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Comparission Between Midazolam and Midazolam Plus Diphenhydramine Efficacy of Sedation in Children Undergoing CT-scan admitted to the Hospital in Tehran

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Sedation is a technical administration of sedative agents that usually is associated with an analgesic drug and makes a situation to allow the patient to tolerate unpleasant procedures, however the patient's cardiopulmonary function remains appropriate. These measures are aimed to improve the quality of care and patient satisfaction, to reduce pain and anxiety and to facilitate the success of diagnostic and therapeutic measures. In this study, the effect of the combination of oral midazolam and oral diphenhydramine with midazolam were studied and compared in CT scans only in the sedation of 48 children aged one to seven years whom their medical records were evaluated before induction and procedures for the presence of contraindication for prescribing and also had no neurologic and vascular deficits. . These individuals were monitored in terms of blood pressure, heart rate, respiratory rate and arterial oxygen saturation. Data obtained from the monitoring was interpreted and analyzed by SPSS software. Finally, it was shown that the combination of oral midazolam and oral diphenhydramine leads to a safer and more effective sedation compared with midazolam alone in children during CT scan. This combination will enable the sedation failure during CT scans for children to get the lowest rates.

Key word : Midazolam, diphenhydramine, CT-scan.

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These measures are aimed to improve the quality of care and patient satisfaction, to reduce pain and anxiety and to facilitate the success of diagnostic and therapeutic measures. One application of sedation is in imaging studies in uncooperative low aged people and patients including one to seven-year- old people. One of the main goals of sedation and anesthesia is to create comfort and convenience before CT scan that many studies have been performed in this field. Studies indicate that parents' anxiety and worry even makes it difficult to separate children. Oral sedation leads

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to patients' and their parents' satisfaction[1].

CT imaging is one of the best tests in children to study their body that needs to remain unmoved for variables periods even for an hour in a closed environment, and cramped and noisy space. Patients less than 7 years and those who have mental retardation requires sedation and anesthesia, also the sedation is needed for older children who have anxiety, stress and fear, despite the assurances[1]. Rapid induction and short recovery time are desirable and appropriate characteristics of the sedation. A suitable sedative medication (sedative) should have minimal respiratory depression[1,2] . In general, different drugs have been used for the sedative of children during various procedures[3], but midazolam is one of the most common drugs for the sedative in children and adults during a set of procedures. This short-acting benzodiazepine is used in different ways to provide an appropriate sedation and amnesia (PTA) and a reduced anxiety, and is preferred to long-acting benzodiazepine such as diazepam and lorazepam[4]. When an oral midazolam is used alone as a sedative drug, without any other drug, it *fail*s significantly to provide the sedation[5] . First-generation histamine-receptor antagonists such as diphenhydramine and promethazine have been known as a responsible for depressing effects on the nervous system. The reduced levels of understanding and the performance of psychomotor following the addition of antihistamine to the sedative drug leads to increased sedative effect[6]. The sedative effects of antihistamines can be respiratory depression, nausea and vomiting, hypotension, drowsiness and etc[1]. In a study by Malinovsky and colleagues, the comparison of intranasal midazolam was performed in different ways including oral, rectal and propofol, and showed that the midazolam is a perfect alternative for that drug[7]. In another study, it was also evident that the various doses play a role in the beginning of drug effects, however, did not affect to complete recovery time[8]. Based on chernow's study in 1987, the average time to discharge from recovery was 60 minutes[9]. A good emtri was also obtained after 20-10 minutes with midazolam, however, the anti-anxiety effect was obvious after 15 minutes[10]. Previous studies aimed to compare the effect of midazolam with other sedatives have shown that promethazine has higher efficacy in comparison with midazolam[11], the combination of promethazine and chloral hydrate also showed a better sedation in the *pediatric intensive care unit* (PICU)[12-13]. In general, oral midazolam is an easy and convenient *way* of *administering drug* in children to separate from parents with a fast recovery time. In this study, the effect of midazolam and oral diphenhydramine with oral midazolam alone in the sedation of one to seven-year-old children was studied in order to perform CT and the effectiveness and efficiency were evaluated based on age, gender, weight and the start and duration time of drug effect and hemodynamic changes including heart pulse rate (PR), *Respiratory rate* (RR), blood pressure (BP), arterial oxygen saturation (SPO2). In general, the ultimate goal of this study was to judge clinically the patients aged from one to seven year who require radiology procedures for a decision to perform sedation with a lowest dose and a maximum effect. The comparison of these two methods can be a basis for further research.

METHODS

The information was provided to parents and a number of children scheduled for CT scan and sedation were assessed according to the sample size which was determined based on ASA classification (I, II) [14] in ages ranged from one to seven years. Before the procedure and induction, the medical records were evaluated for the presence of contraindications medication. Children with neurological and vascular defects were excluded. The other children were randomly divided into two categories, Group D who received 1.25 mg/kg diphenhydremine, Group M who received 0.5 mg/kg oral sugar syrup an hour before CT. Then 0.5 mg/kg oral midazolam (mixed with fruit juice) was given 20 min before CT. In case of vomiting within 15 min, the midazolam administration was repeated again with the same dose. The patient's blood pressure, heart rate, respiratory rate and arterial oxygen saturation were monitored. The sedation was evaluated according to UMSS grading every 10 minutes of midazolam administration until discharge[15]. The study was evaluated by a blind viewer in compared with the two groups. Children who could not sleep in 30 minutes after midazolam administration were received 50% of the initial dose of midazolam for recomplement. The start time of

effect and the period of deep sleep were reported for every child who didn't wake up with low irritation during the imaging. If the sedation was eliminated before *the completion* of *CT*, the sample was not assessable; therefore, a higher dose of midazolam was used. Discordant events such as nausea, vomiting and paradoxical reactions were reported. Hemodynamic changes were checked. Respiratory depression was occurred in SPO2 <92%. Sedation time was measured from the beginning of sedation effect until full consciousness. Other necessary information was obtained through the completion of questionnaires. In this study, paired t-test, chi-square and t-test methods were used. Pvalue was significantly considered <0.05. Statistical analysis was performed with SPSS software.

Calculation of sample size and sampling method

X1 , X2 ,S1 ,S2 were calculated for early study on 10 patients in each treatment group for the variables (Table I) by following formula (α = 0.5 and β = 0.2).

n= (Z(1-α/2) + Z(1-β))^2 × [S1^2+S2^2]/ (X1-X^2)^2

Z(1-α/2)=1.96 , Z(1-β)=0.84

RESULTS

48 children participated in this study. The age was ranged from 1 to 7 years old and the weighing was between 8-18 kg. General Characteristics of the people studied can be seen in Figure. In the group that received midazolam alone (Group M), 9 patients (18%), and in the group that received a combination of midazolam and diphenhydramine (Group D), 3 patients (6%) faced with the problem of anesthesia (P <0.05).

According to tables 1 and 2, an *increased heart rate* was found in *both groups*, however, it was higher in the group received midazolam with diphenhydramine. The respiration rate did not change appreciably in both groups before and after drug administration. The oxygen saturation was not significant in both groups before and after the procedure. SpO2 less than 92% was not observed in any of the groups. A decreased systolic blood pressure was seen in both groups after the treatment, however, it was higher in group D. An opposite trend was observed for diastolic blood pressure in both groups that the diastolic blood pressure increased slightly after the treatment. The start time of effect and the duration of drug effects were higher in group D than M.

Table 1. Parameters measured after consuming the drug Treatment

	D group = 23 people		M group = 25 people	
	mean	P-value	Mean	P-value
Heart rate before	110±7		114±10	
Heart rate after	104±9	0.001	110±12	0.003
Respiratory rate before	18±2		21±3	
Respiratory rate after	17±1	0.001	20±2	0.015
Oxygen saturation before	0.988±.006		0.985±0.009	
Oxygen saturation after	0.9885±0.0079	0.704	0.988±0.008	0.877
Systolic pressure before	98.26±5.9		93.40±9.76	
Systolic pressure after	94.57±4.98	0	90.48±9.75	0
Diastolic pressure before	59.78±4.64		55.8±5.71	
Diastolic pressure after	61.3±6.94	0.245	56.40±6.37	0.478

Table 2. The start of effect and the duration of treatments effects

	Group D	Group M	P-value
The start time of effect	32.39±8.92	23.60±17.84	0.000
The duration of treatments effects	40.87±9.1	25±19.09	0

No child required a special hospital care and CT scan was done and processed well

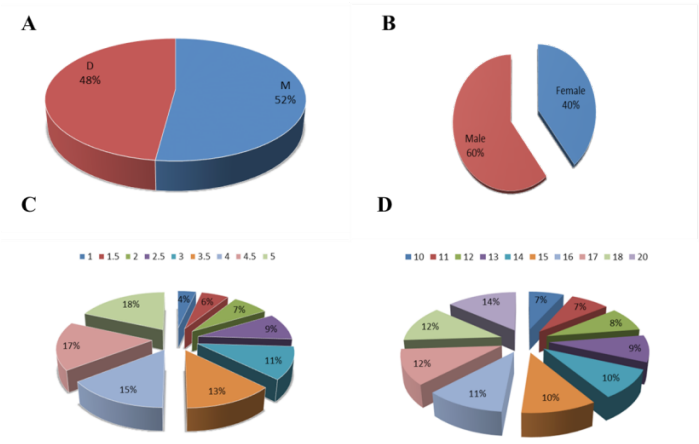

Fig. 1. Summary of the characteristics of studied children. A- The frequency percentage of patients in each group. B- The gender frequency percentage of patients. C- The age distribution of patients. D- The weight distribution of patients

DISCUSSION

Due to noise and closed unfamiliar environment in the CT scan, some children do not calm down successfully to conduct the process due to their low age, hyperactivity and mental retardation. These children are in need of general anesthesia or sedation. The anesthesia is more reliable than sedation but it needs equipments compatible with CT scan, pediatric anesthesiologists and recovery room staff. The main objective of the use of sedatives is to reduce restlessness and additional movements in children which can be obtained by rapid response sedatives. In the present study, we demonstrated that the combination of oral midazolam and diphenhydramine can successfully be used for children to perform CT scan.

Different forms of the administration of various sedative drugs including midazolam (oral- rectal- intravenous), chloral hydrate (oral-rectal), pentobarbital (intravenous- oral), thiopental (rectal), ketamine (rectal), propofol and etc have been used in radiological procedures (4 and 3). Midazolam is one of the most common drugs for sedation in children and adults during the procedures. The short-acting benzodiazepine can be used in different ways which causes a suitable sedation and amnesia and reduces anxiety and are preferred compared to long-acting benzodiazepines such as diazepam and lorazepam[3]. When an oral midazolam is used alone as a sedative drug, without any other drug, it *fails* significantly to provide the sedation[5]. In our study, 59% success was found at sedation with midazolam alone and 86% with the combination of midazolam and diphenhydramine. The sedative effect of this drug is probably due to its effect on CNS cortical areas. Diphenhydramine is used in the symptomatic treatment of allergic rhinitis, vasomotor rhinitis, urticaria, cough, nausea and vomiting caused by travel or move, as a mild hypnotic symptomatic, and the symptomatic treatment of Parkinson and extrapyramidal reactions. The anti-allergic effect of this drug is due to competition for binding to histamine receptors 1H. The anti-vomiting and anti-vertigo effects can be related to anti-muscarinic effect. The antitussive effect of diphenhydramine is due to a direct effect on the cough center in the medulla oblongata. The drug affects the brain 1H receptors and causes the hypnotic effects. The drug is also widely used as hypnotics. In this study, we successfully used diphenhydramine as a sedative along with midazolam as an auxiliary sedative. Children older than 7 years can usually operate in accordance with the instructions for being immobilized, so the age group of 1-7 years was selected for this study. No serious side effects were observed in any of the groups. Nausea was observed in only 2 patients in group C, which according to the anti-nausea properties of drug, the phenomena may be related to its bitter taste. This event was not observed in Group D. Since diphenhydramine was received

before midazolam in this group, the nausea is likely controlled due to the antihistamine properties of diphenhydramine. None of the patients who received the drug required resuscitation, artificial respiration or intubation. Continuous monitoring of oxygen saturation, heart rate, respiratory rate, blood pressure, is very important in the sedation process.

CONCLUSION

The study showed that the combination of oral diphenhydramine (1.25 mg/kg) and midazolam (0.5 mg/kg) leads to a safe and effective sedation in children undergoing CT. This combination is far more effective than the use of midazolam alone and leads to a lower failure in the sedation.

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