Observation on the Therapeutic Effect of Vincamine Sustained-Release Capsules on Vestibular Vertigo

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The study aimed to observe the effect of vincamine sustained-release capsules on the efficacy of patients with vestibular vertigo. 101 patients with vestibular vertigo were randomly divided into two groups, control group (n=51) and vincamine group (n=50); betahistine mesylate tablets (Minshilang) and vincamine sustained-release capsules (Orbran) were given to control and vincamine groups, respectively. The scores of dizziness disability inventory and patient health questionnaire were observed before treatment and after 1 w and 1 mo of treatment, and its influence on vertigo and depression in the two groups was evaluated as well. The data analysis showed that the number of females in the control group was significantly higher than that in males, indicating that the incidence of this disease is higher in females than in males. Dizziness handicap inventory scores of patients of two groups were analyzed and the results showed no significant difference between the groups (F=0.91 and p=0.343); there is a significant difference between different time points (F=427.42 and p=0.000) and interaction between therapeutic drugs at the same time (F=14.74 and p=0.000). Further analysis of the individual effects showed that there was no significant difference between the two groups before treatment (p=0.203), while there was a significant difference between the groups after 1 w and 1 mo of treatment (p<0.01). The patient health questionnaire 9 scores in two groups were analyzed and the results showed no significant difference between the groups (F=0.06 and p=0.938). There was a significant difference between different time points (F=150.13 and p=0.000) and interaction between therapeutic drugs at the same time (F=13.61 and p=0.000). Further analysis of the individual effects showed a significant difference (p<0.05) between the two groups before treatment. The depression level in the vincamine group was higher than that in the control group with no significant difference between the groups after 1 w of treatment (p=0.368). There was a significant difference (p<0.05) between the two groups after 1 mo of treatment and the depression level in the vincamine group was lower than that in the control group. The use of vincamine in the treatment of vestibular vertigo is more effective in controlling dizziness and depression over time than betahistine mesylate and has a long-term effect which is worthy of clinical promotion.

Key words: Vincamine, vertigo, betahistine mesylate, benign paroxysmal positional vertigo, neurology

Vertigo is one of the most common symptoms in neurology, which is the disturbance of orientation or balance of human body to the surrounding environment space. Vertigo can be divided into vestibular vertigo and non-vestibular vertigo, in which the incidence of vertigo caused by vestibular dysfunction accounts for >80 % worldwide[1]. Patients with vertigo have the feeling of rotation, dumping and ups and downs during the attack, and are closely related to the occurrence of depression[2]. In severe cases, the disorder affects life and social interaction. Vincamine is one of the commonly used drugs for clinical treatment of vertigo. It has the effects of improving brain energy metabolism, increasing cerebral blood flow, improving fundus and inner ear circulation, and improving cognition as well[3]. However, the exact functions of vincamine for vertigo patients especially for the espects of vertigo symptoms controlling, anxiety and depression remain unclear. In this work, 101 cases of vertigo patients in our hospital were recruited to explore the effects of vincamine in controlling vertigo symptoms and anxiety and depression over time, and to provide a theoretical basis for clinical drug selection. 200 patients with vestibular vertigo admitted to the outpatient

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department of the First Affiliated Hospital of Zhengzhou University from August 2020 to February 2021 were considered and 101 patients were actually included, among which 25 were males and 76 were females, aged from (24-78) y old. All the individuals were randomly divided into two groups, control group (n=51) and vincamine group (n=50). There was no significant difference in age, gender and condition between the two groups. Betahistine mesylate tablets were currently recommended for vestibular vertigo patients in clinic. All the individuals in control group were administrated with betahistine mesylate tablets while the vestibular vertigo patients in observation group were given vincamine medicine. The patients who had abnormal vestibular function measurement and patients with informed consent were considered as inclusion criteria of the study. Similarly the patients with history of no stroke, brain tumor and other intracranial diseases in the past; pregnant patients and patients having diabetes, drug allergy and vertigo caused by other reasons were excluded. In treatment method, all the individuals from control group were given betahistine mesylate tablets (Eisai China Pharmaceutical Co., Ltd., production batch number 2010033), 3 times/day and 1 tablet each time. At the same time, the individuals from vincamine group were given vincamine sustained-release capsules (Yantai Luyin Pharmaceutical Co., Ltd., batch number 120121411), twice a day, 1 tablet each time. Outcome measures of all the patients such as Dizziness Handicap Inventory (DHI) and Patient Health Questionnaire (PHQ) 9 scores were evaluated for at three time points (before and after 1 w and 1 mo of treatment), according to the quantitative score to evaluate the therapeutic effect of patients. DHI is generally used to evaluate the degree of vertigo. The scale was developed in the Department of Audiology, Henry Ford Hospital, United State of America. It includes three dimensions namely, body, function and emotion. It can evaluate the overall quality of life of vertigo patients and the specific situation of each dimension; evaluation of vertigo has a good representation[4]. Similarly PHQ-9 is the primary tool for assessing depressive status in healthcare settings, which is convenient and concise to use, has repeatability, high specificity, sensitivity, and strong self-evaluation credibility[5]. Further, statistical analysis of the collected data was carried out. Statistical Package for Social Sciences (SPSS) version 21.0 software was used to analyze the data and normality test was carried out to determine whether the data has been drawn from normal distribution. The measurement data was expressed as mean±standard deviation (x±s) and were processed by repeated measures analysis of variance where $p<0.05$ was considered to be statistically significant. Gender parity between the two groups was compared. The results indicated that the number of female patients in the control group were significantly more than that of vincamine group, suggesting that the prevalence of the disease in women was more than that in men, with gender differences, as shown in Table 1. DHI scores between two groups after treatment were compared. Overall, as shown in Table 2, there was a significant difference between different time points ($F=427.42$ and $p=0.000$). There was an interaction between the two drugs at the same time ($F=14.74$ and $p=0.000$), which indicated that the trend of the total value was different with an increase of different drugs with time. Further, analysis of the single effect showed that there was no significant difference between the two groups before treatment ($p=0.203$), but there was a significant difference in the two groups at 1 w and 1 mo after treatment ($p<0.01$); vincamine group was better than control group. PHQ-9 scores between the two groups after treatment were compared. As shown in fig. 1, there was a remarkable difference between different time points ($F=150.13$ and $p=0.000$) in PHQ-9 evaluation. There was an interaction between the treatment drugs at the same time ($F=13.61$ and $p=0.000$), suggesting that the change in trend of the questionnaire value was different with the increase of different treatment drugs over time. Subsequently, analysis of the individual effects showed a remarked difference between the two groups before treatment ($p<0.05$), and the depression degree of the vincamine group was higher than that of the control group. There was no significant difference between the two groups at 1 w after treatment ($p=0.368$), however there was a significant difference between the two groups at 1 mo after treatment ($p<0.05$). The depression degree of the vincamine group was lower than that of the control group. There were also an obvious difference at different time points in each group ($p<0.01$). Over time, the effect of vincamine in

controlling depression was better than that of the control group. Vertigo is the spatial orientation of the human body or the balance barrier and is often considered as a kind of movement illusion[6], of which vestibular peripheral vertigo is an important part. Vestibular peripheral vertigo caused by vestibular organ and vestibular neuropathy which is often rotary, having short duration and strong vertigo and is accompanied by cochlear symptoms and autonomic symptoms[7] such as Benign Paroxysmal Positional Vertigo (BPPV), Meniere's disease and labyrinthitis, etc. Patients with vertigo often display dizziness, head swelling, headache, rotation and quality of life is affected in severe cases. Similarly, most patients often show varying degrees of anxiety and depression[2]. Vestibular vertigo involves multiple disciplines where the cause is complex and the rate of misdiagnosis is high. Some primary hospital neurologists often misdiagnose vestibular vertigo as vertebrobasilar artery, insufficient blood supply, cervical spondylosis and cerebral infarction, etc., leading to repeated medical treatment[6]. At present, symptomatic treatment is the main treatment for vertigo, aiming at controlling vertigo symptoms and relieving depression. The purpose of this study was to investigate whether there was a difference in the effect of vincamine sustained-release capsule in improving vertigo, anxiety and depression compared with betahistine mesylate treatment. The results showed that the vertigo and depression of control group and vincamine group were improved after treatment, and the difference was statistically significant ($p<0.05$). Betahistine mesylate is a classical drug for relieving vertigo, which has obvious antihistamine effect, can dilate blood vessels, improve cerebral circulation[8], inner ear circulation, increase the release of transmitters from nerve endings, reduce symptoms such as dizziness, tinnitus and nausea and vomiting[9]. It is widely used in the treatment of vestibular peripheral vertigo. At the same time, vincamine is an indole alkaloid extracted from *Vinca* plants[10]. It can dilate tiny blood vessels and has the functions of protecting cochlea and vestibular function repair[11]. It can also effectively improve symptoms such as dizziness, headache, tinnitus, etc. Currently, it is mostly used treatment of cerebral arteriosclerosis, cerebral ischemia, cerebral vasospasm, cerebral thrombosis, vertigo, aphasia and Meniere's syndrome, etc. Vincamine can be widely distributed into the tissues, through the blood-brain barrier and mainly through the liver, kidney and brain metabolism without drug accumulation, showing very few adverse reactions[12]. In order to determine whether vincamine is superior to betahistine mesylate treatment in controlling vertigo and improving anxiety and depression, this study was carried out. In this study, 101 individuals were included where the age and gender of patients were not significantly different. The results of statistical analysis showed that the DHI score of vincamine group was lower than that of control group after 1 w of treatment and the difference was statistically significant ($p<0.05$), indicating that the effect of controlling vertigo between the two groups had been different at about 1 w of treatment. Vincamine has faster onset of action than betahistine mesylate treatment, which may be related to its small molecular weight, high lipid solubility, easy to penetrate the blood-brain barrier, improve local blood supply and improve sleep quality and other effects. After 1 mo of treatment, DHI score of vincamine group was lower than that of control group and the difference was statistically significant ($p<0.05$). The effect of vincamine on controlling vertigo symptoms was better than that of control group as well. In the course of this study, the anxiety and depression score of vincamine group was higher than that of control group before treatment and there was a difference ($p<0.05$). After 1 w of treatment, the difference was reduced. After treatment, the anxiety and depression score of vincamine group was lower than that of control group, with statistically significant value, $p<0.05$. The results indicated that the effect of vincamine in controlling anxiety and depression was significantly better than that of betahistine mesylate treatment. At the same time, the study has also shown that vincamine can prolong the relative and absolute values of paradoxical sleep time, promote memory enhancement, improve cognitive function and have an adjuvant therapeutic effect on anxiety control in patients with depression[13]. At present, the effect of betahistine mesylate on the improvement of anxiety and depression has not been accurately reported. In this study, anxiety and depression of patients in betahistine mesylate group also improved over time or there was an improvement in the symptoms of vertigo. In addition, female patients with vestibular vertigo

were significantly more than men in the two groups, which may be related to the higher incidence of anxiety and depression in women than men. To sum up, the use of vincamine treatment of vestibular dysfunction caused by vertigo symptoms is more beneficial than the classic treatment of betahistine mesylate. And for improving anxiety and depression, the use of vincamine treatment has a better effect. Based on the fact of unclear evaluation, combination of the two drugs betahistine mesylate and vincamine can provide relevant clinical experimental observations which have to be conducted in the near future.

TABLE 1: COMPARISON OF GENDER PARITY IN TWO GROUPS, n (%)

Gender	Control group	Vincamine group	Overall
Male	13 (25.49)	12 (24.00)	25 (24.75)
Female	38 (74.50)	38 (76.00)	76 (75.24)

TABLE 2: CHANGES OF DHI QUESTIONNAIRE SCORES IN TWO GROUPS BEFORE AND AFTER TREATMENT

Group	Before treatment	1 w after treatment	1 mo after treatment
Control	54.20±18.45	33.65±13.04	15.55±8.06
Vincamine	59.04±19.51	25.88±9.80	12.00±6.54

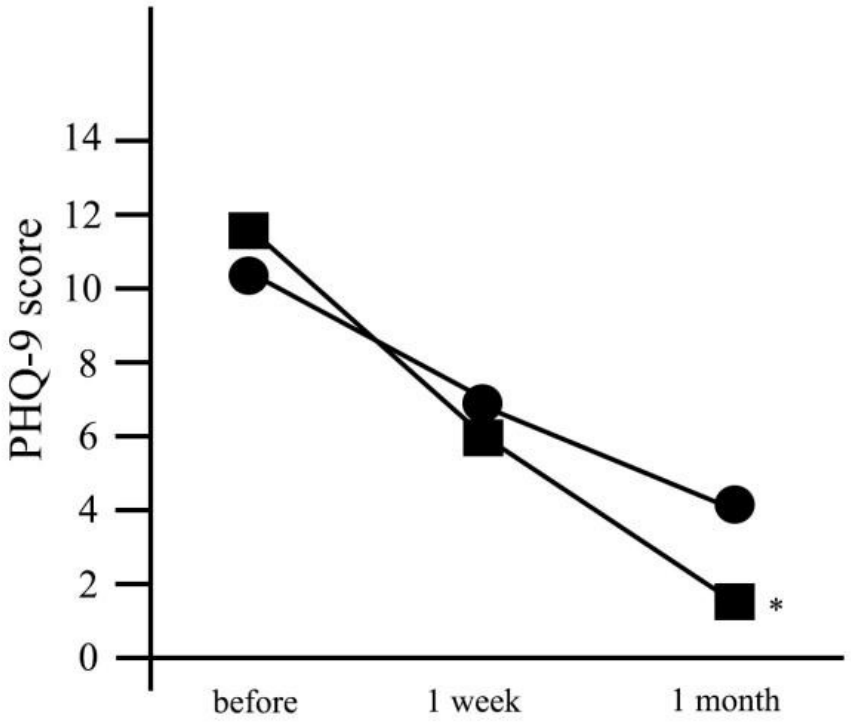

Fig. 1: Changes of PHQ-9 scores before and after treatment in the two groups
Note: *p<0.05, (●): Control group and (■): Vincamine group

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Conflict of interests:

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