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Brief Reports

DIAZEPAM AND MECLIZINE ARE EQUALLY EFFECTIVE IN THE TREATMENT OF VERTIGO: AN EMERGENCY DEPARTMENT RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

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☐ **Abstract—Background: Vertigo is a debilitating disease that is commonly encountered in the emergency department (ED). Diazepam and meclizine are oral medications that are commonly used to alleviate symptoms. Objectives: We sought to determine whether meclizine or diazepam is superior in the treatment of patients with peripheral vertigo in the ED. Methods: We performed a double-blind clinical trial at a suburban, teaching ED. We randomized a convenience sample of adult patients with acute peripheral vertigo (APV) to diazepam 5 mg or meclizine 25 mg orally. Demographic and historical features were recorded on a standardized data form. Patients recorded their initial level (t0) of vertigo on a 100-mm visual analog scale (VAS) and after 30 min (t30) and 60 min (t60). The primary outcome parameter was the mean change in VAS score from t0 to t60. Differences between groups and 95% confidence intervals were calculated. Our a priori power calculation estimated that a sample size of 20 patients in each group was required to have an 80% power to detect a difference of 20 mm between treatment groups. Results: There were 20 patients in the diazepam group and 20 in the meclizine group. The two groups were similar with respect to patient demographics and presenting signs and symptoms. At t60, the mean improvements in the diazepam and meclizine groups were 36 and 40, respectively (difference −4; 95% confidence interval −20 to 12; $p = 0.60$). Conclusion: We found no difference between oral diazepam and oral meclizine for the treatment of ED patients with acute peripheral vertigo.** **© 2016 Elsevier Inc. All rights reserved.**

☐ **Keywords—benign paroxysmal positional vertigo; diazepam; meclizine; vertigo**

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INTRODUCTION

Vertigo is a debilitating disease that is commonly encountered in the emergency department (ED). There are approximately 500,000 medical encounters for the primary complaint of vertigo dizziness in the United States each year (1). Of these, approximately 20% occur in the ED and account for 3% of all ED visits (1–3).

Although preferable diagnostically and for guiding therapy, establishing a specific cause for vertigo is difficult in the ED (3–5). In addition, vertigo as a presentation of stroke or some other central etiologic cause adds to this diagnostic challenge (4–7).

A number of different treatments have been used for ED patients with cases of severe symptomatic vertigo. These include anticholinergics, antiemetics, benzodiazepines, and others (8,9). Of these medications, diazepam and meclizine are commonly used (8–11). Little information exists comparing the effectiveness of these

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agents in the treatment of vertigo. We found no previous study comparing these agents. Our objective was to determine whether meclizine or diazepam is more effective in the treatment of peripheral vertigo in the ED.

MATERIALS AND METHODS

We performed a prospective randomized controlled trial at a suburban ED with an annual patient census of 80,000. All patients between 18 and 65 years of age with a chief complaint of vertigo were eligible if the treating emergency physician diagnosed an episode of vertigo that was peripheral in nature. Patients with mild vertigo (visual analog scale [VAS] score <40 mm on a 0–100-mm scale) or those requiring parenteral therapy were excluded. In addition, any patients with a focal neurologic deficit, presentation consistent with a central cause of vertigo, presentation consistent with syncope or cardiac event, orthostatic hypotension, known pregnancy, presentation consistent with drug-induced vertigo, a known adverse reaction to diazepam or meclizine, or history of recent ingestion (within 24 hours) of a sedative, antihistamine, antipsychotic, or opioid were excluded.

After the patient examination, physicians completed a standardized data collection instrument that included demographic, historical, and clinical questions. Patients recorded their initial level (t0) of vertigo on a 100-mm VAS.

Patients were allowed to refuse or withdraw from participation in the study at any time. After enrollment, patients were randomized to the diazepam or meclizine group by computer randomization in a double blind fashion. Allocation to each group was concealed. The diazepam group received 5 mg orally, while the meclizine group received 25 mg orally. A study pharmacist prepared all the pills so that they looked identical and maintained a locked code of which drug was given to each study participant. The patient, study investigators, and treating physicians were blinded to the study medication used. In addition, this code was not unlocked until the completion of study enrollment and data collection.

Patients recorded the severity of their symptoms on the VAS after 30 min (t30) and 60 min (t60). The primary outcome parameter was the mean change in VAS score from t0 to t60. Differences between groups and 95% confidence intervals (CIs) were calculated. Our a priori power calculation estimated that a sample size of 20 patients in each group was required to have an 80% power to detect a difference of 20 mm between treatment groups in the mean change in VAS scores. We chose 20 mm on a 100-mm scale as a clinically important difference we wished to show.

Data were entered into Excel for Windows (Microsoft, Redmond, WA) and transferred into SPSS for Windows (IBM, Armonk, NY) for statistical analysis. Categorical variables were analyzed by chi-square, interval data using the Mann-Whitney *U* test, and continuous variables using the Student's *t*-test. All tests were two-tailed, with alpha set at 0.05. The study was approved by the institutional review board.

RESULTS

Forty eligible patients were consented and enrolled in this study, 20 in the diazepam group and 20 in the meclizine group. The two groups had similar patient demographics (Table 1). The median age of all enrolled patients was 44.0 years (95% CI 37–50 years; interquartile range 34.2–53.7 years), and the mean duration of symptoms were 6.5 and 6.25 h, respectively.

There were no statistically significant differences in proportions between the groups with respect to headache (0.15; 95% CI −0.15 to 0.45; $p = 0.53$), nausea (0.05; 95% CI −0.21 to 0.31; $p = 1$), hearing changes (0.20; 95% CI −0.01 to 0.41; $p = 0.18$), worsening symptoms with movement, (−0.05; 95% CI −0.21 to 0.411; $p = 1$), and nystagmus (−0.25; 95% CI −0.54 to 0.04; $p = 0.19$). The mean t0 score was 55 mm for the diazepam group and 62 mm for the meclizine group (−6.7; 95% CI −18.2 to 4.8; $p = 0.24$).

Both agents were associated with rapid significant improvement ($p < 0.001$) in vertigo scores (t0 to t60 VAS scores). However, no significant differences were seen when comparing mean decrease in VAS between diazepam versus meclizine at any time points (Table 2). At t60, the mean improvement in the diazepam and meclizine groups were 36 mm and 40 mm, respectively (difference −4, CI −20, 12; $p = 0.60$).

DISCUSSION

There are a number of etiologies for vertigo. Peripheral causes include benign paroxysmal positional vertigo (BPPV), Meniere's disease, labyrinthitis, and bilateral vestibular paresis. Central nervous system causes include migraine, stroke, transient ischemic attack, tumors, and

Table 1. Study Demographics

	Diazepam	Meclizine
No.	20	20
Age (mean ± SD)	42.7 ± 13.2	42.9 ± 11.0
Female sex (n)	11	14
Median duration of symptoms in hours (range)	6.5 (2–72)	6.25 (2–72)
Initial t0 VAS score in mm (95% CI)	55.3 (46–63.6)	62.0 (53.5–70.4)

CI = confidence interval; SD = standard deviation; VAS = visual analog scale.

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Table 2. Mean Change in Symptoms Between Diazepam and Meclizine for 0–30, 0–60, and 30–60 Min

	Diazepam	Meclizine	*p* Value
No.	20	20	—
Time (min)			
0–30	18.7 (4.3–33.2)	24.2 (15.7–32.8)	0.49
30–60	17.2 (8.7–25.6)	15.9 (9.8–22)	0.80
0–60	35.9 (22.7–49.2)	40.2 (29.6–50.8)	0.60

hemorrhages. Additional causes are psychogenic and vertigo of unknown origin. Of these, the most common is BPPV, accounting for 17% to 41% of cases (12).

When a diagnosis of BPPV has been made in the outpatient setting, many experts advocate for the first-line therapy of a canalith repositioning procedure (CRM) (12–14,16). However, the ED literature is less clear on this issue. The preponderance of CRM studies of effectiveness for BPPV were completed in outpatient non-ED settings (12–15). An emergency medicine evidence-based medicine analysis identified ED setting studies (17). However, questions were raised regarding the effectiveness of CRM for BPPV in the ED setting (9,17,18).

Pharmacologic treatment of vertigo, including cases of BPPV, have been well described and are numerous (8,19–21). These include anticholinergics, antihistamines, antiemetics, benzodiazepines, calcium channel antagonists, betahistadine, gentamycin, corticosteroids, droperidol, and others (8,9,19,21–23). Of these agents, two of the most commonly used in patients with symptomatic vertigo are diazepam and meclizine (23,24). Few clinical studies have addressed their usefulness for treating ED patients with vertigo (14). We are not aware of any studies that have compared the effectiveness of these agent head to head. The results of our study were that there was no treatment advantage of one over the other. Sixty minutes after study drug administration (diazepam or meclizine), there was no difference in the mean reductions of VAS vertigo scores between the two ($p = 0.60$). In addition, we did not show any statistical differences in other meaningful outcomes, such as incidence of headache, nausea, hearing changes, worsening symptoms with movement, and nystagmus.

Both diazepam and meclizine have a long history of use in the treatment of vertigo and act as vestibular suppressants to alleviate symptoms. Diazepam has neuroinhibitory effects through gamma-aminobutyric acid receptors at the vestibular level (8,10,21,23,25). Meclizine has anticholinergic effects on acetylcholine receptors at the vestibular apparatus (12,21,25,26).

Both agents were associated with fairly rapid (<60 min) improvement of vertigo scores in our patients. Although they have different methods of suppressing vestibular responses, they appear to have similar efficacy in their usage in the ED for peripheral vertigo.

Limitations

This study had several limitations. The sample size was relatively small. Despite sample size calculations being performed, a larger sample size may have identified small differences that may have existed between these agents. In addition, a larger sample size may have identified differences in side effects between the two agents.

Another significant issue is that our main study outcome measure, vertigo VAS assessment at 60 min, is not the end point of the disease process. Assessment several days or weeks after discharge from the ED may have given us additional useful information. However, ED assessment of vertigo focuses on ruling out serious causes of vertigo and rapid symptomatic improvement. Improvement in patient symptoms allow for ED discharge and referral for follow-up and definitive diagnosis and treatment.

Future Considerations

Although our study addresses the question regarding the treatment of vertigo with diazepam versus meclizine, a number of other issues regarding this topic need additional consideration. Much of the literature on this topic has been performed in the outpatient, non-ED setting. More studies looking at this patient population are needed.

Another area that needs to be addressed is the most optimal method of ED neurologic assessment to differentiate peripheral from central causes of vertigo. The current emergency medicine standard of care focuses on ruling out serious diseases, such as the serious central causes of vertigo (4–7). Although neurologic assessments focused on eye movements may be able to almost eliminate the possibility of a serious central nervous system causes, the additional training and potential extra equipment involved may not be practical in all EDs (3–7,26).

Finally, our study only looked at symptomatic treatment of vertigo in the ED in a time frame that was important for ED diagnosis, treatment, and disposition. Future work could look at effectiveness ≥24 hours after treatment.

CONCLUSIONS

Oral diazepam and oral meclizine were effective agents in the treatment of severe peripheral vertigo presenting to an ED. Both were found to be equally effective as first-line therapy.

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ARTICLE SUMMARY

1. Why is this topic important?

Vertigo is a common complaint in the emergency department (ED), and both diazepam and meclizine are commonly used treatments for vertigo. This study attempts to find out which agent is better for these patients.

2. What does this study attempt to show?

This study, using a double-blind randomized controlled trial design, attempted to determine which agent (diazepam or meclizine) was superior as therapy for patients with vertigo in the ED.

3. What are the key findings?

This study showed that both agents significantly improved patients with vertigo in the ED within the first hour of treatment. However, neither agent was superior to other.

4. How is patient care impacted?

This study allows clinicians to continue using either diazepam or meclizine as therapies for patients with vertigo in the ED.

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