

Hyoscine versus diazepam for the management of true vertigo in the emergency department

Hamid Kariman¹, Firoozeh Vajihi¹, Afshin Amini¹, Ali Shahrami¹, Ali Arhami-Dolatabadi¹, Majid Shojaee¹ and Alireza Baratloo²

¹Department of Emergency Medicine, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran; ²Department of Emergency Medicine, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.

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Abstract

The present study was a double-blind clinical trial to compare the efficiency of hyoscine and diazepam in vertigo treatment. Eligible patients (n=69) were randomly divided into 2 groups of 5 mg hyoscine and 10 mg diazepam. Severity of vertigo was measured in supine and sitting position, and while turning the head. Vertigo severity was assessed before, and 1 and 2 hours after administration of the drug. Treatment success rate of diazepam in relieving vertigo in different positions varied between 88.9 and 100%, while this rate was 31.2–73.5% in hyoscine treatment group (p<0.01). Prescription of diazepam led to complete relief of vertigo in 40–63% of the patients, while this rate was only 2.6–12.5% in hyoscine treatment group (p<0.001). It is likely that diazepam is a better option than hyoscine for management of true vertigo in patients presenting to the emergency department.

Introduction

True vertigo is a type of vertigo identified by failing to sense gravity and spinning feeling. The patient might have hallucinations of self or surroundings' motion (Marple and Meyerhoff, 1998). Currently, there are various methods for treating patients with vertigo such as drug, surgery, and vestibular rehabilitation (Ganancia et al., 2002; Girardi and Konrad, 2005). Treatments in the emergency department are symptomatic and aim to eliminate vertigo and other accompanying symptoms (Kerber, 2009).

Diazepam as a benzodiazepine compound plays a major role in treatment of disorders with central origin. It has also been effective in vertigo treatment as shown in various studies. This drug, as a gamma-aminobutyric acid (GABA) receptor regulator, centrally leads to inhibition of vestibular response. In low doses, this drug is very effective and beneficial. However, its addictiveness, bringing about memory problems, and increasing the chance of falling for the patient are

among the limitations of its consumption. These might be the reasons that researchers are looking for replacement methods and treatments (Tan et al., 2014). Antihistamine, anticholinergic, and anti-nausea drugs have been suggested for this purpose (Hain and Uddin, 2003; Hain and Yacovino, 2005).

On the other hand, hyoscine is one of the oldest medicines. This drug is extracted from a plant called henbane from the family of Solanaceae. Hyoscine is an anticholinergic, antispasmodic, analgesic and sedative drug that exerts its relaxing effect directly on smooth muscles. In addition to its peripheral anticholinergic activities, this drug also affects the central nervous system and has a slow but long sedative effect on the brain (King et al., 2014; Renner et al., 2005). Hyoscine is one of the most commonly used drugs for motion sickness and it has been suggested that it might also be effective in treating or decreasing vertigo symptoms. A systematic review showed that very few studies have been carried out to assess the role of hyoscine in treatment of balance disorders and the existing



evidence and conclusions regarding effectiveness of this drug in reducing vertigo symptoms and motion sickness are mostly based on animal studies and second or third class evidence. As a result, they had suggested carrying out more studies in this field (Spinks et al., 2011). Therefore, the present clinical trial was designed aiming to evaluate the effectiveness of hyoscine compared to diazepam in management of true vertigo in patients presenting to the emergency department.

Materials and Methods

Study design and setting

The present study is a double-blind clinical trial performed during 6 months, from March 2015 to September 2015, in Imam Hossein Hospital, Tehran, Iran. The main goal of the study was comparing the effectiveness of hyoscine with 5 mg dose and 10 mg diazepam in managing and relieving vertigo.

Participants

All patients over 18 years old with complaint of vertigo, who were categorized as true vertigo cases based on clinical definition were included in the study. Receiving prophylaxis treatment with vertigo reducing drugs, allergy to hyoscine or diazepam, pregnancy, lactating, renal failure, and recent visit to the hospital were considered as exclusion criteria.

Sample size

To determine sample size the formula for comparing means in analysis of repeated measures was used. Considering the results of previous studies, sample size for finding significant difference in mean response of the 2 groups after drug treatment with a test power of 90% ($\beta=0.9$), type 1 error of 5% ($\alpha=0.05$), combined standard deviation of 18, individual observation correlation of 0.8 ($\rho=0.8$) and correlation structure of 1 for individual observation was estimated to be 21 patients in each group using the formula. This number was multiplied by 20% probability of loss to reach the final sample size of 26 patients in each group.

Randomization and blinding

Solutions were prepared by an emergency medicine specialist that did not participate in the process of evaluation and prescription of drugs. They were placed in similar packs covered by aluminum foil. The solutions were anonymous and both were diluted in 10 mL distilled water. The solution containing hyoscine was named pack A, and the one containing diazepam was named pack B. It should be noted that the composition of packs was confidential until the end of the study. To ensure double blinding of the study, preparing solutions and drug injection and recording the results were done by 2 separate physicians. Information

regarding the administered drug was only revealed when adverse side effects or other clinical changes were seen in a patient that needed knowledge of the administered drug.

In the present study, randomization was done using random numbers table. For this purpose, each patient was given a number; if the number was odd, pack A was administered and if it was even, pack B was used.

Intervention

Initially, demographic data and baseline characteristics including age, sex, history of using drugs, duration of vertigo and history of vertigo were recorded. Patients were also questioned about accompanying symptoms including nausea, vomiting, hearing loss, tinnitus, ear fullness, double vision, blurred vision, dysarthria, dysphagia, hypoesthesia, paresthesia, and weakness of one side of the face and extremities. There were also questions regarding the characteristics of vertigo including it being spinning or not, its central or peripheral origin and estimated duration of vertigo. Presence and direction of nystagmus were other studied factors. This category was defined in 5 levels of nystagmus free, horizontal, vertical, and rotary nystagmus, and other. In addition, before prescription of drug, the patients' feeling of vertigo was evaluated in supine position, while sitting and while turning their head to one side. After gathering baseline characteristics and demographic data, patients were divided into 2 groups of 5 mg hyoscine and 10 mg diazepam using a random numbers table. After administration of drug, 500 mL normal saline was prescribed for the patients.

Outcome

Severity of vertigo was classified as no vertigo, mild, moderate, and severe vertigo. In the present study, at least 1 level improvement or relief of vertigo was defined as successful treatment. The patients' vertigo sensation was re-evaluated in supine and sitting positions and while turning their head to one side in the first and second hour of drug administration. Probable side effects of the drugs were monitored since injection until 2 hours after administration. They were recorded based on patient's report and clinical appearance. After 2 hours of follow-up, if vertigo was relieved, the patient was discharged with approval of the in-charge physician. In case of unsuccessful treatment, rescue medication was prescribed by the in-charge physician.

Statistical analysis

Data were entered to SPSS 21 and were analyzed using STATA 11.0 software. Severity of vertigo and accompanying symptoms of the patient on admission, and 1 and 2 hours after treatment initiation were reported as frequency and percentage. To evaluate the age difference between the 2 groups, t-test was applied. Duration

of vertigo was compared using Mann-Whitney test. To compare other baseline characteristics and demographic data of the patients between the groups on admission, Chi-squared or Fisher's exact tests were used. Non-parametric chi-squared for trend test and Kaplan-Meier curve were used for comparing the trend of treatment success between hyoscine and diazepam groups in the first and second hours after treatment. For this purpose, at least 1 level improvement in vertigo severity was considered as successful treatment. In another part, to be sure of the findings and approve the analyses, treatment success was considered complete relief of vertigo and findings were separately reported in tables and figures. In all analyses, $p < 0.05$ was considered as significance level.

Ethics

Protocol of this study was assessed by the Ethics Committee of the Shahid Beheshti University of Medical Sciences and was given the code number IR.SBMU.SM.REC.1394.134. Patients voluntarily participated in the study and informed written consent was obtained from them. Throughout the study, the researchers adhered to declaration of Helsinki principles. Protocol of the study was registered on the Iranian registry of clinical trials located at www.irct.ir under the code number IRCT2016100815640N5.

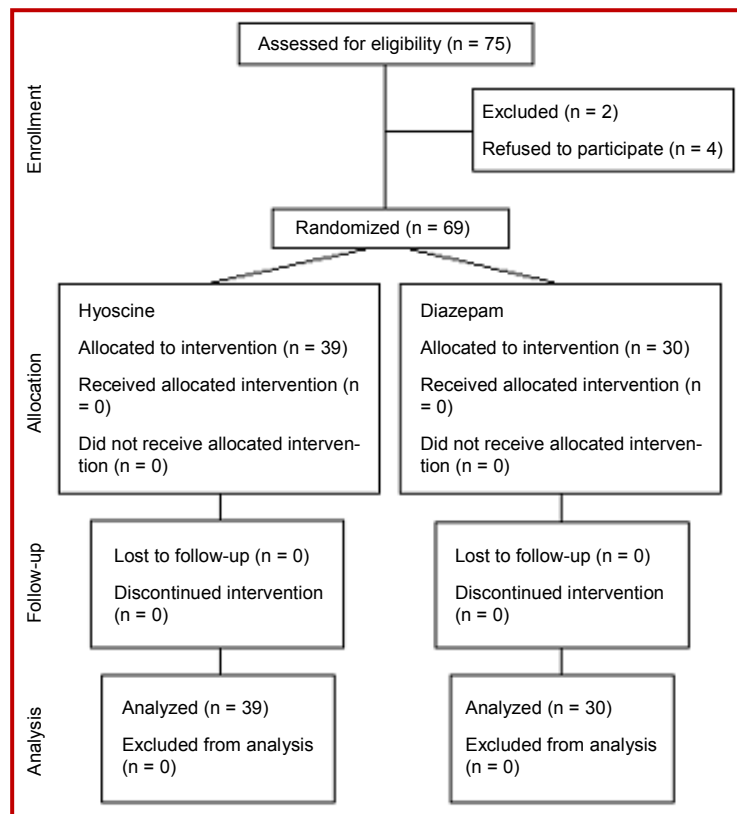


Figure 1: CONSORT flowchart of studied patients

Results

Demographic and baseline findings

Finally, 69 patients with the mean age of 55.4 ± 15.7 years (age range: 21-80 years) were included in the study (68.1% female). 39 patients were treated with hyoscine and 30 received diazepam. CONSORT flowchart of studied patients was showed in Figure 1. Table I shows demographic data and baseline characteristics of the studied patients and the findings of clinical examinations based on the groups. According to the results, there was no significant difference between mean age of the patients ($p=0.57$) and their sex distribution ($p=0.18$). History of vertigo, characteristics and type of vertigo, its duration, direction of nystagmus, and accompanying symptoms were also similar between the 2 groups ($p > 0.05$).

Treatment effectiveness in supine position

Presence of vertigo in supine position did not show a significant difference between the 2 groups ($p=0.18$). Considering at least one level improvement, after 1 hour, 4 patients in hyoscine group and 12 in diazepam group reported improvement in supine position vertigo. These counts were 5 and 16 patients, respectively, 2 hours after treatment initiation. Non-parametric Chi-squared for trend test showed that success rate was significantly higher in diazepam group compared to hyoscine treatment group ($p < 0.001$). Complete relief of vertigo was seen in 1 case after hyoscine treatment and 4 after diazepam administration in the first hour. After 2 hours, these values were 2 and 11 patients, respectively ($p=0.001$).

Treatment effectiveness in sitting position

Presence of vertigo in sitting position on admission did not show a significant difference between the 2 groups on admission ($p=0.99$). Considering at least 1 level improvement in vertigo in sitting position, after 1 hour, 26 patients in hyoscine group and 27 in diazepam group reported feeling better regarding vertigo. These values were 30 and 29 patients, respectively, after 2 hours. Non-parametric Chi-squared for trend test showed that success rate was significantly higher in diazepam group compared to hyoscine treatment group ($p=0.02$). Hyoscine administration could completely relieve vertigo in sitting position in the first hour. However, 2 hours after injection, vertigo was completely relieved for 1 patient in hyoscine group and 12 patients in diazepam group ($p=0.001$).

Table I			
Demographic data and baseline characteristics			
Variable	Hyoscine (n = 39)	Diazepam (n = 30)	P
Age (year)	54.5	56.6	0.57
Sex			
Female	24	23	0.18
Male	15	7	
History of underlying illness	17	14	0.80
History of vertigo	3	2	0.99 ^a
Vertigo characteristic			
Spinning	36	24	0.16 ^a
Non-spinning	3	6	
Type of vertigo			
Central	9	10	0.34
Peripheral	30	20	
Duration of vertigo (hours)	4	3.5	0.99 ^b
Vertigo symptoms			
Nausea	34	27	0.99 ^a
Vomiting	31	25	0.76 ^a
Dysarthria	2	2	0.99 ^a
Dysphagia	1	0	
Hyposthesia	1	0	
Tinnitus	0	1	
Nystagmus			
No	4	6	0.50 ^a
Horizontal	31	21	
Horizontal-vertical	4	3	

^aBased on Fisher's exact test; ^bbased on Mann-Whitney test

Treatment effectiveness while turning the head

Presence of vertigo while turning the head did not show a significant difference between the 2 groups on

admission (p=0.78). Considering at least 1 level improvement in vertigo while turning the head, after 1 hour 21 patients in hyoscine group and 21 in diazepam group reported feeling improvement in their vertigo. These values were 25 and 27 patients, respectively, after 2 hours. Non-parametric Chi-squared for trend test showed that success rate was significantly higher in diazepam group compared to hyoscine treatment group (p=0.03). Hyoscine administration could not completely relieve vertigo for any patients in the first hour. However, diazepam administration led to complete relief of 3 patients during this time. In addition, 2 hours after drug administration vertigo was completely relieved in 4 patients in hyoscine group and 17 cases in diazepam group.

Table II depicts the results in terms of effectiveness of hyoscine and diazepam administration in treatment of vertigo in supine position, in sitting position and while turning the head. Figure 2 presents complete vertigo relief failure rate of hyoscine and diazepam in treating vertigo in various positions.

Side effects

In evaluation of treatment side effects, follow-up did not reveal any side effect of drug administration.

Discussion

Findings of the present study showed that efficiency of diazepam is significantly higher than hyoscine in treatment of vertigo and its symptoms. Treatment success rate of diazepam in relieving vertigo in different positions varied between 88.9 and 100%, while this rate was 31.2-73.5% in hyoscine treatment group. Prescription of diazepam led to complete relief of vertigo in 40-63% of the patents, while this rate was only 2.6-12.5% in hyoscine treatment group.

Although hyoscine, as an anticholinergic drug, has been used for a long time and in various clinical settings, effectiveness of this drug in controlling true vertigo has been evaluated in few studies. For instance, a syste-

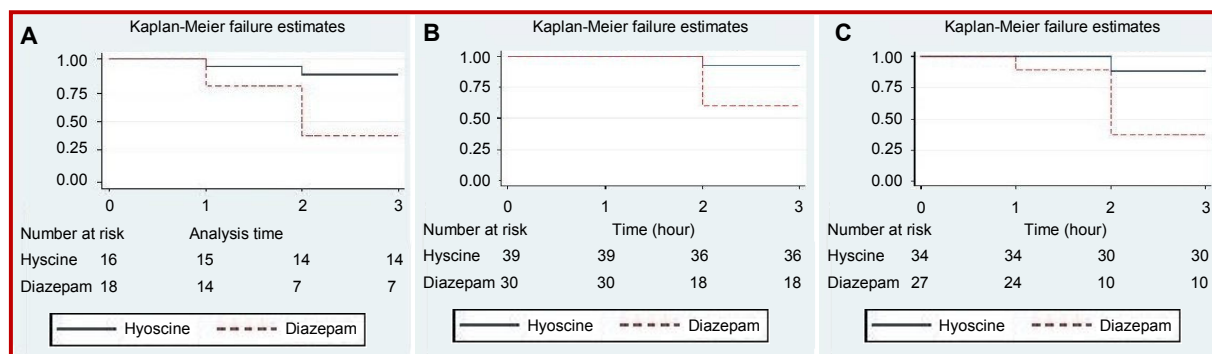


Figure 2: Complete vertigo relief failure rate of hyoscine and diazepam in treating vertigo in supine position (A), in sitting position (B), and while turning the head (C)

Table II
Effectiveness of hyoscine and diazepam prescription in treatment of vertigo in different positions

Variable	In supine position			In sitting position			While turning the head		
	Hyoscine (n = 39)	Diazepam (n = 30)	p value	Hyoscine (n = 39)	Diazepam (n = 30)	p value	Hyoscine (n = 39)	Diazepam (n = 30)	p value
<i>On admission</i>									
None	23	12	0.18 ^a	0	0	0.99 ^a	5	3	0.78 ^a
Mild	10	8		1	1		2	1	
Moderate	0	1		1	0		0	0	
Severe	6	9		37	29		32	26	
<i>An hour after treatment</i>									
None	24	16	---	0	0	---	5	6	---
Mild	10	11		1	10		4	8	
Moderate	3	2		27	17		20	12	
Severe	2	1		11	3		10	4	
<i>Two hours after treatment</i>									
None	25	23	---	3	12	---	9	20	---
Mild	10	6		2	3		4	2	
Moderate	0	1		28	14		19	8	
Severe	4	0		6	1		7	0	

^aBased on Fisher's exact test

matic review on 35 studies in 2011 aiming to assess the efficacy of transdermal hyoscine in motion sickness symptom relief showed that although this drug is effective in relieving the symptoms of this problem, all the evidence obtained are level 2 and 3 evidence and this makes it hard to reach a final decision regarding use of this drug in treating vertigo and motion sickness (Spinks et al., 2011). Even three decades ago, Rahko and Karma also attempted to evaluate treatment value of transdermal hyoscine in treatment of peripheral vertigo in 30 patients. This study showed that using this treatment brings about desirable outcome in reducing symptoms of Menier's disease. However, the researchers stated that blurred vision and dry mouth are observed side effects of this drug. Finally, they concluded that transdermal hyoscine could be used as a replacement option in treatment of peripheral vertigo (Rahko and Karma, 1985). The reason for the contradicting results obtained in this study, compared to other studies, might be the route of administration. All the mentioned studies had evaluated the effectiveness of transdermal hyoscine in relieving vertigo symptoms. The effects of systemic and local administration of a drug might be significantly different.

Findings of the present study show the acceptable effectiveness of diazepam in treatment of acute vertigo. Findings of other studies are also indicative of the same result. For example, Ganança et al. in their study showed that clonazepam leads to complete relief of

vertigo in 77.4% of vertigo patients (Ganança et al., 2002). In another clinical trial lorazepam and dimenhydrinate were compared for treatment of vertigo in patients. Findings of the study also confirmed the effectiveness of lorazepam in vertigo symptom relief and walking of the patients (Marill et al., 2000). Although a study by Amini et al. showed that promethazine is more efficient than lorazepam in treating vertigo, its findings also indicated the effectiveness of lorazepam in this regard (Amini et al., 2014).

Conclusion

It is likely that diazepam is a better option than hyoscine for management of true vertigo in patients presenting to emergency department.

Conflict of Interest

All authors have completed the ICMJE uniform disclosure form and declare no support from any organization for the submitted work.

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Author Info

Firoozeh Vajihi (Principal contact)

e-mail: f.vajihi@yahoo.com

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