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Comparison of the effectiveness of intravenous piracetam and intravenous dimenhydrinate in the treatment of acute peripheral vertigo in the emergency department

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INTRODUCTION We aimed to compare the effectiveness of intravenous piracetam with that of intravenous dimenhydrinate in the treatment of acute peripheral vertigo in the emergency department.

METHODS This double-blind study comprised a total of 200 patients, aged between 18 and 70 years, who had presented to the emergency department of Ankara Training and Research Hospital and were diagnosed with peripheral vertigo. Evaluation of the severity of the patients' vertigo was performed using a visual analogue scale, before and after drug administration.

RESULTS Both drugs were found to be effective ($p < 0.001$) and had comparable effects ($p < 0.474$). Dimenhydrinate was also found to have about two times the side effects of piracetam. Drowsiness was found to be the most common side effect of these two drugs.

CONCLUSION Dimenhydrinate and piracetam have similar levels of effectiveness with regard to acute vertigo. We conclude that piracetam, which has fewer side effects than dimenhydrinate, better vestibular compensation, and is effective for both acute and chronic vertigo, could be more frequently used in the emergency treatment of acute vertigo.

Keywords: dimenhydrinate, emergency department, peripheral vertigo, piracetam

INTRODUCTION

Vertigo and balance disorders are common causes of emergency department admissions. Vertigo may be of peripheral or central origin, and can be treated symptomatically or by treatment of the underlying disease. Many different types of drugs have been used to treat vertigo of peripheral origin, including antihistamines, anticholinergics, benzodiazepines, calcium channel blockers, antiemetics, vasodilators and piracetam.[1] It has been suggested that the use of vestibular suppressants such as antihistamines, anticholinergics and benzodiazepines should last no longer than several days because of their potential to delay vestibular compensation (i.e. recovery), the main mechanism that treats vertigo. In contrast to vestibular suppressants, piracetam increases vestibular compensation. Although the effectiveness of piracetam in treating vertigo has already been proven in a large number of studies, there are limited reports on its effectiveness in the symptomatic treatment of acute vertigo.[1-3] In Turkey, piracetam is not widely used in the acute treatment of peripheral vertigo in the emergency departments of hospitals, including ours.

We conducted this prospective study to address the lack of recent literature on the effectiveness of piracetam in the treatment of acute peripheral vertigo. In the present study, we aimed to compare the effectiveness of intravenous piracetam with that of intravenous dimenhydrinate in the treatment of acute peripheral vertigo in the emergency department.

METHODS

Between May 2010 and January 2011, 200 patients aged 18–70 years, who presented to the Department of Emergency Medicine, Ankara Training and Research Hospital, Turkey, with the chief complaint of vertigo and were diagnosed with peripheral vertigo, were included in this prospective, randomised double-blind study. Patients aged > 70 years were not included in the study, as central vertigo is more frequently encountered in these patients. Informed consent was obtained from all patients who met the inclusion criteria of the study. Written approval for the study was obtained from the Turkish Ministry of Health, Drug and Pharmaceutical Directorate, Clinical Drug Research Ethics Board.

The exclusion criteria were pregnancy, history of allergic reaction or contraindication to any of the test drugs, and history of enrolment in a previous clinical drug trial. In addition, a senior emergency medicine resident evaluated all patients who presented with complaints related to vertigo. Detailed histories of all the patients were obtained, and detailed physical examination was performed, including neurological and ear, nose and throat examinations. Laboratory studies conducted focused on patients' haemograms, biochemistry, cardiac enzymes

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Table I. Characteristics of patients and side effects of drugs.

Characteristic	No. of patients		p-value
	Treated with dimenhydrinate (n = 100)	Treated with piracetam (n = 100)	
Age* (yrs)	44.7 ± 16.1	45.6 ± 16.1	0.710
Gender (female/male)	77/23	74/26	0.622
Past history of vertigo	48	43	0.478
Systemic pathology	–	1	–
Neurologic pathology	11	12	0.825
Nystagmus	10	12	0.651
Pretreatment VAS*	7.78 ± 2.04	7.37 ± 2.18	0.171
Side effects			
None	64	78	0.029
Weakness	26	15	0.054
Drowsiness	2	–	0.497
Dizziness	8	7	0.788

*Data is expressed as mean ± standard deviation. VAS: visual analogue scale

and blood gases. Electrocardiography and cranial computed tomography were also performed. Based on these evaluations, patients found to suffer from vertigo due to dehydration, anaemia, carbon monoxide poisoning and cardiac pathologies were excluded from the study. All included patients received an initial diagnosis of peripheral vertigo based on their history, physical examination findings, consultation reports, and laboratory and other study results. Medical history, physical examination findings, severity of vertigo (evaluated before and after treatment via a visual analogue scale [VAS]) and observed side effects were recorded for all patients.

Dimenhydrinate (50 mg/5 mL) and piracetam (1,000 mg/5 mL) were dissolved in physiological saline in fresh 5-mL syringes daily. Ten syringes containing either dimenhydrinate (n = 5) or piracetam (n = 5) were prepared daily. Before receiving randomised, double-blind treatment of either dimenhydrinate or piracetam, all patients were evaluated using VAS. Syringes containing dimenhydrinate or piracetam were injected into 500 mL of physiological saline solutions, and the drugs were infused over one hour. Subsequently, the researcher conducted a post-infusion VAS evaluation on the patients and recorded the presence of any side effects such as drowsiness, weakness and dizziness. Side effect evaluation was performed only once following the first drug administration. In total, 100 patients were treated with dimenhydrinate and another 100 with piracetam. No other drugs were administered during the first hour unless emergently indicated. Randomisation of the patients was performed by a member of the emergency department who was not involved in the study. Emergency physicians, residents and nurses were given instructions pertaining to the study's protocols and evaluation of patients with vertigo during a two-hour education conference before the study commenced. Patients who did not benefit from the first treatment received additional, random, double-blind treatment in similar doses. After additional treatments, patients were re-evaluated via VAS.

In order to detect a minimal difference of 1.5 points in the mean changes of VAS scores between the two treatment groups with a power of 90% and where p = 0.05 was considered significant, a sample size of 98 patients per group was required. Estimation of the sample size was performed using NCSS and Power Analysis and Sample Size 2000 softwares (NCSS Statistical Software, Kaysville, UT, USA).

Data analysis was performed using the Statistical Package for Social Sciences for Windows version 11.5 (SPSS Inc, Chicago, IL, USA). Mean ages were compared using Student's *t*-test. Mann-Whitney *U* test was applied for comparison of VAS scores. Categorical data were evaluated using either Pearson's chi-square test or Fisher's exact test, where applicable. Statistical significance of the differences between pre- and post-treatment VAS score was evaluated using Wilcoxon signed-rank test. Relative risk (RR) and 95% confidence interval (CI) were calculated to compare the frequencies of adverse events in the two treatment groups. A p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 200 consecutive patients, who presented with a chief complaint of vertigo and were subsequently diagnosed with peripheral vertigo, were included in the present study. The mean age of the study population was 45 (range 18–70) years. Of the 200 patients, 151 (75.5%) were female and 49 (24.5%) were male. Comparing the dimenhydrinate and piracetam treatment groups, we found no significant relationships in the two treatment groups' age, gender, past medical history, presence of nystagmus, systemic examination results, neurological examination results, pretreatment VAS scores and side effects (Table I). The VAS scores of the patients were labelled as: (a) 1st VAS score (before treatment); (b) 2nd VAS score (after treatment); and (c) 3rd VAS score (after any additional treatment). The differences between the 1st and 2nd VAS scores, and the 2nd and 3rd VAS scores were categorised as the 1st and 2nd VAS score differences, respectively. Comparing the 1st and 2nd VAS scores of each drug, a statistically significant difference between the two VAS scores was found ($p < 0.001$). Both drugs were able to decrease the patients' 1st VAS

Table II. Comparison of the 1st and 2nd VAS scores of the patients.

Treatment group	Mean ± SD		p-value
	1st VAS score	2nd VAS score	
Dimenhydrinate (n = 100)	7.78 ± 2.04	2.60 ± 3.03	< 0.001
Piracetam (n = 100)	7.37 ± 2.18	2.37 ± 2.63	< 0.001
p-value	0.172	0.929	

SD: standard deviation; VAS: visual analogue scale

Table III. Comparison of the 3rd VAS scores of patients who underwent additional treatment.

Additional treatment	3rd VAS score*
Dimenhydrinate (n = 46)	2.37 ± 2.37
Piracetam (n = 29)	2.41 ± 1.82
p-value	0.266

*Data is expressed as mean ± standard deviation. VAS: visual analogue scale

Table IV. Comparison of the 2nd and 3rd VAS scores of the patients who underwent additional treatment.

Additional treatment	Mean ± SD		p-value
	2nd VAS score	3rd VAS score	
Dimenhydrinate (n = 46)	4.65 ± 2.14	2.37 ± 2.37	< 0.001
Piracetam (n = 29)	6.66 ± 2.13	2.41 ± 1.82	< 0.001

SD: standard deviation; VAS: visual analogue scale

scores, confirming their effectiveness ($p < 0.001$). However, there was no difference between the mean values of the 1st VAS scores ($p = 0.172$), and the 2nd ($p = 0.929$) VAS scores of both the dimenhydrinate and piracetam groups (Table II). No statistically significant difference was found between the 1st VAS score differences of the dimenhydrinate and piracetam groups ($p = 0.474$), thus confirming similarity in their effectiveness.

Additional treatment was required in 75 (37.5%) patients – 46 (23.0%) patients were treated with dimenhydrinate, while 29 (14.5%) were treated with piracetam. There was no statistically significant difference between the 3rd VAS scores of the dimenhydrinate and piracetam groups ($p = 0.266$) (Table III). Significant differences ($p < 0.001$) were observed between the 2nd and 3rd VAS scores of the two treatment groups, further confirming the effectiveness of both drugs (Table IV). Side effects observed in the patients were also evaluated at the end of the first treatment. Of the 100 patients treated with dimenhydrinate, 36 experienced side effects – 26 (26.0%) reported drowsiness, 8 (8.0%) dizziness and 2 (2.0%) fatigue. Similar side effects were also recorded in 22 patients treated with piracetam (drowsiness [n = 15, 15.0%] and dizziness [n = 7, 7.0%]) (Fig. 1). The risk for side effects was higher in patients treated with dimenhydrinate compared to those treated with piracetam (RR 1.219, 95% CI 1.018–1.459) (Table V).

DISCUSSION

Vertigo is a symptom that is difficult to diagnose and treat, and its treatment can be either symptomatic or specific.[4] The

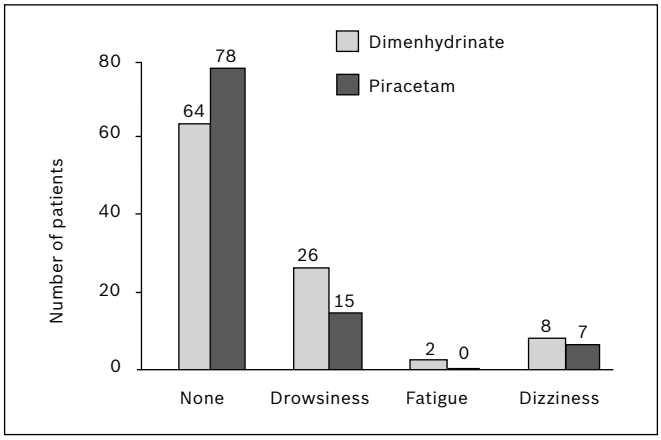

Fig. 1 Graph shows the incidence of side effects in the two treatment groups.

recommended ideal drug treatment should: (a) eliminate vertigo and the associated symptoms that discomfort the patient; (b) increase vestibular compensation; (c) possess minimal side effects and drug interactions; and (d) have the potential to be used to treat the aetiology of vertigo in both acute and chronic periods.[5,6] Females are affected twice as often as males in benign paroxysmal positional vertigo (BPPV).[7] Vertigo was also more frequently observed (61%–66%) in females in a number of previous reports.[8-10] Similarly, our study showed a higher incidence of vertigo in females (75.5%).

In the present study, when the 1st and 2nd VAS scores of the patients in both the dimenhydrinate and piracetam treatment groups were compared, a statistically significant difference was found between the two VAS scores for each drug ($p < 0.001$) (Table ll). A significant decline in the VAS scores of the patients was found after treatment with either dimenhydrinate or piracetam. This finding not only demonstrates the effectiveness of both drugs in the treatment of vertigo, but also highlights the comparable effectiveness of both drugs ($p < 0.001$).

Piracetam is known to be effective in the treatment of vertigo of peripheral and central origin,[11,12] as it increases vestibular compensation and central control of the patient's balance centres. Additionally, piracetam potentiates the effects of sedative drugs and antihistamines. Many previous studies have shown that piracetam accelerates spontaneous recovery in acute vertigo and stabilises adaptation in chronic vertigo.[2,3,13] Furthermore, piracetam decreases the frequency of episodes in patients with chronic recurrent vertigo.[13] All these effects of piracetam positively contribute to the development of chronic compensation.

The mean age of patients with vertigo in a study by Arya and Nunez[10] was 52.6 years, and in a larger series, the mean age of patients with BPPV was reported to be 50 years.[14,15] In our study, the mean age of our patients was 45 years, with vertigo observed mostly in the fifth decade of life (24%). In the piracetam treatment group, the 1st VAS score differences of the subgroups of patients below and over 40 years of age were comparable ($p = 0.189$). Therefore, piracetam was deemed to

Table V. Chi-square comparison of drug side effects experienced in patients (n = 200) after treatment.

Treatment group	No. of patients (%)	
	Side effects absent	Side effects present
Dimenhydrinate (n = 100)	64 (64)	36 (36)
Piracetam (n = 100)	78 (78)	22 (22)
Total (n = 200)	142 (71)	58 (29)

have similar effectiveness in those age groups. Previous studies in the literature, such as Winblad's review,[16] have documented the fact that piracetam has a greater effect on cell membrane fluidity in cases where regular cell membrane fluidity is endangered (e.g. in the geriatric population). Comparing the mean ages of the patients in different studies in which piracetam treatment was evaluated, most patients were noted to be over 55 years of age.[2,17] However, we could not demonstrate any relationship between age and drug effectiveness in the piracetam treatment group in our study.

In the present study, 75 (37.5%) patients needed additional treatment with either dimenhydrinate (23.0%) or piracetam (14.5%) because they did not benefit from the initial treatment. Both dimenhydrinate and piracetam were found to be effective when used in these re-treated patients. However, we found that when piracetam was used in re-treated patients, it was able to decrease patients' 2nd VAS scores more effectively than dimenhydrinate ($p < 0.001$). This finding may be due to the potentiating effect of piracetam on sedative and antihistamine drugs, which inhibit inputs from the vestibular system. The effectiveness of piracetam in the treatment of vertigo is thought to be the result of its effects on neurotransmission and microcirculation.[16] Since piracetam interacts additively with antihistamines, response to treatment in acute vertigo may be accelerated by concurrent or sequential piracetam use.

In our study, patients treated with dimenhydrinate presented more side effects than those treated with piracetam ($p = 0.029$; RR [95% CI] = 1.219 [1.018 – 1.459]). In patients treated with dimenhydrinate, the risk of side effects occuring was approximately twice that of the piracetam treatment group. Dimenhydrinate-related anticholinergic side effects such as somnolence, sedation, dry mouth, and in rare cases, tremor and gastrointestinal side effects, can be observed.[18] In a previous study, diphenhydramine and dimenhydrinate treatments were reported to induce greater sedation than diazepam within 60 mins.[4] In line with this finding, the most frequent side effect in our study was drowsiness. It is mentioned in the literature that side effects such as depression (rare, less than 2%), nervousness, somnolence, hyperkinesia and tremor can be observed after piracetam treatment.[13] However, based on our results, drowsiness was detected in only 15% of our patients who were treated with piracetam.

One of the limitations of our study was that the length of stay in the emergency department, based on side effects of the drugs and their influence on discharge decision, were not recorded. However, our study found that dimenhydrinate and piracetam have similar levels of effectiveness in the treatment of acute vertigo. We thus conclude that piracetam could be more frequently used in the treatment of acute vertigo in the emergency department, as it has fewer side effects and better vestibular compensation than dimenhydrinate, and is effective in both acute and chronic vertigo.

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