# Clinical Observation Of ZhenQi Buxue Oral Liquid in Treating Menstrual Disorders

## Version 3.0 (Mar, 2022)

Research Title：Clinical and Basic Researches Related to ZhenQi Buxue Oral Liquid in Treating Menstrual Disorders

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Research Units：Peking Union Medical College Hospital

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The Second Hospital of Hebei Medical University

Second Affiliated Hospital of Nanchang University

Southeast University Affiliated Zhongda Hospital

Hubei Maternal and Child Health Hospital

Liuzhou Maternity and Child Healthcare Hospital

Zhejiang University Medical College Affiliated Hangzhou First People's Hospital

Guangzhou Women and Children's Medical Center

### 1. Research Backgrounds and purposes

Menstrual disorders are a common disease, and the incidence is increasing year by year under the social background of modern general mental and psychological pressure. The most common causes of menstrual disorders are various psychological and spiritual factors, age factors, iatrogenic factors, etc. The clinical manifestations mainly include oligomenorrhea, amenorrhea, and decreased menstrual flow. Western medicine generally uses hormone supplementation to treat menstrual disorders. At present, the clinical treatment of menstrual disorders is mainly based on progesterone

supplementation, which can protect the uterus and effectively control the amount of bleeding. The theory of traditional Chinese medicine believes that menstrual irregularities are related to people's constitution, and the foundation of menstruation regulation is to nourish the kidneys as the first method. Clinically, Zhenqi Buxue Oral Liquid is mainly used for dizziness, pale complexion, fatigue, lack of energy and lazy speech caused by insufficient qi and blood. , ginger, jujube. The excipients are protein sugar and sodium benzoate. Sheep placenta has the effect of regulating vitality, nourishing essence and blood, and can invigorate kidney qi, nourish essence and blood, and improve the vitality of the body; pearls can soothe the nerves and calm panic; coix seed and ginseng can replenish vitality, nourish blood and promote body fluid; Strengthens the surface and strengthens the muscles; Angelica has the effects of invigorating the spleen and stomach, nourishing qi and promoting body fluid, nourishing blood and soothing the nerves. Therefore, it has a certain theoretical basis of traditional Chinese medicine for the treatment of mental and psychological factors or women's menstrual disorders. This study intends to compare the treatment of Yimaxin (progesterone capsule) and Zhenqi Buxue oral liquid, and analyze and compare the improvement of symptoms, signs and various inspection indicators related to menstrual disorders between the two groups after treatment. Provide more reasonable and safer treatment methods.

**2.Research process and methods**

This clinical study was conducted in multiple centers such as Peking Union Medical College Hospital, Chinese Academy of Medical Sciences; West China Second Affiliated Hospital of West China Medical University; First Affiliated Hospital of Chongqing Medical University; and Second Affiliated Hospital of Hebei Medical University. Patients diagnosed with menstrual disorders were divided into 3 groups according to the type of medication, namely: Group A (Zhenqi Group): Zhenqi Buxue Oral Liquid was taken orally, 10 ml per time, 2 per day times*3 menstrual cycles, orally; Group B (Progesterone group): Yimaxin 200 mg once a day for 10 days*3 menstrual cycles, orally; Group C (combination group): Zhenqi Buxue Oral Liquid, orally , 10 ml at a time, 2 times a day * 3 menstrual cycles + oral Yimaxin 200mg once a day * 10 days * 3 menstrual cycles from the second half of the menstrual cycle. The clinical study lasted for 3 months, and the follow-up was conducted once a month (before the medication, after the first month of medication and after the third month of medication, and after the second month, followed by telephone or WeChat follow-up), during your participation in the study You will take Zhenqi Buxue Oral Liquid or Yimaxin according to the

doctor's order. From the first day you agree to participate in this study, you will receive a subject diary card issued by the doctor in charge, and follow the doctor's request. Complete it daily and submit it to the doctor in charge at each hospital visit. During the whole clinical research process, it is necessary to complete various physical examinations, laboratory tests and corresponding auxiliary examinations according to the requirements of the competent doctor (respectively before taking the medicine, 1 month and 3 months after taking the medicine). , 3 months), about 15-20 ml of venous blood each time (including sex hormones (mainly FSH, LH and E2 and AMH, liver and kidney function tests, etc.).

**3. Benefit from participating in the research:**

During the research, you will receive free related examinations for menstrual disorders, Zhenqi Buxue Oral Liquid and Yimaxin drugs for free; during the research, the doctor will monitor your condition throughout the whole process, and give you timely advice.

This study will not bring risks and discomforts other than disease treatment to the subjects participating in the study. During the study, the doctor will monitor your condition throughout the whole process, and follow up after 1 month of taking the medicine. Patients can consult the research unit at any time regarding the discomfort during the treatment. In the event of side effects related to the test drug, we will provide free diagnosis and treatment and corresponding compensation according to national regulations.

**4. Relevant details consulting:**

You have the right to inquire about the research content, and if you have any questions about the research situation or your rights, or if you think there is any situation related to this research, please contact your doctor in charge. And you have the right to consult about your rights or related risks, consultation telephone (ethical review committee telephone): 69155817.

**5. Right to withdraw from research:**

Your participation in this study is completely voluntary. You may withdraw from the study at any time without reason, and your unwillingness to participate or continue to participate in the study will not affect your rights in any way. Additionally, you have the right to withdraw from this study at any time. (The doctor or investigator may also ask you to withdraw if you do not follow your doctor's instructions, or if your doctor is concerned about your health and well-being.)

**6. Confidential:**

Your medical information from this study will be kept confidential. Research results are also published in academic journals without revealing any personally identifiable information. Peking Union Medical College Hospital will keep all of your records in this study and related hospital and office records, and no one should have access to this information without authorization. When necessary, the sponsor of the trial project, the ethics committee, and the government management department may consult the data of the subjects participating in the research according to regulations.

Signature（Subject）_____ Date：_____

Signature（Researcher）_____ Date：_____

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## A． OBJECT

Menstrual disorders are one of the most common clinical symptoms in women. Since puberty, about 70% of women have experienced menstrual disorders, including early, delayed, shortened, prolonged, and more importantly oligomenorrhea, amenorrhea, and decreased menstrual flow.At present, the main method of western medicine for the treatment of menstrual disorders is hormone replacement therapy, but the incidence of adverse reactions is high, and the clinical effect is mediocre. Traditional Chinese medicine in my country mostly adopts holistic conditioning therapy for the treatment of irregular menstruation.

Zhenqi Buxue Oral Liquid consists of sheep placenta, pearl, red ginseng, wolfberry, astragalus, angelica, coix seed, ginger and jujube. The excipients are protein sugar and sodium benzoate. Nourishes qi and blood. It is suitable for dizziness, pale complexion, fatigue, lack of energy and lazy words caused by insufficient qi and blood. This study will conduct a comprehensive and in-depth study on its treatment of mental and psychological stress and menstrual disorders with "oligomenorrhea, amenorrhea, amenorrhea and decreased menstrual flow" as the main manifestations. The molecular mechanism and clinical improvement, and the safety and adverse reactions of its use paln to be clarified.

## B. STUDY METHOD AND DESIGN

- 330 women with menstrual disorders were observed in a prospective multi-center randomized controlled clinical trial.
- Inclusion Criteria:
    1) Aged between 25 and 40 years old;
    2) Patients with oligomenorrhea or oligomenorrhea or menopause within three months (see Appendix 1: Diagnostic Criteria of Traditional Chinese and Western Medicine)
    3) Meet the clinical medication conditions for progesterone to regulate menstruation
    4) The research subjects were informed and voluntarily participated in this study, and signed the informed consent at the same time.
- Exclusion Criteria:
    1) Age <25 years or >40 years old, pregnant or breastfeeding women
    2) Ovarian dysfunction caused by local ovarian surgery, radiotherapy and

chemotherapy for previous malignant tumors, taking hormones or immunosuppressive drugs;

3) Combined with serious or unstable physical diseases that may affect the efficacy of drugs and the conduct of trials, including liver, kidney, gastrointestinal, cardiovascular, respiratory, endocrine, neurological, immune or blood system diseases, etc., mental patients .
4) Those who were allergic to the drugs used in the trial or had serious adverse reactions in the past;
5) Breast cancer or family history of breast cancer in first-degree relatives, irregular vaginal bleeding, uterine fibroids (≥3cm), endometriosis, atypical endometrial hyperplasia, endometrial cancer and other hormone-dependent reproduction Systemic diseases and other malignant tumors;
6) Those with a history of thromboembolic disease or thrombosis;
7) Participated in a clinical trial of another research drug within 3 months prior to inclusion in this study (the first interview);
8) Those who have used related drugs in the past 3 months or have abused or depended on substances (alcohol or drugs) in the past 3 months; heavy smokers (smokers who smoke 20 or more cigarettes per day);
9) Those who met the inclusion criteria, did not follow the doctor's advice, were unable to judge the curative effect or were unable to evaluate the curative effect due to incomplete data.

- Methods: The participants were divided randomly into 3 groups:
  1) Experimental group1(Zhenqi Buxue Oral Liquid): Zhenqi Buxue Oral Liquid, 10 ml each time, 2 times a day for 3 menstrual cycles, orally
  2) Experimental group2(Zhenqi Buxue Oral Liquid and Progesterone Capsules): Zhenqi Buxue Oral Liquid was taken orally, 10 ml at a time, twice a day for 3 menstrual cycles + orally from the second half of menstrual cycle, Progesterone Capsules 200mg, once a day for 10 days for 3 menstrual cycles
  3) Active Comparator group (Progesterone Capsules): Progesterone Capsules 200mg, qd*10 days*3 menstrual cycles, orally

- Treatment Period: 3 month.
- Outcomes Measurement:
    1) Primary Outcome: Menstrual improvement in women including cycle period, menstrual volume，number of days with bleeding or spotting, monthly rates of amenorrhea
    2) Secondary Outcome:
        a) Sex hormone levels: mainly FSH, LH，E2 and AMH
        b) AFC: Changes in AFC in pelvic ultrasonography
        c) SF-36: The change of the MOS item short from health survey
    3) Safety Assessment: Adverse reactions, Hepatic Function, Renal Function, Blood Glucose, Breast Ultrasound

**C. TECHNICAL ROUTE**

**Screening Period (Day -30~0)**

a) The researcher explained the research situation and informed the subjects, and the subjects signed the informed consent;

b) Evaluate whether subjects can enter the study according to the inclusion and exclusion criteria;

c) Collect basic information, medical history (including menstrual history, pregnancy and birth history) and demographic data, conduct routine physical examination (heart rate, blood pressure, height, weight); and irregular menstrual symptoms and scoring

d) On the 2nd to 3rd day of the menstrual cycle (basic day), draw venous blood to check FSH, LH, E2, prolactin (PRL), testosterone (T), and AMH;

e) Liver and kidney function;

f) Pelvic ultrasound: on the 1st to 3rd day after menstruation is clean, after disinfection of the vulva, transvaginal ultrasound is performed to count bilateral ovarian AFC, breast ultrasound;

g) The investigator and the subject agree on the time of the next follow-up visit.

**Enrollment (Day 1)**

a) Re-evaluate whether the subjects can enter the study according to the test and examination results during the screening period, referring to the inclusion and exclusion criteria;

b) Subjects were enrolled and received medicines according to the random number table;

c) The investigator and the subject agree on the time of the next follow-up visit.

**Follow-up 1 ( equivalent to the end of the first month)**

a) Ask and record adverse events that have occurred since enrollment;

b) Ask the patient about the first menstrual condition (menstrual period, cycle, menstrual volume) and symptoms of irregular menstruation after taking the medicine and make a score;

c) The investigator and the subject agree on the time of the next follow-up visit.

**Follow-up 2 (After taking the medicine in the second month, follow-up by WeChat or telephone)**

a) Ask and record adverse events that have occurred since enrollment;

b) Ask the patient about the second menstrual condition (menstrual period, cycle, menstrual volume) and the symptoms of irregular menstruation after taking the medicine and make a score;

c) The investigator and the subject agree on the time of the next follow-up visit.

**Follow-up 3 (the third month after taking the medicine, equivalent to the end of the third month)**

a) Ask and record adverse events that have occurred since enrollment;

b) perform routine physical examinations (heart rate, blood pressure, weight);

c) Ask the patient about the current menstruation and irregular menstruation symptoms, (or pregnancy), perform symptom scores, and evaluate the effectiveness of the drug;

d) FSH, LH, E2, PRL, T, AMH (blood draw on day 2-3 of menstruation);

e) Liver and kidney function;

f) Pelvic ultrasound (bilateral ovarian AFC) examination, breast ultrasound;

g) Subject returns untaken medication and checks (including used medication packaging) and filled diary card.

**D. STATISTICS ANALYSIS**

Data was analyzed using SPSS Version 25. All quantitative information are expressed as mean values ± standard deviation (SD). Statistical significance was assessed using unpaired Student's t-test or chi-square test. Probability values of less than 0.05 were considered significant and an asterisk identifies such significance in the figures. We will also compare the adverse effect of each group using descriptive statistics.

## E. QUALITY CONTROL MEASUREMENT AND RESULT PUBLICATION

1. Every center of the research possesses the competence of scientific research to conduct clinical studies. Special people from each center will be put in charge of the research and monitoring the whole procedure. The rights and interests, responsibility and obligation of all centers will be standardized with the research agreement.
2. The maintenance, secrecy and safety of data and informations will beguaranteed by Department of Obsterics and Gynecology, Peking Union Medical College Hospital.
3. Every center is responsible to subject enrollment and finish the prospective follow up.
4. The researchers' findings will be released in a paper published online.

## F. SOURCE(S) OF FUNDING

1. This study does not charge any fee to any patients.

2. All the investigational drugs and cost of the study are provided by Qian Jin Pharmaceutical CO., LTD.