

Original Article

Efficacy and safety analysis of gastrodin injection combined with anti-anxiety drug for treatment of climacteric hypertension

Xiao-Lan Zhong¹, Jiang-Xin Jing², Zhi-Min Fang¹, Bannu-Kuken¹, Hai-Jun Miao³, Hong-Yan Song¹, Hua Zhong¹, Yun Lu⁴, Shun-Min Liu¹

¹Department of Cardiology, Second Affiliated Hospital of Xinjiang Medical University, China; ²Department of Ultrasound, Second Affiliated Hospital of Xinjiang Medical University, China; ³Section 1, Cadre Ward, First Affiliated Hospital of Xinjiang Medical University, China; ⁴Cath Lab, Second Affiliated Hospital of Xinjiang Medical University, China

Received January 30, 2016; Accepted April 27, 2016; Epub June 15, 2016; Published June 30, 2016

Abstract: Objective: This study aimed to analyze the effect of gastrodin injection combined with anti-anxiety drugs on climacteric hypertension. Methods: 106 cases menopausal hypertensive patients who were treated in our hospital between September 2013 and September 2014 were enrolled in the study. They were randomly divided into two groups and treated with routine therapy and gastrodin injection combined with anti-anxiety drugs, respectively. After the treatment, baseline data of the study, clinical efficacy, mental status, safety and other data were compared between the two groups. Results: In observation group and the control group total effective rate of hypertension were 85.2% and 61.5%. Comparisons between the two groups showed that in the observation group it was significantly better than the control group ($P < 0.05$). After treatment HAMD score were (14.3 ± 3.6) points and (17.6 ± 3.5) points. In the observation group it was significantly lower than that in the control group ($P < 0.05$). Total efficiency rate of anxiety were 83.3% and 9.6%. Comparisons between the two groups showed that in the observation group it was significantly better than that in the control group ($P < 0.05$); adverse reaction rate were 14.8% and 26.9%. In the observation group it had a significant advantage ($P < 0.05$). That is, for the safety of the two therapies, in observation group it was significantly better than the control group ($P < 0.05$). Conclusion: Gastrodin injection combined with anti-anxiety drugs is safe and effective for the treatment of menopausal hypertensive.

Keywords: Gastrodin injection, anxiolytic, menopause, hypertension, efficacy and safety

Introduction

Climacteric hypertension refers to menopausal women appear main symptoms of high blood pressure and other disease. Treatment of the disease itself is not complicated, and the treatment of hypertension is similar. However, due to menopausal women, many of which accompanied by intense anxiety and other negative mental state, the impact of the disease seriously affected the quality of life for these patients. Its early symptoms of hypertension is similar to menopause symptoms. Clinical misdiagnosis rate is high, thereby it affects clinical efficacy [1]. Studies have supplemented that based on antihypertensive therapy, they were treated with anti-anxiety

drugs for treatment of other adverse psychological symptoms, accessing good effect. But because lack of clinical application, relevant research data were less, therefore related research for this therapy have important guiding values. Gastrodin injection for the treatment of hypertension, not only does it have a significant effect, but also it has high safety, and it has been recognized in clinical and research. But researches about gastrodin injection combined with anti-anxiety drug are less, which need more data to support for the promotion of therapy [2]. Therefore research on efficacy and safety analysis of gastrodin injection combined with anti-anxiety drug for treatment of patients with climacteric hypertension have great value.

Subjects and methods

Inclusion and exclusion criteria of subjects

The research is based on standard diagnosis of hypertension and clinical experience. Inclusion and exclusion criteria for patients was developed in order to enhance the safety and scientific of the research. The specific contents are as follows: (1) Inclusion criteria: ① SBP was not lower than 140 mmHg or diastolic blood pressure was not less than 90 mmHg. The course was six months or more, and their age was between 48 and 51 years around the menopause [3]; ② patients Hamilton depression Scale (HAMD) 1-17 items scored no less than 17 minutes [4]; ③ in line with the principle of informed consent and related associations developed medical ethics [5]; (2) Exclusion criteria: ① diagnosis of secondary hypertension; ② with severe liver and other organs damage disease; ③ with severe mental disorders; ④ with drug allergies; ⑤ during the study, steroids or other drug were used during the research; ⑥ reluctant to participate in research, study and lost to follow-up and other reasons lead to clinical data missing [6].

Characteristics of the participates

According to the research needs, between September 2013 and September 2014-menopausal hypertensive patients who were treated in our hospital were screened. 106 cases were enrolled in the study, and they were randomly divided into observation and control group. The basic information are as follows: (1) study group: 54 cases, ① Age: between 48 and 51 years, mean (49.3 ± 0.8) years; ② course: 6-12 months, the average duration were (9.6 ± 2.8) months; ③ HAMD Rating: scored 17-22 points, the average was (19.8 ± 2.5) min; (2) control group: 52 cases, ① age: 49 between and 51 years, the mean were (49.6 ± 0.5) years; ② course: 7-13 months, the average duration were (9.8 ± 2.6) months; ③ HAMD Rating: scored 18-21 points, the average was (19.4 ± 2.3) Minute. Duration and baseline HAMD score and other information were compared between the two groups and there was no significant difference ($P > 0.05$), indicating that the data of the research were comparable.

Treatment method

Three clinically experienced attending physicians in our hospital were randomly selected as

research physicians; nurses were experienced hospital nurses. Study used double-blind method; all cases received health education and psychological counseling; exercise therapy was performed based on the patient's condition.

Treatment for control group

The control group was treated in accordance with conventional method, using oral antihypertensive drugs plus placebo; specific drug and administration were as follows: metoprolol succinate sustained-release tablets (AstraZeneca AB; Betaloc, National drug approval: No. 2J0100098), 12.5 mg/time, 2 times/day, orally; with two weeks as a period, blood pressure of subjects was detected; undesirable cases were treated with Nifedipine sustained-release tablets (Shanxi Yunpeng pharmaceutical Co., National drug approval: No. H20113056), 20 mg/time, 2 times/d. Meanwhile, placebo (vitamin e) was given referring to the antianxiety drug dose in observation group.

Treatment for observation group

Observation group was treated with gastrodine injection combined with anti-anxiety drug; specific drugs and doses were as follows: (1) Gastrodine injection: 200 mg/times, 2 times/day, intravenous injection; Shaanxi Bosen biopharmaceutical Co., National drug approval: No. 91H130052; (2) Anxiolytics: 50 mg/times, 2 times/day, orally administration, Maprotiline hydrochloride tablets (Hunan Dongting pharmaceutical Co., Ltd., National drug approval: No. H43020562). The collection and evaluation of data were performed after two months of continuous treatment.

Evaluation items and standards

(1) Efficacy: ① Hypertension: With the hypertension efficacy evaluation criteria approved by National Cardiovascular Society as a basis, the study evaluation criteria was developed, as follows: markedly effective: DBP decreased more than 10 mmHg to normal levels or the decreased range was greater than 20 mmHg; effective: diastolic blood pressure interval was between 10 and 19 mmHg or systolic blood pressure decreased more than 30 mmHg; invalid: no significant drop in blood pressure, no improvement or blood pressure further increased. The total effective rate = number of

Table 1. Baseline data comparison between the two groups

| Parameter | Observation group (54) | Control group (52) | T (X ²) | P |
|------------------------|------------------------|--------------------|---------------------|-------|
| Age (Year) | 49.3 ± 0.8 | 49.6 ± 0.5 | 1.368 | 0.265 |
| Disease course (month) | 9.6 ± 2.8 | 9.8 ± 2.6 | 1.256 | 0.258 |
| HAMD scores (points) | 19.8 ± 2.5 | 19.4 ± 2.3 | 1.059 | 0.166 |

Table 2. Treatment effect comparison between the two groups

| Groups (n) | Excellent | Effective | Invalid | Total effective rate (%) |
|------------------------|-----------|-----------|---------|--------------------------|
| Observation group (54) | 22 | 24 | 8 | 85.2 |
| Control group (52) | 18 | 14 | 20 | 61.5 |
| X ² | | | | 4.686 |
| P | | | | 0.038 |

(markedly effective + effective) cases/number of cases in the group * 100%; the higher the total effective rate, the better the efficacy [7]; ② Anxiety and depression: HAMD scale score was used before and after treatment; HAMD reducing rate = (before treatment-after treatment) Score/score before treatment * 100% was taken as efficacy evaluation content. The criteria were as follows: recovery: reducing rate was between 75 and 100%; effective: reducing rate was between 25 and 74%; invalid: HAMD score reducing rate was lower than 25 percent; scores after treatment and the total efficiency were taken as the efficacy evaluation Criteria [8]; (2) Safety: In the course of treatment the drug-related adverse reactions were summarized; incidence of adverse reactions was calculated as the safety evaluation criteria. The higher the incidence of adverse reactions, the better the safety [9].

Statistical analysis

Data were analyzed using SPSS18.2 statistical software; measurement data were expressed as Mean ± SD and compared by *t* test; count data were expressed as X (%) and compared by X² test; when P < 0.05, the difference was significant.

Results

Baseline data

Average age of the study, average duration and average HAMD score and other data were compared and analyzed between groups without significant difference (P > 0.05) indi-

cating the subjects were comparability in the study, **Table 1**.

Efficacy

Hypertension efficacy: In observation group and the control group total effective rate of hypertension were 85.2% and 61.5%. Comparisons between the two groups showed that in the observation group it was significantly better than the control group (P < 0.05). The specific data were shown in **Table 2**.

Anxiety efficacy: After treatment HAMD score were (14.3 ± 3.6) points and (17.6 ± 3.5) points. In the observation group it was significantly lower than that in the control group (P < 0.05). Comparisons before and after treatment showed significant difference (P < 0.05). Total efficiency rate of anxiety were 83.3% and 9.6%. Comparisons between the two groups showed that in the observation group it was significantly better than that in the control group (P < 0.05); The specific data were shown in **Table 3**.

Safety of treatments

During treatment, there was no serious drug-related adverse reactions. In some cases there were minor adverse reactions. After symptomatic treatment, they were improved and did not affect the process. Adverse reaction rate were 14.8% and 26.9%. In the observation group it had a significant advantage (P < 0.05). That is, for the safety of the two therapies, in observation group it was significantly better than the control group (P < 0.05). The specific data were shown in **Table 4**.

Discussion

With increasing age, female ovarian function declines and estrogen secretion is gradually reduced; the most obvious stage is menopause around the age of 49. At this stage, women often present as insomnia, irritability, emotional instability, high blood pressure and other symptoms of autonomic dysfunction, which is clinically called climacteric syndrome. If the blood pressure reaches hypertension level and continues for more than six months, it can be diagnosed as menopause hypertension [10].

Table 3. HAMD scores and anxiety curative effect comparison between the two groups after treatment

| Groups (n) | HAMD scores after treatment (points) | Recovery | Effective | Invalid | Total effective rate (%) |
|------------------------|--------------------------------------|----------|-----------|---------|--------------------------|
| Observation group (54) | 14.3 ± 3.6 | 20 | 25 | 9 | 83.3 |
| Control group (52) | 17.6 ± 3.5 | 2 | 3 | 47 | 9.6 |
| X ² (T) | 8.962 | | | | 7.585 |
| P | 0.036 < 0.05 | | | | 0.002 |

Table 4. Adverse reaction comparison between two groups

| Groups (n) | Flush | Constipation | The rash | Joint pain | other | The incidence of adverse reactions (%) |
|------------------------|-------|--------------|----------|------------|-------|--|
| Observation group (54) | 0 | 2 | 1 | 1 | 4 | 14.8 |
| Control group (52) | 3 | 4 | 2 | 2 | 3 | 26.9 |
| X ² | | | | | | 5.632 |
| P | | | | | | 0.028 |

The anxiety, tension and other symptoms of menopause not only increase the impact of the disease on the quality of life of patients, but also affect drug use and efficacy, so it has important clinical value to study the treatments of menopausal hypertension.

Gastrodine injection has pharmacological effects of conditioning the arterial wall elasticity, dilating cerebral blood vessels, so it can regulate blood pressure on the base of eliminating the dizziness and headache of hypertension patients. Modern research has confirmed that gastrodine injection can improve plasma ET and NO in hypertension patients and thus play a therapeutic role, so as to provide theoretical support for its clinical application [11]. While there are fewer studies on its application in the treatment of menopausal hypertension; its clinical application lacks theory and data to support, which also reflects the value of this research. Maprotiline hydrochloride tablet is the commonly drug in clinical to treat anxiety and depression; it works by blocking nerve endings norepinephrine reuptake, with good effect; it is also the commonly-used drug in the treatment of menopausal syndrome [12]. But its application in menopausal hypertension and combination with gastrodine injection lack research support, so this study not only has important guiding value for clinical practice, but also is innovative.

Menopause hypertensive patients were taken as subjects; according to groups conventional antihypertensive therapy and treatment of gastrodine injection combined with Maprotiline hydrochloride tablet were given, and the blood pressure, psychological status and adverse

reactions were compared between the two groups, in order to demonstrate the clinical value of the therapy. The results confirmed that in gastrodine injection combined with Maprotiline hydrochloride tablet group, hypertension efficacy, anxiety efficacy and adverse reaction rates were significantly better than those in conventional antihypertensive therapy group, thus confirming that the study therapy had good effect and safety and was a viable treatment of menopausal hypertension, to provide guidance for the clinical treatment. Although there were some limitations in time, space, economy, hospital medical level, data analysis capability, research data and settings, through evidence-based research this study acquired selection criteria, grouping method, research data evaluation standards, and screened the medical staff involved in the study, and used double-blind studies to reduce the impact of external factors on the data, enhancing research scientificity and safety; therefore, the results and conclusions of this study were scientific and effective.

In summary, gastrodine injection combined with anti-anxiety drugs for the treatment of menopausal hypertension was safe, effective and feasible, suitable for clinical practice.

Acknowledgements

This work was supported by Xinjiang Uygur Autonomous Region Natural Science Fund Project: 2014211C089.

Disclosure of conflict of interest

None.

Address correspondence to: Zhi-Min Fang, Department of Cardiology, Second Affiliated Hospital of Xinjiang Medical University, China. Tel: +86-0991-4609056; Fax: +86-0991-4609056; E-mail: Fangzhimin15@sina.com

References

- [1] Matsuo K, Gualtieri MR, Cahoon SS, Toboni MD, Machida H, Moeini A, Hasegawa K, Shoupe D, Roman LD. Contributing factors for menopausal symptoms after surgical staging for endometrial cancer. *Menopause* 2015; 438: 11-7.
- [2] Dalago HR, Schuldt Filho G, Rodrigues MA, Renvert S, Bianchini MA. Risk indicators for Peri-implantitis. A cross-sectional study with 916 implants. *Clin Oral Implants Res* 2016; [Epub ahead of print].
- [3] Rusiecki J, Rao Y, Cleveland J, Rhinehart Z, Champion HC, Mathier MA. Sex and menopause differences in response to tadalafil: 6-minute walk distance and time to clinical worsening. *Pulm Circ* 2015; 5: 701-6.
- [4] Briant LJ, Charkoudian N, Hart EC. Sympathetic regulation of blood pressure in normotension and hypertension: When sex matters. *Exp Physiol* 2016; 101: 219-29.
- [5] Allen RH, Cwiak CA. Contraception for midlife women. *Menopause* 2016; 23: 111-3.
- [6] Van Kempen TA, Narayan A, Waters EM, Marques-Lopes J, Iadecola C, Glass MJ, Pickel VM, Milner TA. Alterations in the subcellular distribution of NADPH oxidase in hypothalamic paraventricular neurons following slow pressor Angiotensin II hypertension in female mice with accelerated ovarian failure. *J Comp Neurol* 2016; 524: 2251-65.
- [7] Jang M, Lee Y, Choi J, Kim B, Kang J, Kim Y, Cho S. Association between Parity and Blood Pressure in Korean Women: Korean National Health and Nutrition Examination Survey, 2010-2012. *Korean J Fam Med* 2015; 36: 341-8.
- [8] Kadirogullari P, Atalay CR, Ozdemir O, Sari ME. Prevalence of Co-existing Endometrial Carcinoma in Patients with Preoperative Diagnosis of Endometrial Hyperplasia. *J Clin Diagn Res* 2015; 9: QC10-4.
- [9] Villaverde Gutiérrez C, Ramírez Rodrigo J, Olmedo Alguacil MM, Sánchez Caravaca MA, Argente Del Castillo Lechuga MJ, Ruiz Villaverde A. Overweight obesity and cardiovascular risk in menopausal transition. *Nutr Hosp* 2015; 32: 1603-1608.
- [10] Wang M, Cheng N, Zheng S, Wang D, Hu X, Ren X, Pei H, Ma H, Mu H, Bai Y. Metabolic syndrome and the risk of breast cancer among postmenopausal women in north-west China. *Climacteric* 2015; 18: 852-8.
- [11] Lee J, Kim HJ, Cho B, Park JH, Choi HC, Lee CM, Oh SW, Kwon H, Heo NJ. Abdominal Adipose Tissue was Associated with Glomerular Hyperfiltration among Non-Diabetic and Normotensive Adults with a Normal Body Mass Index. *PLoS One* 2015; 10: e0141364.
- [12] Pollow DP Jr, Romero-Aleshire MJ, Sanchez JN, Konhilas JP, Brooks HL. ANG II-induced hypertension in the VCD mouse model of menopause is prevented by estrogen replacement during perimenopause. *Am J Physiol Regul Integr Comp Physiol* 2015; 309: R1546-52.