Clonidine Sedation Effects in Children During Electroencephalography

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Abstract- It is very important to have proper management in children with Seizure. Electroencephalography (EEG) as a diagnostic instrument has a key role in determining the management method of seizure in children. Because of poor cooperation of some children (especially children with attention deficit hyperactivity disorders and developmental disorders) in performing EEG, it is the best choice to sedate children before EEG. The aim of present study is to evaluate the sedation efficacy of clonidine in children before EEG. In a randomized clinical trial, 45 children age 2 to 12 with seizure, who referred to Children Hospital of Tabriz University of Medical Sciences and candidate for EEG, were studied. Sedation before EEG induced by 0.5 to 2.0 mg clonidine orally. Sedation score (0 to 5) measured by using eyes condition, response to voice, and response to touch. Successful sedation, EEG performing, and hemodynamic stability were evaluated during sedation. Of all patients, 40 patients (88.88%) were sedated successfully, and EEG was performed for all of the children. Mean onset time of clonidine effect was 35.47±13.56 minutes and mean time of that the patients' level of consciousness back to the level before administrating of clonidine was 77.55±26.87 minutes. Hemodynamic states of all patients were stable during the study, and there were no significant changes in vital sign of patients. In conclusion, clonidine can be considered as a safe alternative medication for sedation for EEG, which is fortunately associated with no significant change in vital signs, which may complicate overall status of patients.

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Keywords: Sedation; Clonidine; Electroencephalography

Introduction

Seizure is one of common neurological disorder and also often it is one of the early symptoms of neurologic disease in children, and about 10% of children suffer from seizure during childhood (1). Seizure in children may be associated with serious underlying disease which needs to investigate and critical management, so seizure by itself is an important symptom that often requires further evaluations (2,3).

Electroencephalography (EEG) is a useful method for evaluating of children with symptoms of seizure, and it helps physicians for differentiation between seizures and pseudoseizures (4,5). Because of poor cooperation of children especially those with attention deficit hyperactivity disorders, developmental disorders, and Autism spectrum disorders for EEG, it is advised to perform EEG during sleeping, and also for better evaluation of the epileptiform discharges in EEG, studies recommended performing EEG during sleeping or with induced sedation in children due to its importance and benefits (6,7). Sedation reduces the motion and muscularity artifacts on EEG, and also we can use the electrodes without any anxiety and compulsion in children. Therefore the epileptiform discharges recorded better in this condition (8,9).

Various medications were used to induce sedation in children for performing EEG, but there are some controversial results about the benefits and efficacy of these medications. An ideal medication for sedation should have rapid onset of action with short duration of effects and also with few side effects. A proper medication should not interfere with the EEG waves and not change the background waves as well as not cover the minor diagnostic pattern of EEG (8-10). Chloral hydrate is one of the widely used medications for sedation to perform EEG in children, but it causes vomiting and increase the risk of aspiration in children

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and has some serious side effects like cardiac arrhythmia and severe CNS depression. Some alternative medications of chloral hydrate to induce sedation for performing EEG, are phenothiazine, barbiturates, and benzodiazepines, but using of these alternatives also have some limitations because of the effect the background waves of EEG (11-13).

Clonidine as an alpha-2 agonist agent has antihypertensive effects and also sedative effects. Studies about the pain relief focused on sedation effects of clonidine. Clonidine has dose-dependent sedative effects with cardiovascular stability and without drug intolerance side effects or withdrawal symptoms (14-16). With considering inefficacy of chloral hydrate for sedation of children to perform EEG in some cases, the aim of present study was to evaluate the effects of clonidine in sedation of children during EEG.

Materials and Methods

In a clinical trial study, 45 children with epilepsy who referred Educational-Medical Children Hospital of Tabriz University of Medical Sciences and candidate for EEG, were selected randomly and studied. Inclusion criteria were age between 2 and 12-year-old, history of epilepsy, and history of failure to sedation with other routine medications (except clonidine). Exclusion criteria were cardiovascular disease, gastrointestinal disease, pulmonary or renal disease, and also hemodynamic instability. Also, patients with inadequate sedation were excluded from the study (sedation score>2 based on Table 1).

Patients had dietary restrictions, including solids restrictions 8 hours before sedation and fluid and medications restriction 2 hours before sedation. Patients received 0.05-0.2 mg clonidine orally based on their weight, patients less than 10 kg received 0.05 mg, patients with weight of 10 to 20 kg received 0.1 mg, and patients with weight of more than 30 kg received 0.15 to 0.2 mg of clonidine orally.

Level of consciousness in patients was determined by using the below table (Table 1).

Score of consciousness was determined by total scores of three items, including; eyes, response to voice, and response to touch (based on Table 1).

Onset time of clonidine effect was defined as score≤2, the duration time of clonidine effect was considered as the time that level of consciousness back to the score equal to the score before sedation. Heart rate, respiratory rate, body temperature, blood pressure, and oxygen saturation (SpO_2) before and during sedation (after 2 hours from sedation) were measured and evaluated with sedation score every 15 minutes. Vital signs change and other possible side effects of clonidine were recorded. The primary outcome of present study defined as success in sedation and the secondary outcome considered as adverse effect and failure to sedation. Also, the failure to sedate defined as not to reach proper sedation score 2 hours after administering of max dose of clonidine.

This study program was approved by Regional Ethics committee of Tabriz University of Tabriz Medical Sciences following deceleration of Helsinki. Patients have included the study after taking written informed consent form from parents. This study was registered in Iranian Registry of Clinical Trials (IRCT2016102118946N5).

Software SPSS™ version 15, was used for statistical analysis. Descriptive Statistics including frequency, and Mean±SD were used for data reporting. Kolmogorov-Smirnov test was used for determining the distribution of data, and Chi Square used for comparing the Qualitative data, also we used Paired T-Test for comparing Quantitative data. We considered all cases as statistically significant with *P* less than 0.05.

Table 1. Score of consciousness level in patients

Item score	Eyes	Response to voice	Response to touch
0	Closed	None	Not arousable
1	Open	Incoherent	Sleepy, or arousable
2	-	Coherent	Awake

Results

Among all 45 children, 24 (53.3%) of them were male, and 21 (46.7%) of them were female. The mean age of patients' was 4.35±1.32-year-old in range of 2 to 12-year-old.

Of all patients, 5 had inadequate sedation, so they were excluded from the study. Sedation rate induced by clonidine was 88.88 percent. Mean onset time of clonidine effect was 35.47±13.56 minutes in the range

of 20 to 105 minutes after full dose administration of clonidine. Mean time of that the patients' level of consciousness back to the level before administrating of clonidine was 77.55±26.87 minutes in the range of 45 to 140 minutes after full dose administration of clonidine. Table 2 shows the mean vital sign changes during the study.

All patients hemodynamic during the study were stable, and no significant changes were seen in vital sign of patients, and also in the present study, we did not see any adverse effect of clonidine on patients.

Table 2. Vital sign changes during the study

Time Vital sign	Beginning of study	During study	End of study	*P*
Heart rate	85.76±13.14 per minutes	87.62±12.91 per minutes	88.42±13.43 per minutes	*P*=0.085
Respiratory rate	18.54±1.63 per minutes	18.43±1.74 per minutes	18.75±1.94 per minutes	*P*=0.220
Body temperature	37.34±0.22 °C	37.32±0.19 °C	37.34±0.23 °C	*P*=1.000
Diastolic blood pressure	64.11±8.05 mmHg	64.21±9.71 mmHg	62.62±12.28 mmHg	*P*=0.200
Systolic blood pressure	96.41±8.73 mmHg	96.12±9.81 mmHg	95.05±10.11 mmHg	*P*=0.555
SpO_2	93.18±2.53 %	94.11±1.18 %	93.99±1.44 %	*P*=0.270

Discussion

Epilepsy is known as a medical condition worldwide distribution. Epilepsy might be associated with serious underlying disease which needs to be investigated, so seizure by itself is an important symptom that often requires further evaluations, especially with EEG. Sedation is one of the most important steps toward performing EEG, so in the present study, it was aimed to evaluate the effects of clonidine in sedation of children during EEG. In the present study, it was shown that all patients administered with clonidine had proper sedation level also their vital signs during sedation had no statistically significant change.

In a study by Metha *et al*., investigating clonidine as a sedative agent in children with autism and pervasive developmental disorders, it was shown that 2 of 27 children did not have proper sedation, although they cooperated for EEG. Also, 2 patients experienced asymptomatic heart rate reduction by 40%, and 2 other patients had a decrease in systolic pressure. But at last they concluded that clonidine is a viable alternative for sedation in which is well tolerated without any significant side effects and eases administration, shorter duration of total sedation, lack of EEG drug effect, and high overall success rate (17); this study was similar to present study in terms of methods. Furthermore, results were somehow similar, although some patients had experienced change in heart rate and blood pressure, however, at last, this change was not statistically significant. Although in present study changes in EEG was not assessed, some studies favored some subtle changes in EEG (18-20). Meanwhile, others reported no changes (21,17).

In another study, Hall *et al*., performed a study about sedative, analgesic and cognitive effects of clonidine infusions in humans, which included that there were no statistically significant changes in cardiorespiratory variables throughout the study, but there was a statistically significant analgesia, memory impairment and reduced cognitive performance (21); results of this study was similar to present study, as we observed proper sedation in patients and no significant change in vital signs.

In a study by Fu *et al*., a prospective, randomized, placebo-controlled, cross-over study was designed to assess the effects of four different oral doses of clonidine (0.05-0.3 mg per os) on the acute hemodynamic response to electroconvulsive therapy; it was concluded that all vital signs had not changed except mean arterial pressure which decreased (22); although in this study electroconvulsive therapy it was similar to present study considering drug protocol, results of this study considering blood pressure decrease was in contrast to study.

In a similar study by El-Henawy *et al*., investigating effects regarding addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children, it was concluded that No significant difference was observed in incidence of haemodynamic changes or side-effects (23); this was similar to present study, as we did not detect any hemodynamic changes during the clonidine administration, neither.

In a study by Ambrose *et al.*, about effects of intravenous clonidine infusion in critically ill children and dose-dependent sedative effects and cardiovascular stability, it was concluded that children administered with fixed infusion of clonidine had no statistically significant change in cardiovascular and hemodynamic status (24); although in this study in contrast to present study intravenous clonidine infusion was used, results regarding no statistically significant change in cardiovascular or hemodynamic status was similar to present study.

One of the main limitations of the present study was not enrolling a control groups, so we could not efficiently compare probable clonidine effects between control and intervention group. Another limitation of the present study was the lack of EEG details, which could have enhanced quality of the study and it could help authors to come to a precise conclusion about possible effects of clonidine on EEG.

In conclusion, clonidine can be considered as a safe alternative medication for sedation for EEG, which is fortunately associated with no significant change in vital signs, which may complicate overall status of patients. Further studies are encouraged, to compare effects of clonidine with other Alfa-2 agonists and especially control groups. There is also a controversial probable effect of clonidine on EEG, which may complicate interpretation of EEG, so it is suggested that further studies performed to reveal possible effects of clonidine on EEG in different health conditions.

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