ORIGINAL ARTICLE

Comparative Study of the Effect of Oral Chloral Hydrate and Intranasal Fentanyl on Sedation in Children for Electroencephalography

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Abstract

Objectives

Sedation and stability during electroencephalography (EEG) in pediatrics have high clinical importance. This study compares the sedative properties of oral chloral hydrate (OCH) and intranasal fentanyl (INF).

Materials & Methods

This study was a randomized clinical trial conducted in 2020 in Isfahan City on sixty-two pediatric candidates for EEG. Patients were randomized into two groups receiving 50 mg/kg OCH and 2 µg/kg INF thirty minutes before the process. The heart rate (HR), mean arterial pressure (MAP), respiratory rate (RR), and oxygen saturation (O2 sat) of patients, sedation, and physician's satisfaction were measured and compared between groups.

Results

The HR of patients decreased significantly in both groups ($P< 0.001$), and the patients that received INF had significantly lower HR 15, 30, 45, and 60 minutes after drug administrations ($P< 0.05$). RR evaluation indicated significantly decreased RR in both groups ($P< 0.001$), and patients receiving INF had lower RR 30, 45, and 60 per minutes after drug administrations ($P< 0.001$). Both groups showed significantly increased sedation levels during the study ($P< 0.001$), and patients treated with INF had higher sedation levels 15, 30, and 45 minutes after drug administration. Satisfaction rates were higher among the group that received INF ($P= 0.020$).

Conclusion

The use of INF had significant analgesic and sedative effects on pediatrics undergoing EEG.

Keywords: Intranasal fentanyl; EEG, Sedation; Chloral hydrate

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Introduction

Electroencephalogram (EEG) is a test that measures electrical activity inside the brain. Seizures, recurrent sleep apneas, brain infections, or brain tumors are some of the most important reasons children may need an EEG (1, 2). EEG is commonly used to evaluate patients with clinical epilepsy or unclassified periods of seizure (3, 4).

During the EEG process, the areas for connection of the electrodes are marked on the child's head, and after the electrodes are connected, the EEG process begins. The child must be supine or sitting during this process (5). EEG recording is a long-duration procedure and requires the patient's cooperation to set up the device and perform the work steps. Due to the long recording time of the EEG, many children lose their cooperation and start moving or crying during the operation. Thus, neurologists might find the EEG poorly recorded and difficult to interpret (6).

Sedative administration before EEG could be an acceptable strategy for children lacking cooperation. The sedatives should not affect the brain's electrical activity (7). Oral chloral hydrate (OCH) is a sedative drug that does not affect EEG and is rapidly absorbed from the gastrointestinal tract. Its effects appear about half an hour after oral administration (8). This medicine is used to treat insomnia quickly (9). It is also prescribed as a sedative in pediatrics undergoing EEG (10). Numerous studies have emphasized using chloral hydrate for sedation for diagnostic purposes (10-12).

Fentanyl is a powerful synthetic opioid analgesic similar to morphine but is 50 to 100 times more potent. It is a member of the class of drugs known as fentanyl, rapid-acting opioid (synthetic opiate) drugs that alleviate pain without causing unconsciousness (analgesic) (13, 14). Fentanyl depresses the central nervous system (CNS) and respiratory function. It is a short-acting drug used for sedation in children. This drug has known effects for sedation and reducing pain in children, and its intranasal form is increasingly being used (15).

So far, studies have been conducted in this field that have shown the importance and effectiveness of these drugs in creating proper sedation during surgeries and interventional procedures. The use of chloral hydrate and fentanyl in sedation during EEG in children has been studied, but no study has compared the effects of chloral hydrate and intranasal fentanyl (INF). Given the importance of pediatric sedation during EEG, the present study aimed to investigate and compare the effects of OCH and INF.

Materials & Methods

This randomized clinical trial was performed in 2020 at Imam Hossein Hospital, affiliated with

Isfahan University of Medical Sciences. The current study was conducted on pediatric candidates for EEG using simple random sampling.

The inclusion criteria were as follows:

- children aged between three months to three years
- being a candidate for EEG
- American Society of Anesthesiologists (ASA) classification of 1 or 2
- signing the written informed consent to participate in this study by the parents

Patients with respiratory diseases did not enter the study. The exclusion criterion was EEG cancelation due to any reasons.

The required sample size was calculated using the sample size estimation formula to compare the means with a 95% confidence level and 80% test power, equal to thirty patients in each group.

The data regarding patients' ages, gender, and weights were collected, and the patients' names were inserted into the Statistical Package for Social Sciences (SPSS) software and randomized into two groups. The first group received 50 mg/kg OCH thirty minutes before EEG, and the second group received 2 µg/kg INF thirty minutes before EEG.

The heart rate (HR), mean arterial pressure (MAP), respiratory rate (RR), and oxygen saturation (O2 sat) of patients were measured before the drug administrations (time= 0) and 15, 30, 45, and 60 minutes after the drug administrations. The patients' sedation levels were measured using the Ramsy Scale (16) in the mentioned time intervals. Based on this scale, the sedation was rated from 1 (awake, anxious, agitated, or restless) to 6 (asleep with no response to the pain). At the end of the process, the satisfaction rate of the physicians was rated from 1 (least satisfaction) to 5 (highest satisfaction) using a Likert scale.

The obtained data were inserted into the SPSS software version 24. Independent t-tests and repeated measures were used to compare data between timelines and groups. P-value < 0.05 was considered as the significance threshold.

Results

Sixty-six pediatrics entered the study based on the inclusion criteria and were divided into two groups, each containing thirty-three patients. Four patients were excluded during the study, and the data from 62 children were analyzed.

The study population comprised thirty-two boys (51.6%) and thirty girls (48.4%). The mean age of the first group was 17±9 months, and the mean age of the second group was 16±8 months. No significant differences were observed between the two groups regarding age, weight, and gender (P> 0.05). These data are shown in Table 1.

Hemodynamics evaluation indicated that the patients' HR decreased significantly in both groups (P< 0.001), and the patients that received INF had significantly lower HR 15, 30, 45, and 60 minutes after drug administrations (P< 0.05). The patients' MAP decreased significantly after drug administrations (P< 0.001), but no significant differences were observed between the two groups regarding MAP at different time intervals (P> 0.05). Furthermore, RR evaluation showed a significant decrease in RR in both groups (P< 0.001), and patients receiving INF had lower RRs 30, 45, and 60 minutes after drug administrations (P< 0.001). No significant changes were observed in O2 sat in patients. The data are shown in Table 2.

Evaluating the sedation scales among patients showed significantly increased rates of sedation among both groups during the study (P< 0.001), and patients that were treated with INF had higher

sedation levels 15, 30, and 45 minutes after drug administrations (Table 3).

In addition, Investigating physicians' satisfaction during the procedure showed higher satisfaction rates among the group that received INF (P= 0.020) (Table 4).

Table 1: Comparison of demographic variables between two groups.

		chloral hydrate	nasal fentanyl	P value
Age (month)		17±9*	16±8	0.549
Weight (gr)		11100±2833	10726±3284	0.673
Sex	male	17 (53.1%)	15 (46.9%)	0.611
	female	14 (46.7%)	16 (53.3%)	

* Data is represented by mean±SD or N (%).

Table 2: Evaluation and comparison of hemodynamics between two groups.

group	T=0	T=15min	T=30min	T=45min	T=60min	P2	P3
HR Chloral hydrate (Mean± SD)	135±13	134±11	132±12	131±12	129±13	<0.001	0.006
HR fentanyl (Mean± SD)	134±12	126±12	122±12	119±12	118±13	<0.001	
P1	0.662	0.008	0.002	0.001	0.001		
MAP Chloral hydrate (Mean± SD)	68±6	67±6	65±6	65±6	64±6	<0.001	0.008
MAP fentanyl (Mean± SD)	68±7	66±6	64±7	63±7	62±7	<0.001	
P1	0.794	0.949	0.568	0.389	0.405		
RR Chloral hydrate (Mean± SD)	16±2	14±2	14±2	14±2	13±3	<0.001	<0.001
RR fentanyl (Mean± SD)	16±2	14±2	12±1	11±1	11±1	<0.001	
P1	0.614	0.564	<0.001	<0.001	<0.001		
O2 Sat Chloral hydrate (Mean± SD)	98±2	97±2	98±2	98±2	98±2	0.066	0.891
O2 Sat fentanyl (Mean± SD)	97±2	97±2	97±2	98±2	98±2	0.191	
P1	0.775	0.592	0.449	0.663	0.537		

* Data is represented by mean±SD; P value1: repeated measurements of within group analysis; P value2: between group analysis in one time; P value3: repeated measurements of between group analysis.

Table 3: Comparison of sedation scores between groups.

Variable		Chloral hydrate	Nasal fentanyl	P-value 1
Sedation scale 0	2	31 (50.0%)	31 (50.0%)	Not
	3	0 (0.0%)	0 (0.0%)	
	4	0 (0.0%)	0 (0.0%)	
Sedation scale 15	2	23 (100.0%)	0 (0.0%)	0.000
	3	8 (20.5%)	31 (79.5%)	
	4	0 (0.0%)	0 (0.0%)	
Sedation scale 30	2	3 (100.0%)	0 (0.0%)	0.000
	3	28 (65.1%)	15 (34.9%)	
	4	0 (0.0%)	16 (100.0%)	
Sedation scale 45	2	0 (0.0%)	0 (0.0%)	0.000
	3	28 (71.8%)	11 (28.2%)	
	4	3 (13.0%)	20 (87.0%)	
Sedation scale 60	2	7 (70.0%)	3 (30.0%)	0.412
	3	21 (47.7%)	23 (52.3%)	
	4	3 (37.5%)	5 (62.5%)	
P value2		<0.001	<0.001	
P value3				<0.001

* Data is represented by N (%); P value1: between group analysis in one time; P value2: repeated measurements of within group analysis; P value3: repeated measurements of between group analysis.

Table 4: Comparing the satisfaction rates between groups.

		choloral hydrate	Intranasal fentanyl	P value
Likert	3	2 (100.0%)	0 (0.0%)	0.020
	4	14 (70.0%)	6 (30.0%)	
	5	15 (37.5%)	25 (62.5%)	

* Data is represented by N (%).

Discussion

Proper sedation for pediatrics during interventions such as EEG is essential, and efforts have been made to provide the best sedative options for such procedures. By evaluating the effects of INF and OCH, the present study showed that patients in both groups had significantly decreased HR, MAP, and RR during the procedure, and patients that received INF had significantly lower HR and RR compared to OCH. The physicians' satisfaction with sedation during the procedure was higher in pediatrics that received INF.

These data demonstrate the clinical effectiveness of INF in providing more stable hemodynamics and higher sedation rates. Using INF could result in more stability during the EEG process. The use of INF has been previously studied, and it has been declared that this drug is easy to administer and provides proper pain relief and sedation (17). INF has been used for pain relief in patients with breakthrough cancer pain, and both short-term and long-term results have been reported to be acceptable (18, 19).

INF has also been used in different clinical conditions in the pediatric population. In 2010, Saunders et al. investigated the effects of INF on relieving pediatric orthopedic trauma pain in eighty-one pediatrics. Based on this study, pediatrics that received INF had significantly lower pain severity and higher satisfaction initiating within 10 minutes after the administration (20). A systematic review of the literature by Mudd in 2011 showed that INF is a safe and effective pain management method for children in various clinical settings. It was also mentioned that pediatrics receiving INF had almost similar pain relief to opioids in the short term, and no complications had been reported (21). Another study by Yenigun et al. 2018 evaluated data from sixty-three children undergoing tonsillectomy. It reported that intranasal ketamine and INF provided significantly stronger analgesic effects than intravenous paracetamol administration, and these cases had more stable hemodynamics (22). The results of the present study are in line with these reports. However, the important point of the research is that very few studies have evaluated the sedative properties of INF in painless conditions such as EEG.

The good analgesic and sedative characteristics of INF have been proven in previous studies in pediatric emergency departments (23), cases of vaso-occlusive crisis in sickle cell disease (24), acute pain in children (25), children with suspected extremity fractures (26), and as a premedication during surgical operations (27). These studies have reported significant effectiveness for this drug in pain relief and sedation. Furthermore, the results of our study indicated that INF is easy to use and has significant sedative effects that could increase physicians' satisfaction during the EEG process.

Another important issue is that no complications were observed during this study in children; therefore, this study concludes that both drugs are safe and could be used in clinical practice.

The study population was limited. However, significant results were observed among the patients. Other limitations of this study include not evaluating other variables, such as the time interval between drug administration and loss of consciousness and the duration of unconsciousness. The study authors recommend that anesthesiologists pay more attention to INF's sedative and analgesic characteristics, especially in pediatrics.

In Conclusion

Using INF had significant analgesic and sedative effects on pediatrics undergoing EEG. OCH and INF significantly increased sedation rates, but the INF group had better hemodynamic stability, higher sedation rates, and satisfaction.

Acknowledgment

The study protocol was confirmed by the Ethics Committee of Isfahan University of Medical Sciences: IR.MUI.MED. REC. 1398.359 . IRCT20191205045618N1

Author's contribution

AS and AK contributed to the conception and design of the study, drafting of the study, and final approval of the version to be published and were accountable for all aspects of the study in ensuring that uncertainties regarding the accuracy or integrity of any part of the study are appropriately investigated and resolved. SS contributed to the design of the study, revising the study critically for important intellectual content, and final approval of the version to be published and were accountable for all aspects of the study in ensuring that uncertainties regarding the accuracy or integrity of any part of the study are appropriately investigated and resolved.

Conflict of interest

The authors have declared no competing or potential conflicts of interest

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