from current literature, Triclofos and melatonin were considered comparably effective in triggering sleep for EEG recordings in children [4]. In our study, no side effects were observed in patients receiving melatonin, whereas patients receiving chloral hydrate experienced mild gastric symptoms, although no serious side effects were reported. In one of the aforementioned studies [5], vomiting occurred in some patients receiving melatonin, but no side effects were observed in other studies [5, 7, 11]. Chloral hydrate side effects, up to 15% were reported, with gastric complaints being more common; transient bradycardia and desaturation, which resolved with caution, were also reported [5, 7].

Limitations

Small sample size, short study duration, and the retrospective nature of the study may limit the generalizability of the findings. Additionally, the specific age groups included in the study may not fully represent the broader population. Analyzing patients by age groups in a larger sample size may yield more accurate results. Other factors influencing sedation should be considered, and better-designed prospective studies are needed to address these limitations.

Conclusion

This study determined that chloral hydrate and melatonin were not superior to each other in providing sleep induction for EEG recording. The absence of side effects with melatonin use and the lesser need for post-procedural monitoring may make it a preferred choice.

The drugs and drug doses to be used can be selected depending on the experience and preference of the centers.

Conflict of interest

The authors declare no competing interests. The authors declare they have no financial interests.

Funding

No funding was obtained for this study.

Authors' Contributions: Concept: B.D.D., E.T.; Design: B.D.D., E.T.; Data Collection or Processing: B.D.D., E.T.; Analysis or Interpretation: B.D.D.; Literature Search: B.D.D., E.T.; Writing: B.D.D., E.T.

Ethical Declaration: Ethics committee approval was obtained from local Clinical Research Ethics Committee (Date/Number: 17.07.2024/01).

References

1. Theitler J, Dassa D, Heyman E, et al. Feasibility of sleep-deprived EEG in children. *Eur J Paediatr Neurol.* 2016 Mar;20(2):218-221. doi:10.1016/j.ejpn.2015.12.012

2. Bektas O, Arıca B, Teber S et al. Chloral hydrate and/or hydroxyzine for sedation in pediatric EEG recording. *Brain Dev.* 2014 Feb;36(2):130-136. doi:10.1016/j.braindev.2013.03.002

3. Guler, M. A. Comparing chloral hydrate and hydroxyzine using for sedatıon during electroencephalogram(EEG) recording in children. 2008 p:58. Web site: https://tez.yok.gov.tr/UlusalTezMerkezi/tezDetay.jsp?id=g45UilhFej5l17liF_GA&no=WYK9eCmIojHYeNQUNKV1yw Access date:14 june 2024

4. Panda PK, Panda P, Dawman L, et al. Systematic Review and Meta-analysis of Efficacy and Safety of Melatonin and Triclofos for Inducing Adequate Sedation for Sleep Electroencephalogram in Children. *J Neurosci Rural Pract*. 2021 Dec 30;13(1):3-11. doi:10.1055/s-0041-1736511

5. Dirani M, Nasreddine W, Melhem J, et al. Efficacy of the sequential administration of melatonin, hydroxyzine, and chloral hydrate for recording sleep EEGs in children. Clin EEG *Neurosci.* 2017;48:41–47. doi:10.1177/1550059415621830

6. Proposed Guideline: Minimum standards for recording routine and sleep EEG- web site: https://www.ilae.org/guidelines/guidelines-and-reports/proposed-guideline-minimum-standards-for-recording-routine-and-sleep-eeg . Access date: 14 June 2024

7. Fazli B, Hosseini SA, Behnampour N, et al. Melatonin versus chloral hydrate on sleep induction for recording electroencephalography in children: a randomized clinical trial. *Ann Med Surg (Lond).* 2023 Sep 5;85(11):5478-5483. doi: 10.1097/MS9.0000000000001140.

8. Ashrafi MR, Mohammadi M, Tafarroji J, et al. Melatonin versus chloral hydrate for recording sleep EEG. *Eur J Paediatr Neurol*. 2010 May;14(3):235-238. doi: 10.1016/j.ejpn.2009.06.010.

9. Ibekwe R, Jeaven L, Wilmshurst JM. The role of melatonin to attain electroencephalograms in children in a sub-Saharan African setting. *Seizure.* 2017 Oct;51:87-94. doi: 10.1016/j.seizure.2017.08.002.

10. Holsakul K, Poonmaksatit S, Thiamrakij P, et al. Efficacy of Melatonin for Inducing Sleep in Pediatric Electroencephalogram Recordings: A Single-Blind Randomized Controlled Pilot Study. *Child Neurol Open*. 2023 Aug 13;10:2329048X231194251. doi: 10.1177/2329048X231194251.

11. Bonuccelli A, Santangelo A, Castelli F et al. Efficacy of Liposomal Melatonin in sleep EEG in Childhood: A Double Blind Case Control Study. *Int J Environ Res Public Health*. 2022 Dec 29;20(1):552. doi:10.3390/ijerph20010552