Original Article

Clinical evaluation of Xiaoyao Jieyu prescription in the treatment of persistent postural-perceptual dizziness

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Highlights

Persistent postural-perceptual dizziness is a new disease name. It was proposed by Stabb and Ruckenstein on the basis of chronic subjective dizziness and phobic postural vertigo in 2014. At present, the main treatment methods of PPPD is psychotherapy, vestibular balanced rehabilitation and drug therapy, but each method has its limitations. Xiaoyao Jieyu prescription was adjusted on the basis of the ancient formula "Xiaoyao San". It can improve the clinical symptoms of patients with PPPD, which has the advantages of high efficiency, safety, low price and easy access to materials.

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Abstract

Objective: The objective of this study is to evaluate the clinical efficacy of Xiaoyao Jieyu prescription (XJP) in the treatment of persistent postural-perceptual dizziness (PPPD). **Methods**: A total of 33 PPPD patients were randomly divided into test group and control group. Two groups of patients were given psychological treatment. The test group was given XJP and the control group was given escitalopram. The course of treatment was 12 weeks. Before and after 4 weeks and 8 weeks and 12 weeks, the dizziness handicap inventory (DHI), Hamilton anxiety scale (HAMA) and Hamilton Depression scale (HAMD) were used to evaluate the treatment effect. **Results**: The total scores of HAMA, HAMD, DHI and the respective factor scores of DHI significantly decreased in both groups after 4 weeks of treatment compared with those before the treatment ($P < 0.01$). The DHI scores and the score of function, physiology at 8-week, 12-week, as well as the HAMA and HAMD scores at 4-week, 8-week, 12-week in the test group were significantly lower than those in the control group ($P < 0.05$). The incidence of adverse reactions in the test group was significantly lower than the control group ($P < 0.05$). **Conclusion**: XJP can improve the clinical symptoms of patients with PPPD. It can both improve the physical and functional symptoms of PPPD and reduce anxiety and depression. In the course of treatment, the adverse reaction of the prescription is less and mild. It has the advantages of high efficiency, safety, low price and easy access to materials.

Keywords: Chronic subjective dizziness; Persistent postural-perceptual dizziness; Xiaoyao Jieyu prescription; Anxiety; Depression

摘要

目的：评价中药逍遥解郁方（XJP）治疗持续性姿势-知觉性头晕（PPPD）的临床疗效。

方法：纳入 33 例确诊为 PPPD 的患者，随机分为试验组和对照组。两组患者均给以心理治疗。试验组给予口服逍遥解郁方，对照组给予口服艾司西酞普兰，疗程为 12 周。分别于治疗前及治疗 4 周、8 周、12 周末，采用眩晕残障程度评定量表（DHI）、汉密尔顿焦虑量表（HAMA）、汉密尔顿抑郁量表（HAMD）评估疗效。

结果：两组患者在治疗 4 周后，HAMA、HAMD、DHI 总评分及各因子评分即较治疗前显著降低（$P < 0.01$）；与对照组相比，试验组第 8、12 周的 DHI 总评分及功能、生理评分，第 4、8、12 周的 HAMA、HAMD 积分均明显低于同期对照组（$P < 0.05$）；不良反应发生率试验组明显低于对照组（$P < 0.05$）。

结论：逍遥解郁方可全面改善 PPPD 患者的临床症状，降低 PPPD 患者的功能、生理症状积分，降低患者的焦虑、抑郁及头晕残障程度;在治疗过程中不良反应少而轻；具有高效、安全、价廉、易取材等优点。

关键词：慢性主观性头晕；持续性姿势-知觉性头晕；逍遥解郁方；焦虑；抑郁

Abbreviation: PPPD, Persistent postural-perceptual dizziness; XJP, Xiaoyao Jieyu prescription; CSD, chronic subjective dizziness; PPV, phobic postural vertigo; ICD, International Classification of Diseases; SSRIs, Selective Serotonin Reuptake Inhibitors; HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale; DHI, Dizziness handicap inventory.

Competing interests: The authors declare that there is no conflict of interests regarding the publication of this paper.

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Background

Persistent postural-perceptual dizziness (PPPD) is a new disease name. Stabb and Ruckenstein were proposed the name on the basis of chronic subjective dizziness (CSD) and phobic postural vertigo (PPV) in 2014, this concept has been incorporated into the International Classification of Diseases (ICD)-11 [1].The main manifestations of the patients were continuous or frequent attacks of dizziness, with their own instability, swing, head distension and so on [2-3]. PPPD is a chronic state, the course of which is often delayed for more than a few months. It often associated with anxiety, depression, panic, compulsive or somatization disorders and other mental disorders, or even pseudoataxia, which has a serious impact on the life of patients. A survey shows that the prevalence of chronic subjective dizziness is higher, accounting for about 10% of outpatients with dizziness [4], and 30% of vestibular disease patients in Europe and America can develop chronic subjective dizziness [5]. Domestic scholar Ji Weihua *et al* [6] retrospectively analyzed the etiology of 3 270 outpatients with dizziness. It was found that mental factors were the first cause, accounting for 35.8 g of the total number of patients.

However, PPPD is relatively new , the exact prevalence of the disease has not yet been established. Since the disease is based on chronic subjective dizziness and phobic postural vertigo, it can be inferred that the prevalence of PPPD should not be less than that of chronic subjective dizziness.

The treatment of PPPD mainly includes psychotherapy, vestibular balanced rehabilitation and drug therapy,which therapeutic method has its limitations. Let us take the easiest usable drug “Selective Serotonin Reuptake Inhibitors (SSRIs)” for example. SSRIs is a classic drug for PPPD [7-10]. But SSRIs have many side effects, such as dizziness, lethargy, constipation, gastrointestinal reaction and so on [10-11].Some patients even get worse at early stage, so that they can’t stick with their medication [12].Therefore, seeking more safe, effective and convenient treatment is an urgent problem that medical workers need to solve.

In recent years, Chinese medicine has been used to treat PPPD in China, and the results show that it has certain clinical value [13]. TCM classifies PPPD as “vertigo” and “depression syndrome”. It is considered that the disease is a series of general malaise with dizziness as the main manifestation. Patients are often accompanied by burnout sleepiness, epigastriasis, palpitation, restlessness, neck and shoulder acid, defecation, and other symptoms. The etiology and pathogenesis of the disease are complicated. The principle of treatment is mainly to soothe the liver and regulate qi, and also to promote blood circulation to remove meridian obstruction, to eliminate phlegm and open orifices, and to tranquilize by nourishing the heart.

XJP is formed on the basis of Xiaoyao San in “Taiping Huimin Heji Bureau”. Its therapeutic effect is soothing the liver and regulating qi, promoting blood circulation to remove meridian obstruction, eliminating phlegm and opening orifices, and tranquilizing by nourishing the heart. It gives full play of the clinical advantages of traditional Chinese medicine. It can significantly improve the clinical symptoms, anxiety and depression of PPPD patients, and the efficacy is safe and reliable.

Information and methodology

Source of cases

All the PPPD cases were selected in the Department of Neurology of Cangzhou Hospital of Integrated Traditional Chinese Medicine and Western Medicine of Hebei Province from June 2016 to June 2017.

Diagnostic criteria

Diagnostic Criteria for PPPD referring to documents: A. One or more of the following symptoms: dizziness, instability or non-rotating vertigo, ≥ 3 months. Symptoms are persistent, but unstable.Symptoms gradually increase over the course of the day, but they do not keep active throughout the day, and may occur spontaneously or break a brief out during a sudden movement. B. There are no specific triggers to the symptoms, but the following can make the symptoms worse: ①orthostatism; ②active or passive motion, regardless of direction and position; ③exposure to moving visual stimuli or complex visual patterns. C. The disease usually begins shortly after an event that causes acute vestibular symptoms or balancing problems, although less so. The development of the disease is slow. The evoked events include acute, paroxysmal or chronic vestibular syndrome, other neurological or medical disorders, and psychological distress, such as: a. when it induced by acute or intermittent events, symptoms usually fall into standard A mode when the evoked events recover, which may occur intermittently at first and then be fixed as a continuous process. b. when it triggered by chronic events,the symptoms develop slowly and gradually deteriorate. D. These symptoms cause considerable pain or dysfunction. E. Symptoms should not be attributed to another disease or discomfort [14].

Inclusion and exclusion criteria

All the patients who received the treatment met the above diagnostic criteria, aged 18-80 years. The researcher solicited the consent of the person himself or his family. The person himself or his family sign the patient’s informed consent. Exclusion criteria: ①patients with vestibular system related organic diseases; ②dizziness caused by severe physical disease; ③brain caused by brain organic diseases or cervical vertigo; ④patients with escitalopram contraindications; ⑤drug abuser; ⑥patients using antidepressants within 2 weeks of admission; ⑦person suffering from severe depression with suicidal tendency; ⑧patients with severe heart, brain, liver, kidney, hematopoietic system and endocrine system disease; ⑨a woman who is pregnant, lactating, or preparing to conceive.

Grouping and treatment

In this study, randomized, controlled treatment principles were used for clinical evaluation and random grouping scheme was generated by SPSS 17.0 Statistical Software. A total of 33 PPPD patients were randomly divided into test group and control group.There were 17 cases in the test group, 6 males and 11 females, with an average age of (51.56 ± 13.46) years, and 16 cases in the control group , 4 males and 12 females, with an average age of (52. 02±12.08) years.The course of disease ranged from 3 to 34 months, with an average duration of (18 ± 9) month in the test group,and the course of disease ranged from 4 to 35 months, with an average duration of (19 ± 8) months in the control group.There was no significant difference in age, sex, course of disease, DHI score, HAMA score and HAMD score between the two groups. (P > 0.05).Two groups of patients were given psychotherapy, including: psychological guidance, verbal cues, to eliminate the tension of patients. The test group was given XJP: Chaihu (Bupleuri Radix) 10 g, Shudihuang (Rehmanniae Radix Praeparata) 10 g, Shanzhuyu (Corni Fructus) 10 g, Danggui (Angelicae Sinensis Radix) 10 g, Baishao (Paeoniae Radix Alba) 10 g, Shichangpu (Acori Tatarinowii Rhizoma) 6 g, Yujin (Curcumae Radix) 6 g, Fuling (Poria) 10 g, Baizhu (Atractylodis Macrocephalae Rhizoma) 10 g, Yuanzhi (Polygalae Radix) 6 g, Zhigancao (Glycyrrhizae Radis Et Rhizoma Praeparata Cum Melle) 5 g, Shengjiang (Zingiberis Rhizoma Recens) 3 g, Bohe (Menthae Haplocalycis Herba) 3 g. (Remarks:Name of production Unit: Cangzhou Hospital of Integrated Traditional Chinese Medicine and Western Medicine of Hebei University of Chinese Medicine. XJP is unified in the hospital and is managed by the hospital.1 dose is 2 bags, each bag 200 ml).Take 1 dose daily, 1 bag for breakfast and 1 for half an hour after supper. The control group was given one tablet of estalopram (Name of production unit: Xi'an Yang Sen Pharmaceutical Co., Ltd. 10mg / tablet) .One tablet per day after breakfast. Treatment cycle is 12 weeks.

Observation index and method

Four weeks were used as a period of observation, and the observation time points were before treatment and at the end of treatment 4 weeks/8 weeks/12 weeks respectively. Three neurologists were used to test the related scales. If the test results are inconsistent, take the minority from the majority principle.

Score of related Mental scale. Use the Dizziness Handicap inventory (DHI) [15-16] to evaluate the severity of vertigo subjective symptoms in patients with PPPD; use the Hamilton Anxiety Scale (HAMA) and Hamilton Depression Scale (HAMD) to evaluate the severity of anxiety and depression in patients with PPPD.

The evaluation method of DHI scale: the scale was composed of 25 questions and was evaluated by four indexes: total scores, function (F), emotion (E) and physiology (P). There are three answers to each question, "Yes, sometimes, none," with a score of "4 / 2 / 0". A score of 0 indicates that there is no effect on the patients with vertigo, and the total score is 100. The higher the score is, the more serious the effect of vertigo is on the patients. DHI rating scale: 0 ~ 30 points indicate minor disorders, ~60 points indicate moderate disorders, ~ 100 points indicate serious disorders [17]. The efficacy standard refers to Guidelines for Clinical Research of New drugs in traditional Chinese Medicine [18], and is formulated as follows according to clinical practice: remission: DHI score reduction rate is no less than 95%; excellence: DHI reduction rate is less than 95% and not less than 70%;effective: DHI reduction rate is less than 70% and not less than 30%; invalid: DHI reduction rate is less than 95%.

HAMA is one of the commonly used psychiatric clinical scales developed by Hamilton, including 14 items. The evaluation criteria: < 7 is normal. There may be anxiety in 8～14 and anxiety in 15～21. There is definitely significant anxiety in 22～29, and > 29 may be serious anxiety.

HAMD-24 is also one of the commonly used psychiatric clinical scales developed by Hamilton. There are three versions including 17 items, 21 items and 24 items. HAMD-24 was selected in this study. The evaluation criteria were as follows: < 8 is normal, 8～20 is mild depression, 21～35 is moderate depression, > 35 is severe depression.

Safety assessment. The safety of the drug was evaluated by vital signs and physical examination, blood routine examination, liver function, renal function, electrolyte and electrocardiogram before and after treatment for 12 weeks. Adverse reactions were evaluated by Treatment Emergent Symptom Scale.

Statistical methods. SPSS 17 software was used for statistical analysis. The measurement data were expressed as mean ± standard deviation ($\bar{x}$ ±s). The analysis of variance of two factors repeated measurement was carried out on the observation data of multiple time points, and the comparison between two groups was tested by LSD-t test. The comparison of two independent samples by independent sample t-test or non-parametric test. The count data were statistically described by composition ratio or rate, and comparison by χ^2 test or rank sum test. All the statistical results were tested by bilateral test. When P < 0.05, there was statistical significance, and when P > 0.05, there was no statistical significance.

Results

Two sets of baseline analysis

There were 33 cases in the study group, 17 cases in the test group and 16 cases in the control group, but 32 cases were finally completed. 17 cases were completed in the test group. During therapy, one patient felt that the taste of the Chinese medicine was very bitter and did not want to continue taking Chinese medicine. Finally, the patient persisted in taking the medicine after having been explained patiently by the medical worker. In the control group, 15 cases were completed and 1 case was shed (the abscission rate was 6.25%). The reason is that the symptoms of dizziness of the patient, become worse after

taking medicine for one week, and she was not willing to continue taking medicine, and still unwilling to continue taking medicine after patient explanation. In the control group, 15 patients (4 males and 11 females) finished the clinical test , with an average age of (51.02±12.48) years and the average course of disease was (19±8) months.There was no significant difference between the two groups in age, sex, course of disease and DHI score, HAMA score and HAMD score before treatment (P > 0.05), as shown in Table 1.

Table 1 Comparison of baseline data before treatment between two groups

group	cases	M/F	age	course	function	emotion	physiology	total scores	HAMA	HAMD
Test group	17	6/11	51.56 ±13. 46	18±9	24.35±3. 55	21.06±2 .84	19.06±2.84	64.47±7 .02	18.47±3 .39	19.35± 3.10
Control group	15	4/11	51.02 ±12. 48	19±8	23.07±3. 69	21.33±2 .69	19.07±2.81	63.47±6 .57	18.13±2 .88	20.13± 2.87

Note: the baseline data of the two groups were compared by χ^2 test and independent t-test, P > 0.05

Improvement of mental scale integral

Comparison of total DHI score and factor score before and after treatment between the two groups. Comparison of total DHI scores before and after treatment: In the test group, there were significant differences between the four weeks after treatment and before treatment, the eight weeks after treatment and four weeks before treatment, and the difference between 12 weeks and 8 weeks after treatment (P < 0.001, P < 0.001, P = 0.046).In the control group ,there were significant differences between the four weeks after treatment and before treatment, the eight weeks after treatment and four weeks before treatment, and there were no significant differences between the difference between 12 weeks and 8 weeks after treatment (P < 0.001, P < 0.001, P = 0.132).

Comparison of functional F scores before and after treatment: In the test group, there were significant differences between the four weeks after treatment and before treatment, 8 weeks after treatment and 4 weeks before treatment (P < 0.001, P < 0.001).There was no significant difference between 12 weeks after treatment and 8 weeks after treatment (P = 0.132). In the control group, there were significant differences between the four weeks after treatment and before treatment, 8 weeks after treatment and 4 weeks before treatment, 12 weeks after treatment and 8 weeks after treatment (P < 0.001, P = 0.001, P = 0.066).

Emotional E score changes before and after treatment were compared:In the experimental group, there were significant differences between 4 weeks after treatment and before, 8 weeks and 4 weeks after treatment, 12 weeks after treatment and 8 weeks after treatment, respectively (P < 0.001, P < 0.001, P = 0.045). In the control group, there were significant differences between 4 weeks after treatment and before treatment, 8 weeks after treatment and 4 weeks before treatment (P < 0.001).There was no significant difference between 12 weeks after treatment and 8 weeks after treatment in the control group (P = 0.396).

Comparison of physiological P score before and after treatment: There were significant differences between 4 weeks after treatment and before treatment, 8 weeks after treatment and 4 weeks before treatment in both groups (P < 0.001).There was no significant difference between 12 weeks after treatment and 8 weeks after treatment in both groups (P = 0.531, P = 0.517).

Comparison of changes in DHI total score and factor score between two groups before and after treatment. At 4 weeks after treatment,there was no significant difference in total score of DHI and functional F, emotional E, physiological P score between the two groups (P = 0.937, P = 0.908, P = 0.428, P = 0.645). At 8 weeks after treatment,there were significant differences in the total score of DHI, functional F and physiological P score between the two groups (P = 0.012,P = 0.007,P = 0.049), while there was no significant difference in emotional E (P = 0.402). At 12 weeks after treatment, there were significant differences in the total score of DHI, functional F and physiological P score between the two groups (P = 0.010, P = 0.025, P = 0.031), while there was no significant difference in emotional E between the two groups (P = 0.101).

Comparison of Hamah Hamd score before and after treatment between the two groups. The changes of HAMA before and after treatment comparison: the experimental group 4 weeks after treatment and before treatment, 8 weeks after treatment and 4 weeks before treatment, 12 weeks after treatment and 8 weeks after treatment were significantly different (P < 0.001, P = 0.006, P < 0.001); the control group 4 weeks after treatment and before treatment, 8 weeks after treatment and treatment the first 4 weeks, 12 weeks after treatment and 8 weeks after treatment were not significantly different (P = 0.062, P = 0.062, P = 0.062).

Comparison of HAMD changes before and after treatment: in the experimental group, there were significant differences between 4 weeks after treatment and before treatment, 8 weeks after treatment and 4 weeks before treatment, 12 weeks after treatment and 8 weeks after treatment (P < 0.001, P = 0.005, P < 0.001). In the control group, there was no significant difference between 4 weeks after treatment and before treatment, but there was no significant difference between 8 weeks after treatment and 4 weeks before treatment. There was a significant difference between 12 weeks after treatment and 8 weeks after treatment (P = 0.069, P = 0.069, P =

0.046).

Comparison of HAMA and HAMD score before and after treatment between the two groups. At 4 weeks after treatment, there were significant differences in HAMA and HAMD scores between the two groups (P = 0.027, P = 0.003) .At 8 weeks after treatment, there were significant differences in HAMA and HAMD scores between the two groups (P = 0.003, P < 0.001). At 12 weeks after treatment, there were significant differences between the two groups in HAMA and HAMD scores (P < 0.001, P < 0.001) .

In a word, by statistical analysis, the DHI total score, every factor score and score of HAMA, HAMD at 4 weeks after treatment in both groups were significantly lower than those before treatment (P < 0.01), and the DHI total score, every factor score and score of HAMA, HAMD at 8 weeks after treatment were significantly lower than those at 4 weeks after treatment (P < 0.01), and the score of HAMA, HAMD at 12 weeks after treatment were significantly lower than those at 12 weeks after treatment (P < 0.01).In the test group, the score of DHI and Emotion at 12 weeks after treatment was significantly lower than that at the 8th week after treatment (P < 0.01). In the control group, the score of DHI and Function at 12 weeks after treatment was significantly lower than that at 8 weeks after treatment (P < 0.01).

Compared with the control group, the total score of DHI and the F score of function in the test group at 812 weeks were significantly lower than those in the control group (P < 0.05). The HAMA and HAMD scores at week 4, 8, 12 were significantly lower than those in the control group (P < 0.05). It can be seen that both treatment methods can reduce the degree of dizziness and disability and improve anxiety and depression in patients with PPPD, but the efficacy of the trial group is better than that of the control group in improving the function, physiology, anxiety and depression of the patients with PPPD, as shown in Table 2-3.

Table 2 Comparison of the total scores of DHI and the scores on each factor before and after treatment between two groups of patients

Group	Cases	Time	Function	Emotion	Physiology	Total scores
Test group	17	pretherapy	24.35±3.55	21.06±2.84	19.06±2.84	64.47±7.02
		Treatment for 4 weeks	15.29±3.39**	14.12±2.78**	13.06±2.84**	42.47±5.55**
		Treatment for 8 weeks	4.94 ± 3.01★★◆◆	5.18±2.56★★	3.76±2.63★★◆	13.88 ± 4.27★★◆
		Treatment for 12 weeks	3.29±2.54◆	3.30±2.55△	3.17±2.56◆	9.76±6.44△◆
Control group	15	pretherapy	23.07±3.69	21.33±2.69	19.07±2.81	63.47±6.57
		Treatment for 4 weeks	15.20±3.28**	14.00±2.93**	12.27±2.71**	41.47±6.65**
		Treatment for 8 weeks	8.00±2.93★★	6.01±2.94★★	5.87±3.16★★	19.87±8.05★★
		Treatment for12 weeks	5.73±3.28	5.07±3.37	5.20±3.37	16.01±6.32

Note: The data are analyzed by LSD-t test show that there are significant differences between 4 weeks after treatment and before treatment,*P < 0.05, **P < 0.01; 8 weeks after treatment and 4 weeks after treatment, ★P < 0.05, ★★P < 0.01; 12 weeks after treatment and 8 weeks after treatment, △P < 0.05, △△P < 0.01. The independent sample t-test analysis data, compared with the control group in the same period, ◆P < 0.05, ◆◆P < 0.01.

Table 3 Comparison of the scores of HAMA and HAMD before and after treatment between two groups of patients

Group	Cases	Time	HAMA	HAMD
Test group	17	pretherapy	18.47±3.39	19.35±3.10
		Treatment for 4 weeks	13.71±3.01** ◆	14.72±3.00**◆◆
		Treatment for 8 weeks	10.65±3.10★★◆◆	11.64±3.11★★◆◆
		Treatment for12 weeks	6.06±3.17△◆◆	7.06±3.18△△◆◆
Control group	15	pretherapy	18.13±2.88	20.13±2.87
		Treatment for 4 weeks	16.12±2.90	18.10±2.91
		Treatment for 8 weeks	14.10±2.91	16.13±2.80
		Treatment for12 weeks	12.11±3.00	13.10±3.20△

Note: The data are analyzed by LSD-t test show that there are significant differences between 4 weeks after treatment and before treatment,*P<0.05, ** P < 0.01; 8 weeks after treatment and 4 weeks after treatment, ★P < 0.05, ★★P < 0.01; 12 weeks after treatment and 8 weeks after treatment, △P < 0.05, △△P < 0.01. The independent sample t-test analysis data, compared with the control group in the same period, ◆P < 0.05, ◆◆P < 0.01.

Comparison of clinical efficacy

After 12 weeks of treatment, the total effective rate in the test group was 94.125%. The total effective rate in the control group was 73.33%. The data analyzed by rank sum test showed that the difference between the test group and the control group was statistically significant. ($P = 0.042$), as shown in Table 3.

Table 3 Comparison of the clinical effect between two groups of patients

Group	Remission	Excellence	Effective	Invalid	Total effective rate (%)
Test group	4	7	5	1	94.12*
Control group	1	5	7	3	73.33

Note: by rank sum test, compared with the control group, *$P < 0.05$

Comparison of adverse reactions

In the test group, one case had adverse reactions, mainly because he felt that the taste of Chinese medicine was very bitter. After medical worker explained patiently to the patient, they insisted on taking the medicine. In the control group, 6 cases developed adverse reactions, including 1 case of constipation, 1 case of anorexia, 1 case of dry mouth, 1 case of lethargy and 1 case of insomnia. One case, the symptoms of vertigo becoming heavier after one week of medication, was unable to continue taking the medicine, which eventually resulted in abscission. According to χ^2 test, the incidence of adverse reactions in the two groups was significantly higher than that in the control group ($P = 0.033$), as shown in Table 4.

Table 4 Comparison of the side effects between two groups of patients

Side effects	Astriction	Anorexia	Dry mouth	Drowsiness	Dizzy	Lose sleep	Mouthfeel is poor	Incidence
Test group							1	5.88%*
Control group	1	1	1	1	1	1		37.50%

Note: by χ^2 test of four squares table, compared with the control group,*$P < 0.05$.

Discussion

Origin of PPPD

In clinical practice, dizziness is a common symptom of neuroaudiology, with many causes. However, some patients with dizziness, despite comprehensive tests, often show normal results and cannot be explained by neuro-auricular diseases. This kind of dizziness has been referred to as “psychogenic dizziness” [19]. However, because the concept and diagnostic criteria of “psychogenic dizziness” lack the corresponding scientific basis and there is no support for a large amount of research data. Phobic postural vertigo dizziness is a kind of postural head. The clinical state of halo and volatile instability [20] is a stable, identifiable clinical syndrome. The entire longitudinal process may last for years, with two thirds of patients with significant anxiety or depression [21-22]. 2007 with STAAB *et al* [8] improved diagnostic criteria for the syndrome, classifying trigger events and syndromes. And it was renamed chronic subjective dizziness. In the further investigation, the pathogenesis of CSD was gradually identified. The mechanism and treatment strategy, the evidence that CSD is a kind of dysfunction caused by the two-way interaction of mind and body [19, 23]. On the basis of these research results, Staab and Ruckenstein integrate the core symptom characteristics of PPV and CSD. The concept of body disease diagnosis of syndrome of persistent postural-perceptual dizziness syndrome [24] was proposed and included in international disease. The disease was classified in Classification of diseasesus ICD-11.

Epidemiological investigation and harm of PPPD

Because PPPD is a new disease body name, The clinical data and literature are few, so we should take CSD as the main topic for the analysis. At the Foreign Center for third level Neuroaural Sciences, CSD is the second most common diagnosis of vestibular symptoms. 30%～50% of patients with vestibular disorders can develop CSD [25]. As a typical chronic disease, it can occur from adolescence to later adulthood, but it occurs mostly in people aged 40 to 50, and most of them are women (65% ~ 70) [26], the symptoms often last several months or years, the average course of disease is 4.5 years [27]. 60% of the patients with CSD have clinical depression and 45% of them have bedtime anxiety, which seriously affect the daily life of patients. Therefore, we can infer that PPPD has higher resolution and greater harm.

Pathogenesis of PPPD in modern medicine

The pathogenesis of PPD includes personality traits,

classical-operational conditioned reflex hypothesis, balance control pathway and threat assessment system interaction hypothesis.There is a link between anxiety and depression and vestibular function. Anxiety can cause dizziness, and vestibular dysfunction can cause mental and physical anxiety [28]. Therefore, reducing anxiety and depression and regulating vestibular function are important therapeutic principles.

Treatment of PPPD in modern medicine and its limitations

At present, the main treatment methods of PPPD is psychotherapy, vestibular balanced rehabilitation and drug therapy. Among them, psychotherapy and drug therapy mainly focus on reducing the anxiety and depression state of patients, while vestibular balanced rehabilitation therapy mainly focuses on regulating the vestibular function of patients. But each method has its limitations. 1). Psychotherapy. Psychotherapy is the key to successful treatment [22], but it is not ideal for definite, long-term PPPD patients [23]. Therefore, the timing of psychotherapy is important. Psychotherapy can be beneficial when symptoms of PPPD begin to appear but are not fully developed [29]. Therefore, it is difficult to carry out psychotherapy in clinic. On the one hand, this method is highly demanding for patients. It is necessary for the patients to know the disease and to see the doctor in time. However, in practice, most patients do not know enough about the disease and may miss the best time of treatment. On the other hand, medical workers not only need to fully understand the disease, but also need to grasp the methods of psychological treatment accurately and the appropriate treatment opportunities. Therefore, it is difficult to carry out the treatment accurately in the busy clinical work. 2). Vestibular balanced rehabilitation therapy. Vestibular rehabilitation therapy can reduce the vestibular symptoms by 60% and 80%, which may be effective in alleviating anxiety and depression in patients with PPPD. However, vestibular balanced rehabilitation therapy should be performed for at least 3 ~ 6 months to obtain maximum benefit [30]. The treatment cycle is longer and the patient's compliance is poor. It was observed in clinical practice that some patients who received vestibular balance rehabilitation would have worse symptoms of dizziness and could not insist on the treatment. 3). Drug therapy. SSRI drugs, represented by Escitalopram, as first-line antidepressants, can effectively treat persistent postural dizziness. But the use of SSRI drugs can have side effects such as dizziness, insomnia or gastrointestinal tract, and the side effects are big. Some patients may be prematurely discontinued due to worsening of anxiety symptoms and the patient compliance is poor [31].

This study found that the patients with persistent postural and perceptual dizziness was given three consecutive months of oral administration of Escitalopram, with the following results. ①There was a significant difference between before treatment and 4 weeks after treatment in the total score of DHI and the improvement of symptoms such as function, emotion, physiology ($P < 0.01$).There was no significant difference between this group and test group ($P > 0.05$).But the effect of this group was lower than that of test group and the difference was significant in the total score of DHI and the improvement of symptoms such as function, physiology at the end of 8 weeks and 12 weeks of treatment ($P < 0.05$). ②There was significant difference in anxiety and depression score between 4 weeks after treatment and before treatment in the improvement of anxiety and depression scores ($P < 0.01$), but its effect was lower than that test group ($P < 0.05$). ③The clinical efficacy of this group was lower than that of test group ($P < 0.05$). ④Adverse reactions occurred in 6 out of 16 patients taking Escitalopram, including constipation, loss of appetite, dry mouth, lethargy, insomnia. One case of them, whose clinical symptoms were aggravated when taking Escitalopram one week.,and she could not continue taking the drug and eventually fell off in the clinical test

Traditional Chinese Medicine on PPPD

TCM classifies the disease as "vertigo" and "depression". The description in *Suwen* is "all the wind, dizziness, belong to the liver". *Huang Di*'s Classic of Internal Medicine discusses the etiology and pathogenesis of dizziness. It is considered that this disease is mainly caused by the liver and involves the spleen, kidney and other multiple viscera dysfunction.

The author of Clinical guidance Medical record·Vertigo Gate Hua Xiuyun analyse that, all the wind, dizziness, belong to the liver. The head is the gathering place of Zhuyang, and the ears, eyes, mouth and nose are all clear orifices. Those who suffer from vertigo are not feeling the evil spirit from outside, but the wind and the yang of the liver and the gallbladder, and they are in danger of fainting and falling.

The etiology and pathogenesis of this disease are complicated. The etiology of the disease is mostly due to unobstructed mood, stagnation of liver qi, depression of heat, and internal disturbance of the heart and mind. The etiology of the disease is also due to stagnation of qi, spleen loss of health, body fluid to stop gathering into phlegm, phlegm and qi blocked and cause heart and spirit to lose nourishment. The etiology of the disease may also be due to the deficiency of qi, blood and fluid, the decline of brain spirit and the function of visceral spirit, which may lead to the development of the disease.

Liver regulates emotion. Gallbladder is the organ of the liver. If the liver-qi is not smooth and the liver-qi is depressed, the operation of the qi engine will not be smooth. If the operation of qi is not smooth, it can lead to the qi, blood and fluid stopping running and gathering together. If qi, blood and fluid stop running and gather together, it can cause wind, phlegm, fire and blood stasis to block the meridians and gather in the brain, thus causing dizziness. Stagnation of liver-qi and unease of qi are the core pathogenesis of the disease. Phlegm turbidity and blood stasis are the underlying pathological factors of the disease. Therefore, the treatment is mainly to soothe the liver and regulate qi, taking into account the treatment

methods such as eliminating phlegm and opening orifices, activating blood circulation and dredging collaterals, nourishing the heart and tranquilizing the mind, stopping dizziness.

Study on the effect of Xiaoyao Jieyu prescription on the treatment of PPPD

XJP is based on the clinical application of our department for many years. On the basis of the "Xiaoyao San" of the ancient square, it is formed by chemical analysis. The prescription of Chaihu (Bupleuri Radix) can soothe the liver and relieve the depression, and make the liver qi smooth. Chaihu (Bupleuri Radix) is a monarch drug in the prescription. Baishao (Paeoniae Radix Alba) can nourish Yin and soften liver. Danggui (Angelicae Sinensis Radix) can nourish blood and activate blood. The combination of Baishao (Paeoniae Radix Alba) and Danggui (Angelicae Sinensis Radix) can nourish yin and restrict Chaihu (Bupleuri Radix). The combination of Shichangpu (Acori Tatarinowii Rhizoma) and Yujin (Curcumae Radix) can play the role of eliminating phlegm and opening orifices, activating blood circulation and activating collaterals. The Shudihuang (Rehmanniae Radix Praeparata) and Shanzhuyu (Corni Fructus) can nourish liver and kidney. Baishao (Paeoniae Radix Alba), Danggui (Angelicae Sinensis Radix), Shichangpu (Acori Tatarinowii Rhizoma), Yujin (Curcumae Radix, Shudihuang(Rehmanniae Radix Praeparata) and Shanzhuyu (Corni Fructus) are ministerial drug. Baizhu (Atractylodis Macrocephalae Rhizoma), Fuling (Poria), Yuanzhi (Polygalae Radix) can play the role of invigorating spleen and benefiting qi, nourishing heart and tranquilizing spirit. Shengjiang (Zingiberis Rhizoma Recens) can warm the stomach. Bohe (Menthae Haplocalycis Herba) can help Chaihu (Bupleuri Radix) soothe the liver and dissipate the heat. Zhigancao (Glycyrrhizae Radis Et Rhizoma Praeparata Cum Melle) can play a role in reconciliation .The combination of the drugs can make the liver used again, liver body nourishment, spleen transport health, heart spirit to support, phlegm and blood stasis to get rid of depression. The prescription combined with 12 drugs, plays the role of soothing liver and regulating qi, eliminating phlegm and resuscitation, activating blood circulation and dredging collaterals, nourishing the heart and tranquilizing the mind and stopping dizziness.

In this study, we found that patients with PPPD were treated with XJP for 12 weeks, and the following results were obtained. ①There was significant difference between 4 weeks after treatment and before treatment in the total score of DHI and the improvement of symptoms such as function, emotion, and physiology ($P < 0.01$). There was no significant difference between this group and the control group ($P > 0.05$). The effect of this group is obviously better than that of the control group in the total score of DHI and the improvement of symptoms such as function, physiology ($P < 0.05$). ②In the improvement of anxiety and depression scores, there was significant difference between 4 weeks after treatment and before treatment ($P < 0.01$), and the curative effect of 4 weeks, 8 weeks and 12 weeks after treatment was significantly better than that of the control group ($P < 0.05$). ③The overall curative effect was better than that in the control group ($P < 0.05$). ④As for the incidence of adverse reactions, one case in the test group had adverse reactions, mainly because of the bitter taste of traditional Chinese medicine, and insisted on taking medicine after patient explanation. The adverse reaction rate was significantly lower than that in the control group ($P < 0.05$).

It is concluded that XJP has no serious adverse reactions in the treatment of PPPD. It can obviously improve the symptoms of function and physiology of patients with persistent postural dizziness, reduce the degree of anxiety and depression. Compared with the classic western medicine escitalopram, XJP has the advantages of safety, high efficiency, low price and easy access to materials. It shows the broad prospect of clinical application of XJP.

However, this study is only a small sample of clinical observation, and the observation time is only 12 weeks. There is a lack of a large sample of multicenter randomized controlled long span trials to further verify its exact therapeutic mechanism and prognosis. During the course of treatment, some patients considered that "the side effects of western medicine are large and the side effects of traditional Chinese medicine are small or no side effects". On the one hand, it indicates that psychological cues may have a certain effect on the treatment of the disease, and on the other hand, it also suggests that subjective factors may also have an effect on the evaluation of therapeutic effects. Therefore, there is a need for a further multicenter, double-blind, placebo parallel controlled trial. In addition, this study only included escitalopram as a control, and also needed to compare with other SSRI drugs, in order to balance the advantages and disadvantages of XJP in the treatment of persistent postural and perceptual dizziness better. In addition, whether there is a time window for PPPD treatment remains to be further studied.

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