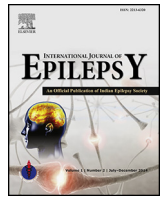




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### Research paper

# Melatonin versus chloral hydrate as the sedating agent in performing electroencephalogram in paediatric patients

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#### ABSTRACT

Electroencephalography (EEG) is a valuable tool in the diagnosis of epilepsy. The attainment of a high quality EEG requires patient's co-operation which is particularly difficult in children. Chloral hydrate has been used as a sedating agent in EEGs but it has potential serious adverse effects and anti-epileptic activity. Melatonin is used increasingly in different investigations as a safe alternative. Our study is to compare their effectiveness as sedating agents in performing EEGs and the detection rate of abnormal EEGs. This is a retrospective study performed in a regional hospital in Hong Kong. One hundred and ninety two EEG studies were included from December 2010 to July 2014. One hundred and two children were given chloral hydrate (50 mg/Kg) in the first half of the period and 90 children were given melatonin (3 mg for  $\leq 5$  years or 6 mg for  $> 5$  year) in the later half. The two groups are compared with Pearson's Chi-squared test with Yates' continuity correction. The successful rate in sedation was similar between the two groups while the pick up rate of abnormal EEGs was 52.56% in the melatonin group and 21.57% in the chloral hydrate group ( $p < 0.05$ ). Subgroup analysis among patients with epilepsy or mental retardation and intellectual disability shared same findings with higher detection rate of abnormal EEGs in the melatonin group. No side effect was documented in the study. Compare with chloral hydrate, melatonin is a safe and effective alternative and probably has less interference with the electrographic activity.

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## 1. Introduction

A high quality EEG requires cooperation of the individual which is particularly difficult for paediatric populations and patients with intellectual problems. Behavioural trainings and sleep deprivation can work in selected cases but they are time consuming and require immense input from both the carers and medical staff.<sup>1</sup> Chloral hydrate has been widely used as an effective sedating agent in EEGs in adult and paediatric populations. However, it has the drawback of altering the sleep architectures, potential anti-epileptic effects as well as the rare occurrence of serious side effects due to deep sedation. Therefore the exploration of an alternative sedating agents is warranted. Melatonin (N-acetyl-5-methoxytryptamine), a natural hormone, is found effective and safe as a sedation in different diagnostic procedures.<sup>2</sup> The aim of this study is to compare the effectiveness of melatonin against

chloral hydrate as a sedating agent for EEGs and would there be any difference in the detection rate of abnormal electrographic discharges.

## 2. Methods

This study is a retrospective study of patients requiring sedation for routine EEGs in the department of paediatrics of a regional hospital in Hong Kong from December 2010 to July 2014. There was a change in sedation protocol in the middle of this period in October 2012 from chloral hydrate to melatonin as the primary sedative agent. There was no change in all other details of the sedation protocol. Sleep deprivation before the EEG session is a standard, parents were instructed to put the children in bed 2 h later and wake the children 2 h earlier. Patients who were unable to cooperate for EEG setups were indicated for sedation. Under the old protocol, oral chloral hydrate (50 mg/kg, maximum 2 g) in syrup form was given to patients requiring sedation, additional dose of chloral hydrate at 25 mg/kg would be given if the child was not sedated. In the new policy, syrup melatonin (3 mg for  $\leq 5$

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**Table 1**  
EEG abnormalities [3].

Recognised EEG abnormalities
<i>Epileptic discharges</i>
Ictal epileptic discharges with or without clinical event seen during recording
Interictal epileptic discharges:
Sharp/spike wave, spike and slow wave complex
Polyspikes/polyspike and slow waves complex
Periodic lateralised epileptiform discharge (PLEDS)
Hypsarrhythmia
<i>Non-epileptic discharges</i>
Burst suppression
Hypoactivity
Focal/generalised slowing
Excessive slowing/encephalopathic pattern

years old and 6 mg for >5 years old) was provided as the primary sedative agent, if the child was not sedated, supplemented syrup chloral hydrate (50 mg/kg, maximum 2 g) was given. Patients who did not require sedation or with known hypersensitivity to the studied drugs were excluded. A total of 192 EEG recordings were included with 102 cases in the chloral hydrate group and 90 cases in the melatonin group. The respective drug was given orally 30–45 min prior to the EEG studies by nursing staff. Regular body parameters including heart rate, respiratory rate and oxygen saturation were monitored before and after the investigation. The patients were discharged when they became fully awake and able to tolerate a meal.

All the EEGs were performed in a single neurophysiological laboratory with the same EEG machine (Biologic EEG) under the international 10–20 system for 20–60 min. The EEGs were performed by the same electrophysiological technicians and were interpreted by the same paediatric neurologists. Asleep state, awake state, activations including photic stimulation and hyperventilation (if cooperation allowed) were included as the standard procedures. Data were collected from the hospital records and EEG request forms. The primary outcome is the effectiveness of melatonin as a sedation when compared with chloral hydrate. The sedation was considered a failure if there was a need of additional doses of chloral hydrate in the chloral hydrate group or the need to provide chloral hydrate on top of melatonin in the melatonin group. Successful EEG was defined as being able to complete the whole session with acceptable motion artefacts for interpretation. The secondary outcome was the number of abnormal EEGs in each group and subgroup. The different EEG abnormalities are listed in Table 1. The data were compared with the Chi-squared test with Yates' continuity correction. A *p* value of less than 0.05 was taken as statistically significant.

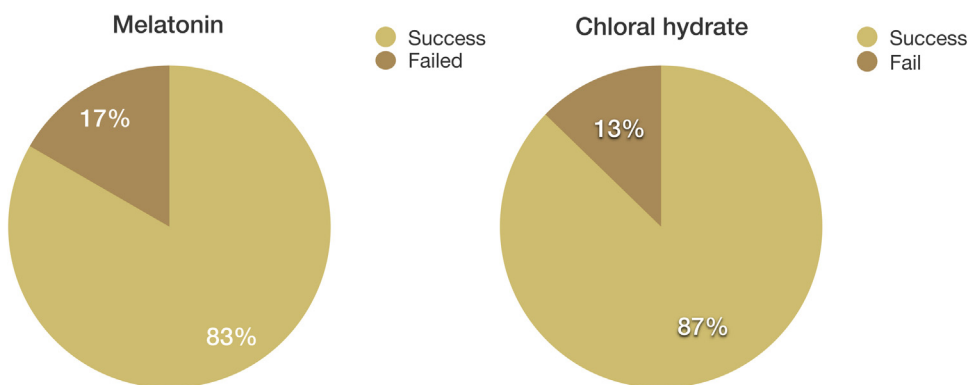
**Table 2**  
Baseline characteristics.

	Chloral hydrate (n = 102)	Melatonin (n = 90)	<i>p</i> value
Boys:girls	59:43	57:33	0.53
Median age (year)/range	3.34/11 days to 19 years	3.65/6 days to 22 years	0.10
History of febrile convulsion	31	28	1.00
Pre-existing diagnosis of epilepsy	47	50	0.93
Patients on anti-convulsant	31	29	0.91
Mentally retardation/ developmental delay	48	58	0.08
Cerebral palsy	6	11	0.20
History of ADHD/autism	18	14	0.85
History of prematurity	8	13	0.22

**3. Results**

Baseline characteristics, including age, sex and underlying conditions were similar in both groups, they are summarised in Table 2. The background information about any previous history of febrile convulsion, whether or not the patient was on anti-epileptic agents, the pre-existed diagnosis of epilepsy, developmental delay or intellectual disability, cerebral palsy, hyperactivity and attention deficiency, autism and history of prematurity are of particular interests as these conditions associate with a increased potential of having epilepsy. Moreover, patients with underlying developmental problems are less readily to cooperate, we performed a subgroup analysis to assess the efficacy of the two studied sedative agents in sedating this group of patients.

For the primary outcome in assessing the effectiveness in sedating patients (Fig. 1), there is no statistically significant difference between the 2 studied agents, melatonin's sedation effect is comparable to chloral hydrate: 75 (83.33%) in 90 cases of those in melatonin group succeeded in completing the EEGs without the need for additional drugs while in chloral hydrate group, 89 (87.25%) in 102 cases succeeded (*p* = 0.57). A subgroup analysis regarding patients with chronic neurological problems as mentioned above was performed. Melatonin is equally effective among patients with chronic neurological problems (Fig. 2): 46 (79.31%) in 58 cases of patients with developmental delay, mental retardation or cerebral palsy succeeded in completing the EEG in melatonin group and 40 (83.33%) in 48 cases of patients with similar conditions succeeded in the chloral hydrate group (*p* = 0.78). There is no statistically significant difference. The cases which were successfully sedated by either melatonin or chloral hydrate alone were then included in the comparisons of the detection rate of abnormal EEGs. The cases failed to be sedated by any one of the above agents were excluded because they either



**Fig. 1.** Successful EEG (*p* = 0.57).

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