Original Research

Oral Piracetam vs Betahistine in Outpatient Management of Peripheral Vertigo; a Randomized Clinical Trial

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Abstract: Introduction: Although vertigo is a common complaint in patients presenting to the emergency department (ED), its ideal treatment is still under debate. This study was conducted to compare oral betahistine and oral piracetam in management of outpatients with peripheral vertigo. Methods: This was a randomized clinical trial performed on patients who were presented to the EDs of 4 teaching hospitals, with complaint of true vertigo. Patients were randomly allocated to either betahistine or piracetam group and their 7-day outcomes were compared. Results: 100 cases with the mean age of 54.72 ± 14.09 years were randomly allocated to either group (62.0% female). The two groups were similar regarding age, sex, and intensity of symptom at the time of presenting to the ED. Twelve (24%) patients in piracetem group and 6 (12%) patients in betahistine group experienced adverse events (odds ratio: 2.32, CI 95%: 0.79-6.76; p = 0.125). There were 3 (6%) patients in each group that experienced a recurrence of their symptoms and 2 (4%) patients in each group saw another physician for vertigo. Conclusion: Oral piracetam is a potentially proper treatment for management of peripheral vertigo and there are few adverse effects associated with it.

Keywords: Vertigo; piracetam; betahistine; emergency medicine; treatment outcome


1. Introduction

Vertigo is an illusion of movement when there is no motion (1, 2). It is a common complaint in patients presenting to the emergency department (ED) and categorized as peripheral or central vertigo (1-3). Although ideally the underlying cause of vertigo should be treated, peripheral vertigo is usually treated symptomatically. Different drugs from various pharmacologic categories are used to treat peripheral vertigo, including antiemetics, anticholinergics, antihistamines, and calcium channel blockers. Despite the availability of various options for symptomatic treatment of vertigo, a drug of choice has not been defined yet. There are sometimes paradoxical data on the effectiveness of each drug for symptomatic treatment of vertigo (1, 4). Betahistine is one of the common medications, which is currently used to treat peripheral vertigo. Piracetam is a cyclic derivative of neurotransmitter gamma-aminobutyric acid, which might be effective in treatment of vertigo (5-10).

By using the combination of betahistine and piracetam in management of peripheral vestibular vertigo Oleg and colleagues concluded that this combination may be more effective than piracetam alone in this regard (11). Intravenous piracetam was as effective as intravenous dimenhydrinate in relieving symptom of vertigo patients in Dugan et al. study (12). However, the evidence regarding effectiveness of oral piracetam after acute manifestation of peripheral vertigo is sparse. Therefore, this study aimed to compare oral betahistine and oral piracetam in outpatient management of peripheral vertigo.

2. Methods

2.1. Study design and setting

This randomized clinical trial was conducted on patients who presented to the emergency departments of Imam Hossein, Shohadaye Tajrish, Loghman Hakim and Sina Hospitals, Tehran, Iran, throughout 2016, complaining from true vertigo. All of these hospitals are teaching hospitals. Ethan...
ical approval was obtained from Shahid Beheshti medical University ethics committee (IR.SBMU.SM.REC.1394.25) and the study was registered on Iranian registry of clinical trials with code number: IRCT2016011921063N3. Informed consent was obtained from each patient prior to his or her enrollment in the study.

2.2. Participants

Patients with acute vertigo who were discharged from the emergency department were included. Exclusion criteria were age below 18 years, prior history of sensitivity to betahistine or piracetam, consumption of drugs which can possibly improve vertigo (antihistamines, benzodiazepines or anticholinergics), history of peptic ulcer disease or pheochromocytoma, patients who did not give consent to participate in the study, patients with central vertigo and patients who were lost to follow-up.

2.3. Intervention

Patients were enrolled using convenience sampling method and were randomly assigned to either piracetam or betahistine group. Upon discharge, piracetam group patients received 800 mg piracetam tablets (Darou Pakhsh Pharma Chem Co., Tehran, Iran) every 8 hours for 7 days and betahistine group patients received 8 mg betahistine tablets (Betaserc®, Abbott Healthcare SAS, Châtillon-sur-Chalaronne, France) every 8 hours for 7 days. Simple randomization was done using a random numbers table, which was generated using Stattrek website “http://stattrek.com/statistics/random-number-generator.aspx”.

2.4. Outcomes

The primary outcome was vertigo intensity control 7 days after discharge from ED. The secondary outcomes were nausea and fatigue intensities control 7 days after discharge from ED, drug compliance, and adverse events.

2.5. Data gathering

Data were acquired using face to face interview with patients at the times of presenting to ED and discharge from ED and using telephone interview 7 days after discharge. Patients’ vertigo, nausea, and fatigue intensities were investigated using 10-point numeric rating scale (NRS). We asked patients about their compliance (taking piracetam or betahistine) using 5-point Likert scale and the occurrence of any complication while taking medications. Patients were asked about the recurrence of their vertigo symptoms, visiting another physician for vertigo or requiring hospitalization because of vertigo during the 7-day period after discharge from ED. An emergency physician and a 3rd year emergency medicine resident were responsible for patients’ allocation and data gathering. The prescribing physicians and the patients were not blinded. However, both the physician who interviewed the patients 7 days after their discharge and the statistical analyst were blinded to the prescribed drug.

2.6. Statistical Analysis

We analyzed data using SPSS software version 21 and intention to treat analysis method. Categorical data were analyzed using chi-square or Fisher’s exact tests. Quantitative data were analyzed using t-test, Mann-Whitney or Kruskal-Wallis tests. The sample size of 48 patients in each group was calculated. Failure to control symptoms was defined as score ≥ 3 7 days after taking medicines. P < 0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

One hundred twenty-two patients were assessed for eligibility, out of which 18 cases were excluded for various reasons (flowchart 1). There were 4 (3.8%) cases of loss to follow up. Finally, 100 cases with the mean age of 54.72 ± 14.09 (18-90) years were randomly allocated to each group (62.0% female). Baseline characteristics of the studied patients are compared in table 1. The two groups were similar regarding age, sex, and intensity of symptom at the time of presenting to the emergency department and discharge.

3.2. Outcome

There were no statistically significant differences between two groups regarding intensity of vertigo, nausea and fatigue 7 days after discharge from ED. Twelve (24%) patients in piracetam group and 6 (12%) patients in betahistine group experienced adverse events (odds ratio: 2.32, CI 95%: 0.79-
Table 1: Baseline characteristics of the studied patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Piracetam n=50</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>56.36 ± 12.92</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male 21 (42.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female 29 (58.0)</td>
<td></td>
</tr>
<tr>
<td>Intensity of symptom (on presentation)</td>
<td>8.36 ± 1.98</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.44 ± 1.63</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>8.24 ± 2.50</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>4.98 ± 3.18</td>
<td></td>
</tr>
<tr>
<td>Intensity of symptom (on discharge)</td>
<td>1.82 ± 1.08</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.58 ± 0.73</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>1.22 ± 0.55</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>1.42 ± 1.07</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation or frequency (%).

Table 2: Comparing the outcomes between the two groups 7 days after discharge from emergency department

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Groups</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Piracetam n=50</td>
<td></td>
</tr>
<tr>
<td>Vertigo Intensity</td>
<td>1.78 ± 1.38</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.84 ± 1.20</td>
<td></td>
</tr>
<tr>
<td>Success</td>
<td>48 (96.0)</td>
<td></td>
</tr>
<tr>
<td>Failure*</td>
<td>2 (4.0)</td>
<td></td>
</tr>
<tr>
<td>Nausea Intensity</td>
<td>1.12 ± 0.52</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.10 ± 0.21</td>
<td></td>
</tr>
<tr>
<td>Success</td>
<td>49 (98.0)</td>
<td></td>
</tr>
<tr>
<td>Failure*</td>
<td>1 (2.0)</td>
<td></td>
</tr>
<tr>
<td>Fatigue Intensity</td>
<td>1.28 ± 0.67</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.36 ± 1.41</td>
<td></td>
</tr>
<tr>
<td>Success</td>
<td>49 (98.0)</td>
<td></td>
</tr>
<tr>
<td>Failure*</td>
<td>1 (2.0)</td>
<td></td>
</tr>
<tr>
<td>Drug compliance</td>
<td>4.52 ± 0.58</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.58 ± 0.50</td>
<td></td>
</tr>
<tr>
<td>Adverse events</td>
<td>12 (24.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 (12.0)</td>
<td></td>
</tr>
</tbody>
</table>

*: score ≥ 3 seven days after discharge. Data are presented as mean ± standard deviation or frequency (%).

4. Discussion

Based on the findings, there was not any significant difference between oral betahistine and oral piracetam regarding recurrence, relieving vertigo, nausea, and fatigue symptoms 7 days after discharge from ED. Adverse events in the two groups were comparable as well. Despite being a common presentation in both ED and general settings, the ideal treatment for vertigo is still under debate (1, 4). Betahistine dihydrochloride is a drug with structural similarity to histamine (13, 14). Betahistine is a strong H3 receptor antagonist and a weak H1 receptor agonist, which is relatively inactive at H2 receptor (13-15). Betahistine increases cochlear blood flow via H3 receptor antagonism (16). It also increases histamine turnover in central and vestibular nervous systems and decreases vestibular sensory input through the same mechanism. Betahistine has excitatory effects on cortical and sub-cortical neuronal activity by H1 receptor agonist (13-15). Betahistine has been used for treating vertigo for years and its effectiveness was shown in many studies (7, 13-15, 17-22). In a Cochrane review conducted by Murdin, 16 studies comparing betahistine and placebo in different vertigo types were included. Pooled data showed that betahistine was better than placebo in reducing vertigo symptoms and the proportion of patients reporting an overall reduction of their vertigo symptoms was higher in the betahistine group (risk ra-
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5. Limitation

The patients and allocating physician were not blinded to the prescribed drugs. There was no placebo group in the study. We cannot rule out the probability of spontaneous recovery of vertigo, nausea and fatigue symptoms of the patients in the seven-day period after the initial presentation to ED. Because of the small sample size and differences in the settings of previous studies, it is hard to reach a definite conclusion about the role of piracetam in vertigo treatment. It seems that there is a need for larger, multicenter studies and meta-analyses for a strong conclusion.

6. Conclusion

Based on the findings, there was not any significant difference between oral betahistine and oral piracetam regarding recurrence, relieving vertigo, nausea, and fatigue symptoms, as well as adverse events 7 days after discharge from ED.

7. Appendix

7.1. Acknowledgements

The authors wish to thank all Emergency Department staff of Imam Hossein, Shohadaye Tajrish, Loghman Hakim and Sina Hospitals for their contribution. This article is extracted from the residency thesis of Seyedeh Roghieh Larimi.

7.2. Author contribution

Ali Arhami Dolatabadi: idea development, and supervising the team.
Seyedeh Roghieh Larimi: patient allocation, initial interview, and writing the manuscript.
Arash Safaie: follow up interview with the patients, statistical analysis, and writing the manuscript.

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7.3. Funding/Support

None.

7.4. Conflict of interest

None.

References


