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RESEARCH ARTICLE

Comparison of the Effect of Intramuscular Promethazine and Ondansetron in the Treatment of Peripheral Vertigo in Patients Presenting to the Emergency Ward

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ABSTRACT

Background & Objectives: Vertigo is often recognized as a gruesome clinical symptom in the emergency ward. Physicians often encounter problems with this complication in both the diagnosis and treatment phase. Vertigo is one of the most common causes for patient attendance at the emergency ward. Drug therapy is the most appropriate treatment for acute peripheral vertigo. Promethazine is one of the medicines used to treat acute vertigo in the emergency ward. This study evaluated the effect and complications of muscular promethazine and ondansetron in the treatment of peripheral vertigo.

Materials & Methods: This study was performed as a double-blind randomized clinical trial in teaching hospitals of Yazd. In so doing, 160 patients observing inclusion criteria were selected for the study and randomly assigned into promethazine and ondansetron groups. Then, 25 mg of intramuscular promethazine was administered to the promethazine group and 4 mg of intramuscular ondansetron was administered to the ondansetron group. Next, the severity of complications and clinical symptoms and the severity of vertigo at the time before and after receiving the drug for up to 2 hours were assessed.

Results: The results of the present study showed that there was no significant difference between the two groups in terms of age, sex, underlying diseases, duration of vertigo and clinical symptoms of patients ($P<0.05$). Matching of the groups was carried out correctly. The mean severity of vertigo in the promethazine group was 6.9, 5.8, 4.1, 2.8 and 2.4, respectively at 0, 30, 60, 90 and 120 min after treatment, while in the ondansetron group, the severity of vertigo was 6.6, 5.5, 3.8, 2.5 and 1.8, respectively at these times. Although the severity of vertigo was lower in the ondansetron group than in the promethazine group, except for 120 min after treatment, there was no significant difference between the two groups. The result of Greenhouse-Geisser test also showed that there was totally no significant difference between the two groups over time ($P=0.39$). Besides, all side-effects were higher in the promethazine group.

Conclusion: The findings of the present study showed that due to the similar effect of ondansetron and promethazine and the numerous complications of promethazine, ondansetron can be used as an alternative to promethazine in the treatment of peripheral vertigo in the emergency ward.

KEYWORDS:
Acute peripheral vertigo, emergency, promethazine, ondansetron.

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INTRODUCTION

True vertigo is a feeling of imbalance as well as a feeling of movement and motion. Real vertigo is either objective (feeling the movement of the environment) or subjective (feeling the movement of the person himself/herself). True vertigo is divided into peripheral and central categories. Peripheral vertigo is sudden, severe, short-term, exacerbated by a change in head position in one direction, and has no neurological symptoms. There may be auditory symptoms such as tinnitus. Central vertigo is, nonetheless, gradual, mild, prolonged, does not change with head posture, has neurological symptoms, and there are no auditory symptoms (1, 2). Although vertigo is not considered a disease by itself, it is one of the most common complaints of emergency ward patients (2, 3). The prevalence of vertigo in the community is about 5% and the annual incidence is 1% (4). Peripheral vertigo occurs due to disturbances in balance/equilibrium organs such as the ear whereas central vertigo happens due to problems in the brainstem (3, 5). Treatment of peripheral vertigo is symptomatic and mainly includes inhibitors of the ear equilibrium and proprioception system and antiemetics. However, there is no fixed standard for choosing the type and length of treatment (5, 6). The ideal treatment is one that relieves the patient's symptoms, has few side-effects, and does not interfere with the central adaptation process of the ear's equilibrium system. Common medications in the treatment of vertigo include benzodiazepines, anticholinergics, and ondansetron (6, 7). Promethazine is one of the treatments that is mostly used intramuscularly. Its significant complications are drowsiness, excitement, restlessness, anger and reduction of consciousness. Ondansetron is a new medicant in the treatment of peripheral vertigo that is used both intramuscularly and intravenously and has none of the side-effects of promethazine. Significant complications include headache, feeling hot, and hot flashes. Due to the fact that no studies have been found on the effects of ondansetron on peripheral vertigo, this study aimed at investigating the effects and complications of promethazine and ondansetron in the treatment of peripheral vertigo.

METHODOLOGY

This study was a double-blind randomized clinical trial conducted in the emergency ward of teaching hospitals of Shahid Sadoughi University of Medical Sciences in Yazd. The statistical population consisted of patients referring to the emergency ward of the teaching hospitals affiliated to Shahid Sadoughi University of Medical Sciences of Yazd (Farrokhi Hospital and Shahid Sadoughi Hospital). They complained of vertigo and were diagnosed with acute peripheral vertigo. Patients aged 18 to 65 years with vertigo, and without contraindications to intramuscular administration of promethazine and intramuscular ondansetron were included in the study. Patients with a definitive diagnosis of vertigo with life-threatening CNS causes, pregnancy, a history of coagulatory disorder, a history of low platelet count, brain damage caused by trauma, simultaneous use of antihypertensives such as thiazides, taking antihistamines, cortone, and calcium channel antagonists, patients under treatment with benzodiazepines due to sleep disorders and anxiety, and all patients who had been taking anti-vertigo drugs for the past week were excluded from the study. Moreover, patients who were not willing to participate in the study were excluded from the study. After admission of patients in the emergency room, first a complete history was taken from each patient in terms of the pattern of vertigo, the length of time, the history of vertigo attacks and underlying diseases such as head trauma, brain tumor, cerebrovascular problems, history of taking anti-vertigo, anxiolytic, anti-allergy, and hypnotic medicines, and also a history of drug allergy. Subsequently, a complete neurological examination of the ear, throat and nose was performed and if necessary, paraclinical procedures were done for the patient including laboratory tests such as electrolyte, renal function test, and biochemistry test. Having obtained patient’s consent and informing them about the method of conducting the study and informing them about possible complications, patients were randomly assigned into two groups: Group A and Group B. In this study, Group A received intramuscular promethazine according to routine treatment and Group B, as the intervention group, received intramuscular ondansetron. For all patients, the demographic information questionnaire including name, age, gender, medical history, severity of vertigo upon arrival at the emergency ward, accompanying symptoms upon arrival, thorough examination of the patient, patient response to treatment based on alleviation of symptoms, treatment complications, and treatment periods was completed. According to the principle of randomization for conducting a clinical trial of the drugs manufactured by the same factory and tested in this study, the drug was first prepared in separate syringes in equal volumes (1 mL) in counted packs and labeled by the study coordinator randomly. The surface of the syringes was then completely covered with a label so that its color could not be determined. The drugs were given to the nurse in charge of the emergency shift in numbered packages and then these packages were randomly injected by the nurse in charge of the emergency shift to the eligible patients. In this study, the patient, the person injecting the drug and the assessor were blind to the type of drug injected until the end of the study. It should be noted that 25 mg of promethazine is equivalent to 1 cc and 4 mg of ondansetron is equivalent to 1 cc, which were used in this study. In group A, 25 mg of intramuscular promethazine was injected whereas in group B, 4 mg of intramuscular ondansetron was administered. Symptoms and severity of vertigo were assessed by the VAS scale for one hour before and after receiving the drug. On this scale, scoring ranged from 1 to 10, with 1 indicating the lowest intensity of vertigo and 10 indicating the highest intensity of vertigo. Patients were examined 30 min and 1 hour later, and finally, after 1 hour of response to treatment, patients were divided into 4 groups: 1. Poor, 2. Moderate, 3. Good, and 4. Very good. During the course of treatment, if the patient did not respond to one of

the drugs, another drug was used to control vertigo. Patient information and signs and symptoms were collected and recorded in special forms at the time of admission to the emergency ward and then in subsequent evaluations. Then, the collected data were compared in both groups of patients. The collected data were analyzed with SPSS22 using descriptive statistics for quantitative variables such as age and VAS scores, i.e., a tool for determining the severity of vertigo, (Mean±SD). For qualitative variables such as gender, tables of frequency and percentage were used. To analyze the data and compare the two groups under study, the two-sample t-test was used. Repeated measures ANOVA was used to evaluate the effect of treatment methods on the VAS score. The Greenhouse and Mauchly test was applied to evaluate the sphericity of variance. Finally, chi-square test and Fisher's exact test were used to compare the ratio of gender in both groups. Benferroni post hoc tests were used for pair-wise comparison of times in each of the two groups.

RESULTS

In this study, 120 patients were randomly assigned into two groups. Patients in the promethazine group (Group A) received 25 mg of intramuscular promethazine. The ondansetron group (Group B) received 4 mg of intramuscular ondansetron. The symptoms and severity of vertigo were assessed at different times based on the VAS scale. The results of the present study revealed that the mean age of patients was 52.5±14.4 years in the promethazine group and 49.1±18.8 years in the ondansetron group. Besides, in promethazine group, 39 (65%) patients were female and 21(35%) male. In ondansetron group, 35 (58.3%) patients were female and 25 (41.7%) were male. There was no significant difference between the two groups in terms of age and gender of patients (P<0.05) so that the two groups were the same in terms of age and gender. Among the patients in the ondansetron and promethazine groups, 15 and 12 patients had a history of taking anxiolytic and sedative/hypnotic drugs, respectively (P=0.51). Moreover, 34 (59.6%) patients in the ondansetron group, and 33 (57.9%) patients in the promethazine group had horizontal nystagmus (P=0.85). The severity of vertigo was 6.6±1.3 in the ondansetron group and 6.9±1.3 in the promethazine group (P=0.17) according to the VAS scale at the time of admission and initial evaluation of patients. All patients in the promethazine group developed complications, while in the ondansetron group, only 17 (28.3%) patients developed complications (P=0.001). In studying hemodynamic variables, the results of the study for the two groups showed that systolic blood pressure and respiratory rate were not significantly different between the two groups. However, diastolic pressure and heart rate were slightly lower in the ondansetron group than in the control group. Additionally, the mean intensity of vertigo in the promethazine group was 6.9, 5.8, 4.1, 2.8 and 2.4, respectively at 0, 30, 60, 90 and 120 min after treatment, while in the ondansetron group the intensity of vertigo was 6.6, 5.5, 3.8, 2.5 and 1.8, respectively at these times. Even though the severity of vertigo in the ondansetron group was lower than the promethazine group, there was no significant difference between the two groups according to the T-test at different times except for 120 min after treatment. The result of Greenhouse-Geisser test also suggested that there was totally no significant difference between the two groups over time (P=0.39).

Table 1: Determining and comparing the average severity of vertigo at different times in the two groups

Time / Group	0 min	30 min	60 min	90 min	120 min	P-value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Promethazine	6.9±1.3	5.8±1.3	4.1±1.2	2.8±1.1	2.4±1.3	0.39
Ondansetron	6.6±1.3	5.5±1.5	3.8±1.3	2.5±0.90	1.8±1.1	
T-test	0.17	0.34	0.24	0.26	0.005	

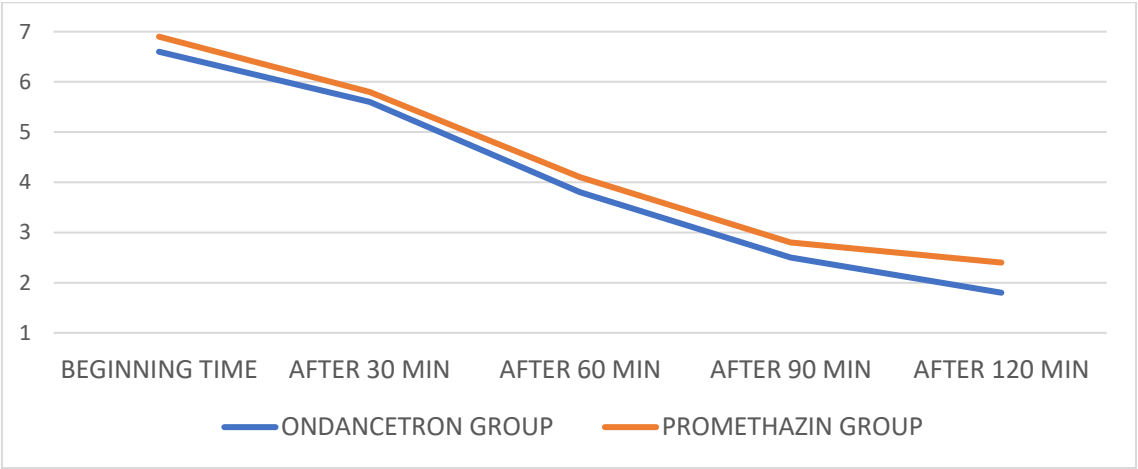

Fig.1: Determining and comparing the average severity of vertigo at different times in the two groups

Table 2: Determining and comparing the frequency distribution of complications in the two groups

Complications	Group	Yes	No	Total	P-value
Drowsiness	Ondansetron	0(%0)	60(%100)	60(%100)	0.001
	Promethazine	59(%98.3)	1(%1.7)	60(%100)	
Restlessness	Ondansetron	1(%1.7)	59(%98.3)	60(%100)	0.001
	Promethazine	16(%26.7)	44(%73.3)	60(%100)	
Headaches	Ondansetron	8(%13.3)	52(%86.7)	60(%100)	0.11
	Promethazine	3(%5)	57(%95)	60(%100)	
Hot flashes	Ondansetron	4(%6.7)	56(%93.3)	60(%100)	0.001
	Promethazine	28(%46.7)	32(%53.3)	60(%100)	
Hypotension	Ondansetron	4(%6.7)	56(%93.3)	60(%100)	0.001
	Promethazine	18(%30)	42(%70)	60(%100)	
Hypertension	Ondansetron	0(%0)	60(%60)	60(%100)	---
	Promethazine	0(%0)	60(%60)	60(%100)	

DISCUSSION

In many cases, the etiology and pathology of vertigo are unknown. The main goal of treatment is to alleviate the symptoms of the disease without changing the physiological mechanisms. A routine history is the first step in diagnosis, followed by various tests (8). Different methods are used to alleviate the symptoms of the disease, including therapeutic methods, drug therapy with a variety of medications including anticholinergics, antihistamines, benzodiazepines, calcium channel blockers, dopamine receptor antagonists and ondansetron (9, 10). Along with drug therapies, repositioning maneuvers are also used to treat vertigo; in some studies, the effect of drug therapy and physical maneuvers have been the same (11). Nevertheless, the most appropriate treatment for acute peripheral vertigo is drug therapy (1, 12). Promethazine is one of the drugs used in the treatment of acute attack of vertigo in the emergency room (13). Vertigo is often recognized as a gruesome clinical symptom in the emergency room. Physicians often encounter problems with this complication in both diagnosis and treatment phase. By far, vertigo is one of the most common causes for patient attendance at the emergency room (14, 15). For the past several decades, the treatment of vertigo has been considered as a challenge for researchers and physicians, and a variety of treatments have been proposed. In all these cases, the purpose of treatment is to diminish the symptoms of the disease or to affect the process of vertigo. However, since in many cases the etiology and pathology of vertigo are undetectable, so the main goal of treatment is to alleviate the symptoms of the disease (16, 17). Yet, no single treatment protocol is mentioned in any of the sources. Promethazine is a first-generation antihistamine of phenothiazine group whose anti-vertigo effects are exerted through a central anti-muscarinic effect (18). Given the noticeable common complications of promethazine such as drowsiness, excitement, restlessness, anger and reduced consciousness, this study was performed to evaluate the effects and complications of promethazine and ondansetron intramuscularly as a double-blind clinical trial in the treatment of peripheral vertigo. The results of the present study demonstrated that there was no significant difference between the two groups in terms of age, gender, history of previous diseases, hemodynamic symptoms, and duration of vertigo ($P<0.05$). Matching of the groups was done correctly. The mean severity of vertigo based on the VAS scale was 6.9, 5.8, 4.1, 2.8 and 2.4, respectively, in the promethazine group at 0, 30, 60, 90 and 120 min after treatment, while in the ondansetron group the severity of vertigo at these times was 6.6, 5.5, 3.8, 2.5 and 1.8, respectively. Although the severity of vertigo was lower in the ondansetron group than in the promethazine group, there was no significant difference between the two groups at different times except for 120 min after treatment. The result of Greenhouse-Geisser test also revealed that there was totally no significant difference between the two groups over time and in the number of times measured. The present study suggested that all the complications of treatment including drowsiness, restlessness, headache, hot flashes and hypotension were higher in the promethazine group than in the ondansetron group, indicating the untoward sequelae of promethazine. The findings of the present study on the severity of vertigo indicated that ondansetron had the same effect as promethazine and was effective in reducing the severity of vertigo in patients. Amini et al.'s study showed that 25 mg intravenous promethazine is more effective than intravenous lorazepam in improving vertigo and reducing associated symptoms. Their results revealed that promethazine is more effective than benzodiazepines in treating acute peripheral vertigo (19). Golikhatir's study also showed that 25 mg intravenous promethazine was more effective than diazepam in reducing the severity of vertigo in patients based on the VAS scale (20). In their study, the mean VAS scores in the promethazine group were 9.56, 5.63, 3.51 and 1.07, respectively, before intervention, 30 min, 2 h and 4 h after treatment. In the present study, while the mean intensity of vertigo in the promethazine group was 6.9, 5.8, 4.1, 2.8 and 2.4, respectively at 0, 30, 60, 90 and 120 min after treatment, in the ondansetron group, the intensity of vertigo at these times was 6.6, 5.5, 3.8, 2.5 and 1.8 respectively. Ondansetron was even slightly better than promethazine. In another study by Barzegari et al., 113 patients with peripheral vertigo were evaluated. One group was given intravenous diazepam and another group received intravenous methylprednisolone. The mean intensity of vertigo was not significant between the two groups at different times and it was higher than the mean intensity estimated in the present study. Hence, it appears that ondansetron is more effective than other medicants such as benzodiazepines and corticosteroids (21). Another study by

Marill et al. reported that patients who received dimenhydrinate had a greater reduction in the severity of vertigo compared to patients treated with intravenous lorazepam. In their study, the mean intensity of vertigo was higher in the ondansetron group compared to the present study. Besides, the decrease in the intensity of vertigo in the ondansetron group was greater in the present study, indicating the effect of ondansetron. Dimenhydrinate, like promethazine, is part of the H1 blocker antihistamine group and is probably as effective as promethazine (18). Findings of Saberi et al.'s study on evaluating the effect of ondansetron and promethazine in the treatment of peripheral vertigo showed that intravenous ondansetron administration can be effective in reducing the severity of vertigo in patients; Nonetheless, unlike the present study, the difference between promethazine and ondansetron was significant. The severity of vertigo was lower in the promethazine group, while in the present study, no significant difference was observed between the two groups. This demonstrates the similar effect of ondansetron and promethazine. Yet, this difference is probably related to the type of medication prescribed and the patients' expression of pain intensity, which is not very accurate. In general, in their study, the mean intensity of vertigo based on the VAS scale was higher than the present study. The results of Saberi et al.'s study showed that the severity of nausea and vomiting in the ondansetron group was significantly lower than the promethazine group; this was consistent with the present study. Also, similar to the present study, hemodynamic variables did not differ between the two groups except for a slightly lower heart rate. In the study by Saberi et al., the time of patients' getting asymptomatic was similar in the two groups of promethazine and ondansetron, indicating the positive effect of ondansetron (22). Due to the fact that ondansetron is a very appropriate medicine in controlling nausea and vomiting and this finding has been proven in various studies, so because in the ondansetron treatment group, the rate of vomiting, nausea, and patients' symptoms improves to a greater degree and given that the most important distressing symptoms in vertigo are nausea and vomiting, thus, patients are more satisfied with ondansetron treatment due to better recovery and report a greater reduction in the severity of their vertigo. In another study by Braude et al., the results showed that administration of 4 mg of ondansetron compared to 25 mg of promethazine had similar effects on nausea and vomiting for unknown reasons in the emergency room; yet. promethazine was associated with more side-effects and more sedation (23). Similar to the present study, the findings by Saberi et al. suggested that the complications of promethazine were significantly higher than ondansetron. The most common side-effect of promethazine was drowsiness. Other complications such as hallucinations, apnea, and blurred vision are rare (22). Finally, due to the fact that studies on ondansetron are very limited and due to the similar and even better effect of this medication in reducing the severity of vertigo compared to promethazine and also the limited complications of ondansetron compared to promethazine, it can be used in treating patients in hospital emergencies instead of promethazine. However, confirmation of the findings of this study requires more extensive studies.

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