Comparison of Intraveneous Diazepam, Dimenhydrinate and Diphenhydramine on Patients with Acute Peripheral Vertigo in the Emergency Department: A Randomized, Double Blind, Clinical Trial

Acil servise akut periferik vertigo ile başvuran hastalarda intravenöz diazepam, dimenhydrinate ve diphenhydramine tedavisinin etkinliğininin karşılaştırılması

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SUMMARY

Objectives: The aim of this study is to compare treatment and side effects of intraveneous (IV) diazepam, diphenhydramine and dimenhydrinate on patients with vertigo.

Materials and Methods: Patients over 17 years of age who presented with vertigo as a chief complaint were included in the study. 2 mg diazepam, 50 mg diphenhydramine, or 50 mg dimenhydrinate were given IV over 2 min. Patients evaluated their vertigo perception with Likert numeric (1-10) scale during walking, standing, sitting, and supine positions. Patients also evaluated additional symptoms and side effects at the same times. Principal outcome measures were evaluated at 60 minutes.

Results: 74 patients were entered into the study. All three medications were found equally effective to decrease vertigo symptoms. There was no statistical difference between groups for side effects, but at 60 minutes diphenhydramine and dimenhydrinate caused more sedation than diazepam (p=0.015). Mean level of change in sedation and drowsiness was significantly less in the diazepam group than others (p=0.025, p=0.033, respectively).

Conclusion: Diazepam, diphenhydramine and dimenhydrinate are equally effective to treat vertigo in the emergency department. Diazepam has less sedation.

Key words: Emergency department; diazepam; dimenhydrinate; diphenhydramine; vertigo.

ÖZET

Giriş: *Acil servise başdönmesi şikayetiyle başvuran hastalarda intravenöz (İ.V.) olarak uygulanan diazepam, diphenhydramine ve dimenhydrinate'in tedavi etkinliği ve görülen yan etkilerini karşılaştırmayı amaçladık.*

Gereç ve Yöntem: *On yedi yaş üzerinde acil servise esas başvuru şikayeti başdönmesi olan bütün hastalar çalışmaya alındı. 2 mg diazepam, 50 mg diphenhydramine veya 50 mg dimenhydrinate 2 dakikanın üzerinde İ.V. olarak uygulandı. Daha sonra hastaların başdönmesi şikayetlerinin şiddeti (yürür, ayakta, oturur ve supin pozisyonlarında) Likert numeric (1-10) skala ile değerlendirildi. Bu sırada hastalarda oluşan ek semptom - bulgular ve yan etkilerde değerlendirmeye alındı. Bu temel değerlendirme ve ölçümler 60 dakika içerisinde yapıldı.*

Bulgular: *Çalışmaya 74 hasta dahil edildi. Üç ilacında başdönmesi semptomlarını azaltma da etkili olduğu bulundu. Gruplar arasında yan etki oluşması konusunda istatistiksel bir fark bulunmadı. Ama diphenhydramine ve dimenhydrinate'in 60 dakikalık sürede diazepamdan daha fazla sedasyon yaptığı görüldü (p=0.015). Diazepam grubunda sedasyon ve sersemlik hissi oluşmasının diğer gruplardan daha düşük düzeyde olduğu bulundu (p=0.025, p=0.033).*

Sonuç: *Diazepam, diphenhydramine ve dimenhydrinate acil serviste baş dönmesi tedavisinde etkin olarak aynı derecede kullanılabilir. Diazepamın daha düşük düzeyde sedasyon yaptığı unutulmamalıdır.*

Anahtar sözcükler: *Acil servis; diazepam; dimenhydrinate; diphenhydramine; vertigo.*

Introduction

Acute peripheral vertigo is a frequent emergency department complaint for which there have been only limited studies of choices for initial therapy. A wide variety of treatment options are used by clinicians, such as anticholinergics,[1,2] histamine receptor blockers,[1] benzodiazepines,[2] calcium channel blockers,[3] neuroleptics,[4] glucocorticoids,[5] and Epley's maneuver.[6,7] Variations on treatment may be from departmental guidelines, or personal experiences. In addition, country to country differences may affect vertigo treatment in the emergency department because of governmental health and medication policies.

Dimenhydrinate is the most common drug used for acute peripheral vertigo in Turkey. However, with starting the new specialty of emergency medicine in 1993, treatment of acute peripheral vertigo became more varied than ever. Today, intravenous (IV) antihistamines, anticholinergics, and benzodiazepines are used, especially in the academic emergency departments in Turkey. However, there is little usage of neuroleptics, glucocorticoids, and Epley's maneuver.

There are limited comparative studies in the literature for acute peripheral vertigo treatment in the emergency department setting. Consequently, some myths about various medications' safety and efficacy are prevalent in clinical practice. Benzodiazepines, for example, are the least used drugs for this purpose because of clinicians' hesitation to use strong sedative agents for vertigo in Turkey. Therefore, the aim of the current study was to compare the efficacy to relieve acute peripheral vertigo and the side effects of the most available drugs in our emergency departments (Diazepam, Dimenhydrinate, and Diphenhydramine).

Materials and Methods

Study Design, Study Setting and Study Population

This was a prospective, randomized, double-blind clinical trial which was held in a university hospital emergency department staffed by attending emergency physicians and residents of an academic department of emergency medicine during a three month period. The university hospital emergency department has 56.000 patients (adult and pediatrics) annually, and serves a medium sized metropolitan area.

Study Protocol

Patients who were older than 17 years of age and presented with symptoms of vertigo were evaluated for vestibular or non-vestibular origin of vertigo perception, and peripheral versus central origin. Exclusion criteria included patients who had a known allergy to the study drugs and to theophylline (because dimenhydrinate is the chlorotheophylline salt of difenhydramine) and non-vestibular origin of vertigo, central vertigo findings, previous enrollment in the study, or were pregnant. Patients who had acute peripheral vertigo symptoms and no exclusion criteria were asked to sign an informed written consent for the study.

Patients were evaluated by attending emergency physicians and senior emergency medicine residents. Data recorded included gender, age, approximate time of onset of vertigo, current medications, specific medical diagnosis, and additional symptoms. Complete physical examination was done in all cases to rule out non-vestibular and central origin. Vertigo data sheets for each patient who met the entry criteria were filled out by senior emergency medicine residents.

Medications were prepared as diazepam 2 mg IV, dimenhydrinate 50 mg IV, and difenhydramine 50 mg IV by a registered nurse (RN) who had no other involvement in the study. All medications were placed in 5 cc syringes with normal saline (NS). Syringes were covered with colored tape to ensure similar appearance, and kept in the study box labeled as "vertigo study". Patients and physicians were blinded to treatment. Medications were updated by the RN each 24 hours if they weren't used. Nurses were instructed to inject the medication over 2 minutes. All patients received 10 NS bolus after the medication injection. Unless there was an emergency indication, no other drugs were permitted during the first hour period. Randomization of patients was performed by a faculty member who had no involvement in the study. Emergency physicians, residents and nurses were instructed in study protocols, and evaluating vertigo patients, which had been well described in recent literature,[8-11] with a 2 hour education conference before the study.

Patients' results were documented before treatment, at 30 and 60 minutes and before discharge. At the same time points, patients evaluated their nausea, vomiting, sedation, drowsiness, dry mouth, vertigo perception while supine, sitting, standing, walking, and with head movement by using 10-point Likert scale (10 was the maximum, 1 was none). In addition, patients were asked to evaluate their readiness to go home at the same time points, and if they needed additional medication for vertigo at 60 min. Patients who were unable to stand because of vertigo were scored as a 10 on the Likert scale for "walking".

There was no routine laboratory testing or imaging modalities mandated by the protocol of the study. However, labora-

tory or radiological measurements were done while the study was continuing, if necessary. After the 60 minute measurements, the emergency physician was free to use dimenhydrinate 50 mg IV, and then diazepam 2 mg IV, if necessary, as an additional medication for cases who needed additional treatment. The study for each case was completed when the discharge time measurements were done. The final emergency department diagnosis was recorded. All patients who discharged were directed in the out patient clinic of the Ear-Nose-Throat service for follow-up.

The Key Outcome Measures and Data Analysis

The key outcome measures evaluated for each group at 60 min, and these were the mean decrease in Likert score "while walking", the mean increase in "ready to go home" Likert scores, the mean change in Likert score for additional symptoms, and common adverse effects without further emergency department intervention, and the number of cases seeking additional medication in each group. Measurements regarding changing on vertigo, ready to go home, side effects and additional symptoms at discharge time were also evaluated in the group of cases who did not need additional drug therapy. A secondary outcome measure was treatment to discharge time in cases who did not need additional medication therapy. Descriptive tests, Pearson Chi-square, Student t, Paired Samples t, and Analysis of Variances (ANOVA) and ANOVA for repeated measures were used for statistical comparison as appropriate. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS, version 11.0).

Results

There were 87 patients who presented with vertigo to the emergency department. 13 cases were excluded from the study because 3 cases were determined to have non-vestibular findings, one case had central vertigo after the first evaluation, 2 cases wanted to quit from the study group in the middle of study, 2 cases had previously enrolled in the study, one case was pregnant, one case was resistant to the medications and was admitted to the hospital clinic and then was diagnosed with cerebellar infarction on magnetic resonance imaging, and vertigo data sheets were found incomplete in 3 cases. Statistical analyses were applied to 74 cases in three treatment groups (Table 1).

Demographic and Presenting Features

74.3% of cases were female. Mean age was 49.2±14.3 years (minimum 18, maximum 74, median: 50, range: 56). There was no significant difference between gender by mean ages (47.9 in female versus 52.8 in male). 70 cases have no previous vertigo diagnosis; only 4 cases had a history of vertigo. Two of them had a history of using vertigo medication, but they denied any medicine use in the last 24 hours. 26 cases presented to the emergency department 24 hours after symptoms started, and only 3 cases presented in less than 1 hour. There was no difference between treatment groups for time of onset of the symptoms and current medication use.

Nausea was found in 74.3%, vomiting in 40.5%, and tinnitus in 41.9% of cases. There was no difference between treatment groups for vital signs at time zero (pretreatment), 30 and 60 minutes, and at discharge.

There was no significant difference between treatment groups for number of cases, gender distribution, mean age, triage to treatment time, and treatment to discharge time. There was an average 53 minutes delay between triage time and administration of the medication. Mean vertigo and "ready to go home" scores of the medication groups are shown in Table 2.

There was no significant difference between groups for vertigo score while lying, sitting, standing and walking at 30 and 60 minutes, and at discharge. The diazepam group had a significantly higher vertigo score while lying and standing than the other two groups at the pretreatment time point.

Table 1. *Medication groups: gender, age, triage to medication time and medication to discharge time distribution of cases.*

	n	Female	Male	Mean age±SD	Triage to medication time (hour:min)*	Medication to discharge time (hour:min)*
Diazepam	25	21	4	49.24±15.85	0:48	2:17
Dimenhydrinate	24	15	9	49.88±12.60	0:50	3:26
Diphenhydramine	25	19	6	48.56±14.90	1:00	2:54
Total	74	55	19	49.22±14.35	0:53	2:52

SD: Standard deviation; * mean time in hours and minutes.
There is no significant difference between medication groups (p>0.05).

Table 2. *Mean vertigo scores in time periods.*

	Treatment group	Time zero (pretreatment)	Value at 30 minutes	Value at 60 minutes	Value at discharge
Vertigo while lying	Diazepam	6.44±2.944[a]	4.32±2.80	3.48±2.97	2.04±2.35
	Dimenhydrinate	4.16±3.67	3.20±2.79	2.45±2.34	1.20±0.65
	Diphenhydramine	4.44±3.65	4.12±3.24	3.08±2.81	1.64±1.65
Vertigo while head motion	Diazepam	7.80±2.78	5.56±3.05	4.12±3.32	2.28±2.22
	Dimenhydrinate	6.29±3.77	5.20±2.87	3.83±2.92	1.91±1.47
	Diphenhydramine	7.24±2.90	6.28±2.90	4.60±3.29	2.32±2.17
Vertigo while sitting	Diazepam	7.44±2.61	5.48±3.30	3.66±3.06	1.58±1.28
	Dimenhydrinate	5.95±3.58	5.25±3.33	3.85±2.97	1.71±1.28
	Diphenhydramine	5.96±3.14	5.48±3.26	4.00±3.11	1.60±1.19
Vertigo while standing	Diazepam	8.84±2.30[b]	6.44±3.05	4.92±3.70	2.12±2.24
	Dimenhydrinate	7.00±3.47	5.95±3.32	4.95±3.58	2.08±1.52
	Diphenhydramine	6.84±2.76	6.32±3.24	4.64±3.35	2.28±1.76
Vertigo while walking	Diazepam	8.44±3.00	6.16±3.35	4.68±3.56	2.08±2.05
	Dimenhydrinate	7.37±3.30	6.33±3.35	5.00±3.70	2.083±1.52
	Diphenhydramine	7.24±2.98	6.72±3.12	4.80±3.22	2.28±1.76
Ready to go home	Diazepam	2.12±2.58	4.48±3.12	6.48±3.48	8.20±3.20
	Dimenhydrinate	2.95±2.91	4.58±3.10	5.41±3.57	8.66±2.44
	Diphenhydramine	2.56±2.38	4.04±2.80	6.16±3.19	8.56±2.25

[a]p: 0.048; [b]p: 0.029.
"p" value represents significance between treatment groups.

The Key Outcome Measures Decrease in Mean Vertigo Score while Walking at 60 Minutes

Each drug showed a significant decrease for vertigo while walking at 60 minutes (p<0.001). Vertigo decreased more in the diazepam group (3.84 units) (Table 3).

Increase in "Ready to Go Home" Score

Each drug showed significant increase in the "ready to go home score" at 60 minutes (p<0.001). Diazepam showed more increase (4.32 units) compared with dimenhydrinate and diphenhydramine. Diazepam was significantly different from dimenhydrinate (p=0.039, Table 3).

Additional Symptoms and Adverse Effects

There was no difference between treatment groups for mean nausea, drowsiness, and dry mouth scores in the time periods, but diazepam had significantly less sedation effect than the other two medications at 60 minutes (p=0.015, Table 4). Nausea was significantly decreased in the diazepam and diphenhydramine groups, but not dimenhydrinate (p=0.012, p=0.004, and p=0.063, respectively) at 60 minutes. Drowsiness was significantly decreased in the diazepam (p=0.001) and diphenhydramine groups (p=0.046) at 60 minutes. Diazepam was significantly different in the mean level of decrease in drowsiness (p=0.033), and sedation (p=0.025)

Table 3. *Mean vertigo score "while walking" decrease and mean "ready to go home" score increase at 60 minutes.*

	Decrease in vertigo score while walking at 60 minutes		Increase at ready to go home score	
	60 minutes	95% CI	60 minutes	95% CI
Diazepam	3.84	2.30 – 5.37	4.32[a]	2.84 – 5.79
Dimenhydrinate	2.37	1.21 – 3.53	2.45	1.36 – 3.55
Diphenhydramine	2.44	1.34 – 3.53	3.60	2.35 – 4.84
Total	2.89	2.16 – 3.61	3.15	2.74 – 4.20

[a]p: 0.039.

Table 4. *Additional symptoms and adverse effects measurements in time periods.*

	Treatment group	Time zero (pretreatment)	Value at 30 minutes	Value at 60 minutes	Change at 60 minutes	Value at discharge
Nausea	Diazepam	4.20±3.18	2.88±2.58	1.96±1.94	2.32*	1.32±0.90
	Dimenhydrinate	4.00±3.56	2.75±2.54	2.50±2.32	1.50*	1.20±0.72
	Diphenhydramine	3.44±3.01	2.68±2.26	1.96±1.83	1.48*	1.20±0.57
Drowsiness	Diazepam	5.04±2.83	3.88±2.40	3.28±2.24	1.76[a,*]	3.12±2.50
	Dimenhydrinate	3.87±2.72	4.08±2.84	3.63±2.60	0.25*	3.04±2.57
	Diphenhydramine	5.08±3.35	5.28±3.28	4.24±3.44	0.84*	3.40±2.78
Sedation	Diazepam	3.12±3.08	2.60±2.56	1.92±1.82[b]	1.08[c,*]	2.00±2.10
	Dimenhydrinate	2.33±2.03	4.12±3.37	3.50±3.13	1.56	3.00±3.10
	Diphenhydramine	3.40±3.29	4.84±3.84	4.40±3.68	1.00	3.84±2.97
Dry mouth	Diazepam	4.16±2.89	3.64±2.81	3.16±2.68	1.00*	2.76±2.57
	Dimenhydrinate	4.37±3.54	4.66±3.11	4.41±3.41	0.04	3.70±3.34
	Diphenhydramine	3.60±2.91	4.88±3.17	4.36±3.30	0.88	2.68±2.15

[a]p: 0.033; [b]p: 0.015; [c]p: 0.025; * represents decreased values.
"p" value represents significance between treatment groups.

at 60 minutes. Only diazepam showed a significant decrease in dry mouth score (p=0.003). Dry mouth score increased in the dimenhydrinate and diphenhydramine groups, but it was not significant for each group.

No patients in the study reported pain with injection, no visual hallucinations, and no hypotension. However, an asymptomatic decline in blood pressure was seen in 8 (10.8%) cases, and there was no difference between treatment groups for blood pressure decrease (2 cases in Diazepam, 2 in Dimenhydrinate, and 4 in Diphenhydramine).

Additional Treatment Need

Forty-two cases requested an additional medication after the 60 minute evaluation. There was no difference between cases

Table 5. *Patients who did not need additional treatment.*

	Treatment group	Value at Time zero	Value at 60 minutes	Change at 60 minutes	Value at Discharge	Change at discharge
Nausea	Diazepam	4.09±3.01	1.09±0.30	3.00±3.03	1.09±0.30	3.00±3.03[a]
	Dimenhydrinate	3.20±3.79	1.20±0.42	2.00±3.55	1.00±0.00	2.20±3.79
	Diphenhydramine	2.54±2.20	1.09±0.30	1.45±2.06[b]	1.09±0.30	1.45±2.06[b]
Drowsiness	Diazepam	5.54±3.20	3.00±2.40	2.54±2.91[c,*]	2.72±2.32	2.81±2.99[d,*]
	Dimenhydrinate	3.00±2.26	2.80±2.34	0.20±1.39*	2.70±2.26	0.20±1.99*
	Diphenhydramine	3.00±2.32	2.36±2.80	0.54±2.76*	2.45±2.79	0.54±2.16*
Sedation	Diazepam	2.63±2.83	1.63±2.11	1.00±3.47*	1.63±2.11	1.00±3.46*
	Dimenhydrinate	2.90±2.23	4.40±3.53	1.60±3.37	3.90±3.57	1.20±3.67
	Diphenhydramine	2.45±2.80	4.36±3.95	1.90±3.01	4.00±3.66	1.45±2.42
Dry mouth	Diazepam	3.18±2.67	2.45±2.80	0.72±1.00[e,*]	2.36±2.54	0.81±0.98[f,*]
	Dimenhydrinate	4.40±3.47	3.60±3.02	0.70±3.49*	3.20±2.74	0.50±4.24*
	Diphenhydramine	2.54±1.63	2.18±1.40	0.36±2.20*	2.09±1.44	0.36±2.20*
Vertigo score while walking	Diazepam	8.54±3.23	1.90±1.81	6.63±3.29*	1.09±0.30	6.09±3.44*
	Dimenhydrinate	6.30±3.26	1.90±1.28	4.40±2.71*	1.30±0.67	3.30±2.31*
	Diphenhydramine	6.18±3.28	1.90±0.94	4.27±2.83*	1.63±0.67	4.54±3.14*
Ready to go home score	Diazepam	2.36±2.80	8.54±2.87	6.18±3.51	8.90±2.77	6.54±3.58
	Dimenhydrinate	4.40±2.87	8.60±1.64	4.20±2.57	9.30±1.49	4.90±2.80
	Diphenhydramine	3.09±2.16	8.45±1.57	5.36±2.54	8.63±1.62	5.54±2.58

[a]p: 0.021; [b]p: 0.042; [c]p: 0.016; [d]p: 0.011; [e]p: 0.038; fp: 0.020; * represents decreased levels.
"p" value represents significant changes of medication group in measurement category, not significance between groups.

who requested and who did not additional drug therapy for the time the symptoms started, gender, mean age, time difference between triage and drug therapy, and their distribution to the treatment groups (14 cases in each group needed additional medication).

The cases who needed additional medication therapy had a lower decrease in their mean vertigo score while walking at 60 minutes compared with cases whose did not need additional medication (1.19 versus 5.12, $p<0.001$). The mean time difference between medication administration to discharge was higher in cases who need additional drug therapy (3:47 versus 1:39, $p<0.001$). The mean "ready to go home score" at 60 minutes was lower in patients who needed additional medication (2.09 versus 5.28, $p<0.001$).

Patients who needed additional medication therapy received dimenhydrinate in 24, and dimenhydrinate and diazepam in 18 cases. There was no difference in these two groups for gender, mean age, time the symptoms started, and their distribution to the three treatment groups. However, mean medication to discharge time was significantly different (2:48 and 5:06, respectively, $p<0.001$).

Patients discharged without needing any additional treatment in the emergency department

In the treatment groups of patients who do not need additional medication, 11 cases were in the diazepam and diphenydramine group, and 10 in the dimenhydrinate group. Diazepam had higher mean age patients than the other two groups (53.2, $p>0.05$). Triage to treatment time was 55, 38, and 67 minutes in diazepam, dimenhydrinate, and diphenhydramine respectively ($p>0.05$). Time difference between treatment to discharge was 125 minutes in the dimenhydrinate group, 90 minutes in diazepam, and 85 minutes in diphenhydramine group ($p>0.05$). All three treatment groups had significant decreases in mean vertigo scores at discharge time ($p<0.001$). The mean decrease in vertigo score was higher in the diazepam group at discharge (6.09 units), and diazepam was significantly different from dimenhydrinate ($p=0.044$). All three medications showed significant increases in "ready to go home score" at discharge ($p<0.001$). The increase was higher in the diazepam group at discharge (6.54 unit), but there was no difference between groups. The diazepam group was the only group which had no decline in blood pressure. The mean decrease in drowsiness was higher in the diazepam group than the others at discharge (2.81 units, $p=0.027$). The dry mouth score decreased in diazepam group (0.81 unit at discharge) more than in the other groups, but there was no significant difference between groups.

Discussion

We performed a prospective, randomized, double-blind clinical trial comparing 3 intravenously administrated agents frequently utilized for acute peripheral vertigo in the emergency departments of Turkey: diazepam, dimenhydrinate and diphenhydramine. The demographic results of the study group were similar to those reported in the literature.[13,14,17]

The patients in diazepam group experienced slightly more vertigo at pretreatment time, but there was no significant difference between groups for mean vertigo score while walking at pretreatment time. Similarly, "ready to go home score" was lower in the diazepam group at pretreatment time, but it was also not significant. Interestingly, level of change in these categories at 60 minutes was greater in the diazepam group. Therefore, we thought that the difference in the diazepam group at the pretreatment time would not have led to qualitative error in our results.

Principal outcome measures were evaluated at 60 minutes. Vertigo sensation while walking decreased more units in the diazepam group, but there was not a significant difference between treatment groups. However, diazepam had a significant increase in the "ready to go home score" than dimenhydrinate.

Diazepam had significantly less sedation effect than the other 2 medications at 60 minute measurement. The diazepam group had also the lowest sedation score at all time points.

We found that all three medications showed a considerable decrease in vertigo, and increase in "ready to go home" scores at 30 minutes-which was our earliest measurement time.

As a secondary outcome measure, treatment to discharge time in cases who did not need additional therapy was higher in the dimenhyrdinate group, but this was not significantly different. All three medication groups did not show any severe side effect such as hypotension, and there was no difference between groups for needing additional medication. We consider that these outcome measures support the conclusion that diazepam is an effective treatment choice for vertigo in the emergency department setting, and it has no more side effects than dimenhydrinate and diphenhydramine at the dose administered.

We did not include a placebo group in the study, because we and ethical consultants considered that this would be unethical. The same concern was also expressed in comparative drug studies for vertigo.[2] We could not find in the literature

what level of change in outcome measures was clinically important. Therefore, we did not mention in the methods an estimated clinically significant level of change for outcome measures. Although it was reported that alleviation of vertigo perception was linked to a decline of nystagmus in the literature,[21] we did not measure decline in nystagmus in our cases. We did not measure patient's weight for weight-based medication dosage because we thought it could be time consuming, and could give the patient more distress. Therefore, the medication dosage in the study was utilized for each medication as is standard practice in Turkey.

Dizziness is a common presenting complaint in emergency department patients, and it is more prevalent in patients older than 50 years of age.[12,13] A large number of entities cause vertigo ranging from the benign such as vestibular neuritis, to life threatening causes such as cerebellar hemorrhage. Peripheral vertigo is more common in females.[14] The general principle with respect to treatment of vertigo is to identify and manage the underlying cause. Therefore, the differential diagnosis of central vestibulopathy, peripheral vestibulopathy and non-vestibular causes in vertigo is very important for emergency physicians. Because most causes of vertigo are peripheral and not life threatening, the primary therapeutic goal is to provide symptomatic relief from the vertigo, as well as the neurovegetative and psychoaffective signs (nausea, vomiting, and anxiety).[9,15] The clinical trials evaluating antivertigo medication have often been questionable because of methodological limitations, and this explains why the habits of emergency treatment and prescription are mainly empirical, and why striking differences can be noticed from one country to another.[15] Meclizine is the most commonly used agent to suppress symptoms. Dimenhydrinate an diphenhydramine reported equally effective, has been reported to have more sedative effect than meclizine. However, diazepam has been regorded as the most potent vestibular suppressant but causes significant sedation.[9] A widely used resource of medical information, eMedicine, also makes the same recommendation of dimenhydrinate and diphenhydramine for vertigo treatment over benzodiazepines.[16]

Some comparative studies including benzodiazepines reported that there were favorable results for dimenhydrinate.[2,18] Diazepam has active metabolites and has at least two times more half life time compared to Lorazepam. Lorazepam can be a good option because its elimination is not much affected by age and liver disease. Because we do not have intravenous Lorazepam in Turkey, we have no chance to use it. Correspondingly, in a study, diazepam and dimenhydrinate were reported equal efficacy compared to the placebo.[19] In an acute attack, diazepam was reported as a widely used drug for acute vertigo attack because of its additional tranquilising effect.[20]

Diazepam had significantly less sedation effect than the other 2 medications at 60 minute measurement. The diazepam group had also the lowest sedation score at all time points. These results were different from a study done by Marill et al.[2] and the comment of Walker and Barnes.[13] Nausea, drowsiness, and dry mouth scores were remarkably decreased in the diazepam group. Dimenhydrinate was reported more effective than the other medications using for nausea and vomiting.[21,22] Dimenhydrinate had also reported as rapid action. However, in our study, we found that all three medications showed a considerable decrease in vertigo, and increase in "ready to go home" scores at 30 minutes-which was our earliest measurement time.

Diazepam showed considerable decrease in mean vertigo score and increase in "ready to go home score" at 60 minutes. In addition, diazepam had significantly less sedation and drowsiness score, and also had positive effect on improvement of other symptoms such as nausea at the dose we used. Based on these results, we think diazepam is an effective alternative to dimenhydrinate and diphenhydramine for the relief of acute peripheral vertigo in the emergency department setting.

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References

1. Mira E, Guidetti G, Ghilardi L, Fattori B, Malannino N, Maiolino L, et al. Betahistine dihydrochloride in the treatment of peripheral vestibular vertigo. *Eur Arch Otorhinolaryngol* 2003;260:73-7.
2. Marill KA, Walsh MJ, Nelson BK. Intravenous Lorazepam versus dimenhydrinate for treatment of vertigo in the emergency department: a randomized clinical trial. *Ann Emerg Med* 2000;36:310-9.
3. Pianese CP, Hidalgo LO, Gonzalez RH, Madrid CE, Ponce JE, Ramirez AM, et al. New approaches to the management of peripheral vertigo: efficacy and safety of two calcium antagonists in a 12-week, multinational, double-blind study. *Otol Neurotol* 2002;23:357-63.
4. Irving C, Richman P, Kaiafas C, Eskin B, Allegra J. Intramuscular droperidol versus intramuscular dimenhydrinate for the treatment of acute peripheral vertigo in the emergency department: a randomized clinical trial. *Acad Emerg Med* 2002;9:650-3.
5. Ariyasu L, Byl FM, Sprague MS, Adour KK. The beneficial effect of methylprednisolone in acute vestibular vertigo. *Arch Otolaryngol Head Neck Surg* 1990;116:700-3.
6. Epley JM. Particle repositioning for benign paroxysmal positional vertigo.

Otolaryngol Clin North Am 1996;29:323-31.

7. Radtke A, Neuhauser H, von Brevern M, Lempert T. A modified Epley's procedure for self-treatment of benign paroxysmal positional vertigo. *Neurology* 1999;53:1358-60.
8. Hoffman RM, Einstadter D, Kroenke K. Evaluating dizziness. *Am J Med* 1999;107:468-78.
9. Walker JS, Barnes SB. Dizziness. *Emerg Med Clin North Am* 1998;16:845-75, vii.
10. Hotson JR, Baloh RW. Acute vestibular syndrome. *N Engl J Med* 1998;339:680-5.
11. Luxon LM. The medical management of vertigo. *J Laryngol Otol* 1997;111:1114-21.
12. Gizzi M, Rosenberg M. The diagnostic approach to the dizzy patient. *The Neurologist* 1998;4:138-47.
13. Kroenke K, Mangelsdorff AD. Common symptoms in ambulatory care: incidence, evaluation, therapy, and outcome. *Am J Med* 1989;86:262-6.
14. Baloh RW, Honrubia V, Jacobson K. Benign positional vertigo: clinical and oculographic features in 240 cases. *Neurology* 1987;37:371-8.
15. Rascol O, Hain TC, Brefel C, Benazet M, Clanet M, Montastruc JL. Antivertigo medications and drug-induced vertigo. A pharmacological review. *Drugs* 1995;50:777-91.
16. Chang AK, Samuels MA. Benign positional vertigo. (Accessed: November 12, 2006) http://www.emedicine.com/emerg/topic57.htm. Last updated: July 12, 2006.
17. Froehling DA, Silverstein MD, Mohr DN, Beatty CW,Offord KP, Ballard DJ. Benign positional vertigo: incidence and prognosis in a population-based study in Olmsted County, Minnesota. *Mayo Clin Proc* 1991;66:596-601.
18. Mulch G. Comparison of the effectiveness of antivertiginous drugs by double blind procedure. The effect of diazepam, dimenhydrinate and sulpirid on the human vestibular spontaneous nystagmus (author's transl). [Article in German] *Laryngol Rhinol Otol* (Stuttg) 1976;55:392-9. [Abstract]
19. McClure JA, Lycett P, Baskerville JC. Diazepam as an anti-motion sickness drug. *J Otolaryngol* 1982;11:253-9.
20. Claes J, Van de Heyning PH. Medical treatment of Meniere's disease: a review of literature. *Acta Otolaryngol Suppl* 1997;526:37-42.
21. Pyykko I, Padoan S, Schalen L, Lyttkens L, Magnusson M, Henriksson NG. The effects of TTS-scopolamine, dimenhydrinate, lidocaine, and tocainide on motion sickness, vertigo, and nystagmus. *Aviat Space Environ Med* 1985;56:777-82.
22. Scherer H, Bschorr J. Considerations about methods to test the effectiveness of anti-vertiginous drugs (author's transl). [Article in German] *Laryngol Rhinol Otol* (Stuttg). 1980;59:477-84. [Abstract]