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Original Article

Comparison of diazepam and promethazine effects in relieving ataxia in patients with Benign Paroxysmal Positional Vertigo

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ABSTRACT

Introduction: Vertigo is one of the most common reasons for referring to emergency departments and benign positional vertigo is the most common cause of peripheral vertigo. Unlike reposition-ing manoeuvres in this Vertigo, evidences regarding drug therapy in this vertigo is little. The aim of this study was to investigate a comparison of diazepam and promethazine effects in relieving ataxia in patients with Benign Paroxysmal Positional Vertigoin Arak emergency department of Valiasr hospital. Materials and Methods: This study was a double-blind clinical trial on patients with BPPV and ataxia admitted to Valiasr Hospital of Arak, Iran. Patients were divided randomly into two eqaul groups (35 persons) on the basis of the inclusion and exclusion criteria for the study. One group was treated with a dose of 12.5 mg of intramuscle promethazine and the other was placed under the administration of 5 mg of intravenous diazepam. The walking ability of patients and patients' vital signs, at the moment 0, 60 and 120 minutes after injection were examined. Data were analyzed by SPSS 18 software. Results: The mean age of patients (p=0.272) and sex distribusion (p=0.05) in the two groups were matched. 60 min after injection, the gait of the all patients were ataxic in both groups. In 120 minute, the results showed that in the diazepam group, 30 (85.7%) patients and in the promethazine group, 31 (88.5%) of the patients had no ataxia. Therefore, no significant differences were observed between the two groups (p>0.05). Conclusion: Our results showed that, promethazine and diazepam are equally effective in improving ataxia caused by benign positional vertigo. However, due to lack of evidence, further studies in the future is recommended.

Keywords: Benign Paroxysmal positional vertigo, Diazepam, Promethazine.

Introduction

Vertigo is one of common complaints in the emergency department(ED) [1], and it is responsible for 5 % of all ED visits [2]. Due to the peripheral or central causes of vertigo, the patients have symptoms such as nystagmus, nausea and vomiting, dysarthria, hearing loss and tinnitus, symptoms of cerebellar and brainstem and ataxia [3, 4]. Relieving of ataxia is important factor in the disposition of patients with vertigo so that a prestigious Setting of admission and discharge of patients with dizziness in the emergency department is considering the patient's ataxia. According to these guidelines, patients who can walk will be discharged after the initial check [5, 6].

Antihistamines (e.g. meclizine, promethazine), benzodiazepines (diazepam), anticholinergic (e.g. scopolamine), and corticosteroids, diuretics and sympathetic mimics are used to treat of vertigo, [6] However, if patients don't responsible, another drug should be used. Parenteral medication is choice to improve vertigo symptoms in patients admitted to the emergency department [7]. However, the first medication choice in the treatment of patients with vertigo has not been introduced so far, and only a few clinical studies are conducted on the treatment of the above as a first-line treatment. Due to the low clinical studies comparing the drugs used for vertigo in emergency, and since the relieving of ataxia in vertigo can be a criterion for improve vertigo and disposition of patients in the emergency department, the purpose of this study is to compare the effects of diazepam and promethazine in reliving ataxia disorders in patients with true vertigo admitted to the emergency unit of Valiasr hospital in Arak.

Material and Method:

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In a randomized, single-blind, clinical trial study, 70 patients of 18 to 60 years' old who admitted to emergency department with benign positional vertigo and ataxia were selected based on inclusion and exclusion criteria. The patients were in accordance with Class 1 or 2 of ASA (American Society of Anesthesiologists). Benign positional vertigo was diagnosed based on clinical history and Hall, Pike maneuver and its diagnostic criteria [8].

The sample size was selected based on the 0.05 = α, the prevalence in the general population of 0.016 and 20% sample size lost including 35 persons in each group.

Patients were entered the study and they randomly divided in two group, group 1 (35 patients received 5 mg of intravenous diazepam) and group 2 (35 patients, received 12.5 mg of intramuscular promethazine).

It has been explained adequately orally and in written to the patients, about the injection dosage and to inform them in about possible side-effects of drugs.

Then patients were examined 60 and 120 min after receiving the drug in about their ataxia, vital signs (systolic and diastolic blood pressure, and heart rate), and also side effects including drowsiness, lethargy, mental confusion, disartria (if patients not have these symptoms when referring to the emergency unit), tremor, muscle cramps, skin rash or hives, diplopia, blurred vision, nausea and vomiting (if patients not have these symptoms when referring to the emergency unit), extrapyramidal symptoms, hypothyroidism and hypertension, dry mouth, metallic taste in the mouth of the patients. The ataxia was examined using two Romberg tests (positive or negative) and Tandemgait (positive or negative).

Exclusion criteria for selection patients with vertigo

1) Loss of consciousness (GCS less than 14) and neurological deficit (FND)
2) Respiratory depression and alcohol poisoning
3) Hypotension (systolic blood pressure <90) and generally patients with unstable hemodynamic
4) Multiple trauma (injury to the internal abdominal organs, significant bleeding, head trauma)
5) Drug addiction
6) History of uncontrolled systemic underlying disease (asthma, COPD, heart disease, kidney disease, hepatic, pulmonary, metabolic, diabetes, CVA and other neurological and neuromuscular diseases, etc.)
7) Pregnancy and lactation
8) History of seizures
9) History of using antihistamines and other sedatives and hypnotics before referral
10) Allergy to diazepam and promethazine and other antihistamines in the past
11) Patients with fever (T> 38)
12) Occurrence of life-threatening medical complications during the study
13) History of closed and open-angle glaucoma, psychosis, myasthenia gravis, Parkinson's blockage disease, kidney disorders, liver, bone marrow disorders, peptic ulcer, Pyloroduodenal, BPH, bladder neck stenosis, hypertension, sleep apnea,
14) The concomitant use of depressant drugs, CNS, cimetidine, levodopa, rifampin, barbiturates and acid valproic.

During the study patients with lack of consent to participate in the study or deterioration of general condition were excluded and replaced with similar cases based on inclusion and exclusion criteria in random.

A physician (not blind to treatment) was responsible for task initial evaluation of patients for inclusion in the study and prescribing medication. Another physician (was blind to the patient's medical condition) was responsible to fill the checklist on demographic and clinical data of patients during the study.

Patients' names remained confidential and no additional cost was imposed to the participants. The Research Project has been approved under No. 747 and the code of ethics14-157-92 in the ethics committee of the Arak University of Medical Sciences.

Data analysis was performed by SPSS 18 software, and the mean, standard deviation, standard error, and frequency used for descriptive analysis and t-test, Chi-square, Mann-Whitney and Friedman tests were used for analytic analysis.

Results:

70 patients with mean age of 56.56 ±14. 38 years old and consisting 46 female (%65.71) and 24 male (%34.28) were studied. There was no significant different between two groups regarding age (p=0.5) and sex (p=0.272). Table 1

Mean systolic blood pressure at T_0, T60 andT_{120} were respectively, 142.8±24.5, 131±21.4 and 124.5±16.1 mm Hg. Diastolic blood pressure at the same time was respectively, 86±14.5 80.9±14.9 and 80.5± 10.6 mm Hg. there was no significant difference between the two groups. And the heartbeat was respectively, 85.1± 12.6, 84.5 ± 6.8 and 85.5 ± 9.05 beats per minute. The heartbeat rate, 60 min after treatment in diazepam group (81.6± 7.23) was significantly less than Promethazine group (86.6± 9.06 beats per minute) (p =0.011/). Table 2

According to Friedman's analysis about checking each hemodynamic factors of patients within each group showed that systolic blood pressure in the diazepam group (p =0. 0001) and promethazine (p =0. 0001), and diastolic blood pressure in the diazepam group (p =0. 001) and promethazine (p =0. 001) was significantly reduced over 120 minutes. The analysis also showed that in Promethazine group heart rate was significantly increased in 60 minutes (p =0. 07) In the next 60 minutes significantly decreased (p=0.02). However, the results showed that heart rate in the group treated with diazepam had no significant change over 120 minutes of the study, (p>0.05). fig (1-6)

Gait of all patients, 60 min after injection in both groups was ataxic and 120 min after the start of treatment, 51 (85%) patients had normal walking and 9 (15%) patients had ataxia.

In 120 min examination, the results showed that 30 (85.7%) of patients in group treated with diazepam and 31 (88.5%) of patients in the group treated with promethazine, were without ataxia and walked normally, that showed no significant difference between the two groups (p>0.05).

The results showed that, during the study, no medical complications occurred in both groups treated with diazepam and promethazine.

Table 1. Data on age, sex, and way of walking in two groups under study

variables	Promethazine group (no: 35)	Diazepam group (no: 35)	p-value
Age (mean ± SD)	56.2±13.15	56/15±82/38	5/0
Sex (female/male)	15(42.8)/20(57.1)	(25/7)9/(74/2)26	272/0
Normal walking in 120 min	31(88.5)	30(88.5)	05/0<

Table 2. Data on hemodynamic variables of patients in two groups during study

Hemodynamic variables	Promethazine group (no: 35)	Diazepam group (no: 35)	p-value
SBP0 (mean±SD)	30±142/6	12±144/24	97/0
SBP1 (mean±SD)	23±131/6	18±130/25	673/0
SBP2 (mean±SD)	123/17±4/7	13±126/84	359/0
DBP0 (mean±SD)	17±86/85	8±86/16	84/0
DBP1 (mean±SD)	79/18±4/1	8±83/89	135/0
DBP2 (mean±SD)	80/12±2/24	8±81/16	595/0
PR0 (mean±SD)	85/8±9/7	16±84/8	537/0
PR1 (mean±SD)	86/9±6/06	81/7±6/23	011/0
PR2 (mean±SD)	83/8±7/4	9±88/4	99/0

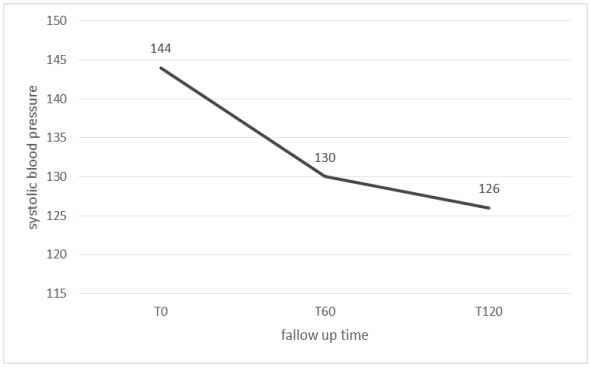

Figure 1: systolic blood pressure change fallowing diazepam administration during 120 minutes

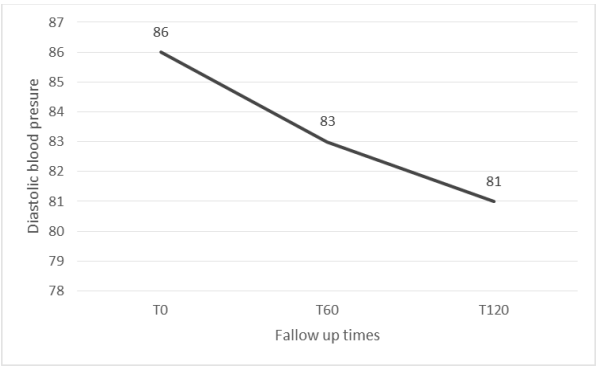

Figure 2: diastolic blood pressure change fallowing diazepam administration during 120 minutes

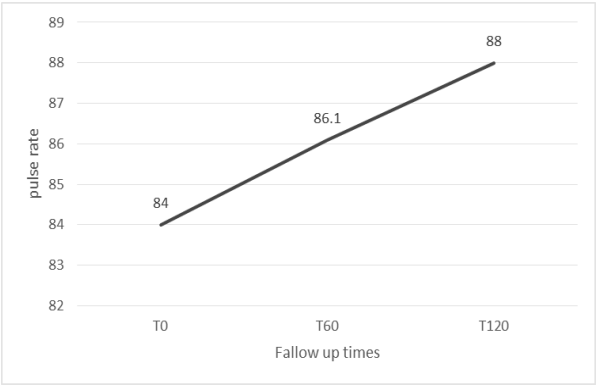

Figure 3: heart RATE change fallowing diazepam administration during 120 minutes

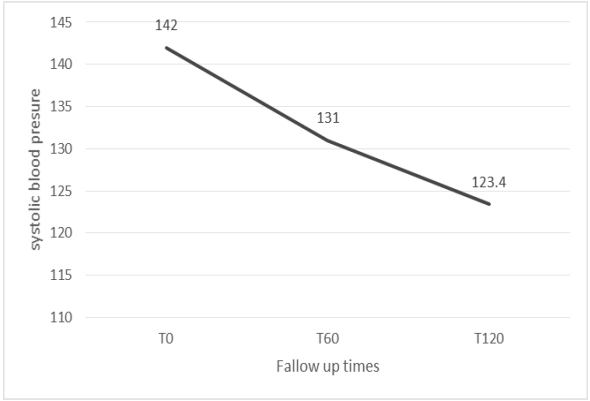

Figure 4: systolic blood pressure change fallowing promethazine administration during 120 minutes

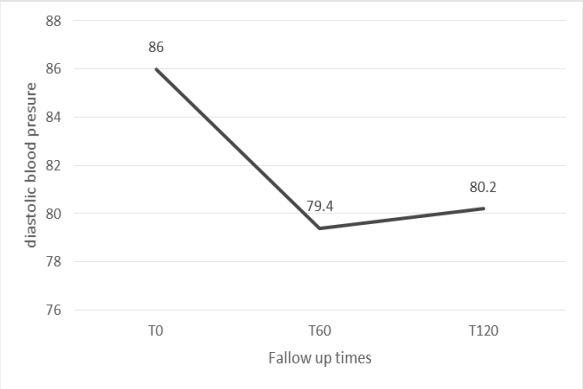

Figure 5: diastolic blood pressure change fallowing promethazine administration during 120 minutes

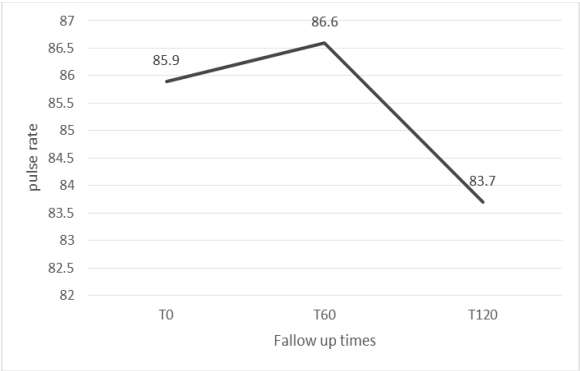

Figure 6: Heart Rate change fallowing promethazine administration during 120 minutes

Discussion:

Based on our results, both diazepam and promethazine improve ataxia in patients with BPPV are equally. Also, based on our results, it was found that systolic and diastolic blood pressure in both groups had a similar decline throughout the study; however, this reduction did not result in hemodynamic instability in patients. In addition, heart rate had no significant change in diazepam group but had significantly changed with no worthwhile clinical significance in promethazine group, since use of these drugs did not cause bradycardia or tachycardia in both groups.

In benign positional vertigo, the most common cause is peripheral vertigo. The cause of this vertigo is separating autolites of the semicircular duct in endolymph (canalolithiasis), their movement in this space gives vertigo. [8] The most common cause of BPPV is idiopathic; however, the most common identifiable cause of vertigo is head trauma. Based on the evidence, the basis for treatment of this disorder is the repositioning maneuver (Epley maneuver), which aims to transfer floating particles in the semicircular duct to their original location. Many references [2, 9, 10] have recommended use of drugs for the treatment of vertigo; however, some studies have reported no effect of the drug in the treatment of BPPV [11-13].

However, in some cases, such as the lack of response to treatment with therapeutic maneuvers in BPPV, medical treatment is used. Drug groups used in the treatment of this disorder include benzodiazepines such as diazepam and antihistamines such as dimenhydrinate and meclizine. Although, based on the evidence, the maneuver treatment is more effective in reliving BPPV than medical treatment [14-18], due to issues such as lack of response to treatment with therapeutic maneuvers, improved conditions and symptoms of BPPV patients admitted to emergency unit, and finding a treatment for symptoms of the disorder, such as ataxia seems reasonable for early improvement of the clinical status of the patient and improving the quality of diagnosis and treatment for patients, especially in emergency situations [14, 15].

According to studies by Ebadi H [12], Richard W [16], Mompo Romero L [17], Soto Varela A. [18], treatment with Epley maneuver is more effective to improve medical treatment in patients with BPPV. However, as mentioned above, examining the effect of drug treatment more accurately is reasonable.

Based on the evidence, benzodiazepines, such as diazepam with GABA-mediation and suppressive effects on the vestibular system (although the exact mechanism is not completely understood [2]), is used as a treatment for patients admitted to the emergency with vertigo, BPPV [14, 15]. However, the side effects of these drugs, such as the development of habit, memory disorders and seizures are illustrated for this class of drugs [15]. Antihistamines also have shown a positive impact on the improvement of patients with vertigo. The purpose of this study was to investigate the first choice in the treatment of ataxia in BPPV (as one of the most common symptoms of this disorder) using diazepam and promethazine which are both the most common drug used in the emergency room for improvement vertigo. However, there are few studies of the effects of promethazine as an antihistaminic and comparing effect of benzodiazepines with antihistamines, especially promethazine (which was used in the present study).

Marill KA, et al. [1] in 2000 conducted a study to evaluate the effects of lorazepam and dimenhydrinate in patients with vertigo referred to the emergency. In this clinical trial, 74 patients in two groups were treated with 2 mg of lorazepam and 50 mg of dimenhydrinate and were compared 1 and 2 hours after injection in terms of clinical response and recovery of vertigo.

The results showed that dimenhydrinate was significantly more effective than lorazepam in the treatment of emergency patients with vertigo. According to the study by McClure JA [19], after 4 weeks of using lorazepam and diazepam for benign paroxysmal positional vertigo, no appropriate response was observed compared to the control group. Izadi P et al. [15] conducted a study to evaluate the treatment response of BPPV patients with therapeutic maneuver alone, or therapeutic maneuver associated with dimenhydrinate therapy. In this randomized clinical trial study, 75 patients were treated with dimenhydrinate and 73 patients were exposed to therapeutic maneuver with placebo. The results showed that therapeutic maneuver is very effective in BPPV, and associating that with treatment with medication (dimenhydrinate) increases the therapeutic effect. In the present study, the condition of ataxia

in BPPV was considered as a therapeutic target, and only patients who had both BPPV and ataxia were included in this study. Due to quick and accurate assessment ability of clinical symptoms, especially in emergency situations, and appropriate relationship of improved ataxia and with improved patient's condition, we used this clinical symptom in patients with BPPV. However, from the point of view, our study was somehow differences from similar studies [8].

Finally, given the high prevalence of patients admitted to the emergency department with complaints of vertigo as well as the following reasons, further studies in the future, in other medical centers and larger sample size is recommended.

1) Rapid treatment of BPPV, as one of the most common causes of true vertigo of patients referring to the Emergency, is very important due to the role of treatment in enhancing compliance of patients to continue the diagnosis and treatment.
2) Although in clinical situations and emergencies, benzodiazepines such as diazepam and antihistamines such as promethazine are used in the treatment of patients with true vertigo and BPPV, the reliable evidence, especially in the case of some antihistamines such as promethazine, is very small. In addition, the best choice as the first step drug in vertigo with appropriate side effects and response is important.

Conclusion:

Our results showed that promethazine and diazepam are equally effective in reliving ataxia caused by benign positional vertigo. However, due to lack of evidence, further research in this area is recommended.

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Authors' contributions

All authors wrote the manuscript equally.

Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

Conflict of interests

The authors declared no competing interests.

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