

# *Review on the Research Progress of Premenstrual Syndrome*

Dingyao Fan, Tong LI, Siqing MA, Qiao LIU, Huiping TAN, Xiaoyue WU, Chunting DIAO\*

*Hubei University of Chinese Medicine, Huangjiahu Campus of Hubei University of Traditional Chinese Medicine, Wuhan city, Hubei Province*

*\*corresponding author*

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**Abstract:** Premenstrual syndrome (PMS) refers to physical discomfort and psychological symptoms that occur before menstruation (luteal phase of the menstrual cycle). This article will summarize the relevant research on premenstrual syndrome, make statements from two aspects of drug therapy and psychological therapy, and discuss the future research and from the perspective of Traditional Chinese medicine. Currently, there are few studies on premenstrual syndrome, and its treatment theory is still in the exploratory stage, and there is still a gap in international research. For this disorder in the future, not only the participation of modern medicine, but also the multi-dimensional diagnosis and treatment combined with traditional Chinese medicine theory should be carried out.

## **1. Introduction**

Premenstrual syndrome (PMS) refers to physical discomfort (headache, lower back pain, breast pain, lower abdominal discomfort) and psychological symptoms (irritability, irritability, anxiety, depression) before menstruation (the luteal phase of the menstrual cycle). These symptoms appear before menstruation, and then gradually weaken until disappear, the common population is mainly young and middle-aged women. The incidence is about 30%-40%, and the symptoms are more severe in 2%-15%. Premenstrual syndrome (PMS) has a certain impact on people's life, study and work, which has aroused widespread concern. [1] This article will summarize the related research on PMS and discuss the future research.

## **2. Symptoms and diagnostic criteria of PMS**

The symptoms of premenstrual syndrome (PMS) are varied and vary from person to person, so the key to diagnosis is to determine the timing and severity of symptoms and whether they are relieved after menstruation has ended. Currently, there are three diagnostic criteria for premenstrual syndrome in the world: ① Diagnostic criteria for PMDD in the American Psychiatric Association's (APA) Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), ② Diagnostic criteria for PMS recommended by the American College of Obstetricians and Gynecologists

(ACOG), ③ Diagnostic criteria for premenstrual tension syndrome (PMTS) in the International Classification of Diseases (ICD-10).[2-4]

In the American Diagnostic Statistical Manual of Mental Disorders, Fifth Edition (DSM-V, code N94.3), premenstrual syndrome was renamed premenstrual dysphoria disorder and categorized under the heading "Mood disorders" [5]. The English version is Premenstrual Dysphoric Disorder. Defined as recurrent anxiety disorder, loss or irritability in the week or so before menstruation begins. The criteria for diagnosis are as follows: in most menstrual cycles, five or more of the following symptoms are present and resolve with the onset of menstruation. Symptoms must include any of the first four symptoms. ① Significant depression, feeling of despair, or thoughts of inferiority; ② Significant anxiety and tension; ③ Significant mood swings; ④ Obvious anger or irritability, interpersonal relationship is prone to conflict; ⑤ Decreased interest in daily activities; ⑥ I feel it difficult to concentrate; ⑦ Often feel tired and tired; ⑧ Significant changes in appetite; ⑨ Excessive sleep or insomnia; ⑩ Feeling ready to collapse; For example, breast tenderness, headache, joint muscle pain, etc. These symptoms obviously affect the patient's work, study, and daily life, and should be observed for at least two consecutive periods.

The American College of Obstetricians and Gynecologists (ACOG) defines premenstrual syndrome as "foreseeable premenstrual symptoms closely related to the menstrual cycle that significantly affect normal living" [6] in the diagnostic criteria for PMS. The diagnostic criteria are: ① Body: water and sodium retention, hypoglycemia, breast pain, headache and so on; ② Behavior: sleep disorders, inattention, appetite changes, decreased interest in things; ③ Emotional aspects: irritability, emotional volatility, anxiety, depression and so on.

The International Classification of Diseases (ICD-10) names premenstrual symptoms as premenstrual tension syndrome, classified as a physical disorder, and describes it as "a series of repeated mental, behavioral and physical symptoms during the luteal phase of the menstrual cycle, which disappear after menstruation".

There is no clear name and definition for premenstrual syndrome. In terms of diagnosis, although different criteria have different focuses, there is still much overlap or similarity in the main symptoms. For example, the three criteria respectively in the cycle, physical and psychological aspects are mentioned in the following several items: ① symptoms in menses about a week began to appear, in the end of menstruation began to reduce until disappeared. ② There are significant mood fluctuations, such as anxiety, tension, depression or irritability, increased social conflicts, etc. ③ breast pain, abdominal pain, headache or joint pain, lethargy or insomnia, etc.

### 3. Relevant epidemiological investigation

Due to the social cognition of women's status has not reached a certain level, the defects of some women's self-knowledge and attitude towards menstruation, and the problems in the statistical process, there are few large-scale clinical investigation reports on premenstrual syndrome. It is reported abroad that the incidence is 30%-40%. 80% of women report mild premenstrual symptoms during menstruation, and 20% to 50% report mild to moderate premenstrual symptoms. In 5 to 8 percent of these patients, social functioning is affected. Thus, in each menstrual cycle, one in four women of reproductive age is affected by PMS, which often affects social roles, reduces work productivity and living standards, and can lead to a high direct and indirect burden of disease. In a survey of 454 women of childbearing age, Zhao Gengli et al. found that the incidence of PMS was 30.4%. Qiao Mingqi et al. pointed out in their epidemiological investigation of PMS that the incidence of the disease accounted for 41.9% of adult women. Li Yanqin reported that the incidence of PREmenstrual syndrome in women of childbearing age is as high as 30%-79%. [7]

In terms of patient age, the incidence of PMS is higher in women of childbearing age. But in recent years, the incidence of premenstrual syndrome in female college students also presents a high trend. The incidence of PMS among female college students is increasing due to physiological and psychological factors such as irregular eating habits, insufficient sleep and exercise, high pressure in study and interpersonal relationship, etc., which needs continuous attention from the society.

At the same time, often in negative emotions: anxiety, depression, tension or a long time in a high stress state of women are also prone to premenstrual syndrome. PMS women have great mental stress and poor mental health, and often adopt a dull coping style in the face of life events. Follow-up studies should also investigate psychosomatic problems.

## **4. Etiology and pathogenesis of premenstrual syndrome (PMS)**

### **4.1. The cause of**

#### **4.1.1 Endorphin theory:**

Since changes in endorphin levels can affect mental and neurological factors, intravenous administration of endorphins can increase prolactin concentration.[8] Animal studies have also shown an increase in vasopressin after endorphin administration. The effect of endorphin inhibitor naltrexone on endorphin receptor can change the secretion of luteinizing hormone, and  $\beta$ -endorphin changes with the menstrual cycle, so it is suggested that premenstrual stress syndrome is caused by the change of endorphin concentration in luteinizing phase.[9]

#### **4.1.2 Imbalance of progesterone ratio:**

PMS can be caused by high estrogen level and low progesterone level. It may also be due to abnormal tissue sensitivity to progesterone. Under normal circumstances, progesterone promotes distal renal tubular excretion of sodium and water, while estrogen through renin, angiotensin | water sodium retention, aldosterone system. Therefore, the imbalance between estrogen and progesterone can cause signs of weight gain.[10]

#### **4.1.3 Insufficient vitamin B6:**

Vitamin B6 promotes the elimination of excess estrogen in the body, easing mood and behavior. Lack of vitamin B6 is likely to cause premenstrual synthesis.

#### **4.1.4 Spiritual factors:**

Some patients with prominent mental symptoms, mood swings, mental tension and other symptoms can aggravate the original.

## **4.2. Pathogenesis of premenstrual syndrome**

### **4.2.1 Imbalance of neuromedia-neuroendocrine system:**

Endorphin ( $\beta$ -ENDORphin,  $\beta$ -EP) theory: normal menstrual cycle  $\beta$ . An EP begins to rise before ovulation and continues until the next menstruation. The  $\beta$ -EP level in the luteal phase of PMS patients was significantly lower than that in the normal control group. The use of the endorphin inhibitor Naloxone can produce symptoms similar to those of PMS. Abnormalities or sensitivity to  $\beta$ -ep during the luteal phase are responsible for a series of neuroendocrine processes that lead to various manifestations of PMS.[11]

Serotonin (5-HT): 5-HT plays a role in the development of PMS. During the premenstrual period, the 5-HT can be impaired in the nervous system of PMS patients, resulting in variations in their responsiveness to stimuli. PMS can be effectively treated with drugs that release 5-HT or block its reabsorption.[12]

#### **4.2.2 Hormone changes:**

Progesterone deficiency: PMS often occurs during ovulation cycles, and can be caused by decreased progesterone levels during the luteal phase or by changes in the E/P ratio. Progesterone deficiency causes estrogen to be relatively excessive, resulting in electrolyte imbalance, increase of extracellular fluid, headache, edema, irritability, breast distension and so on.

Increased secretion of prolactin (PRL) PRL plays a significant role in the regulation of osmotic pressure in animals, but has little effect on humans. It may only act on the mammary gland, affecting the balance of local osmotic pressure and causing breast swelling and tenderness. PMS symptoms are rare in women with hyperPRL. The theory of increased PRL excretion due to the fact that bromocriptin only alleviates breast symptoms and has no significant effect on other symptoms is still lacking reliable and strong evidence.[13]

#### **4.2.3 Sodium hydrate retention:**

High aldosterone causes systemic fluid retention and is often used to explain the development of PMS. The change of 5-HT in PMS patients leads to the increase of pituitary corticotropin, and the increase of aldosterone and angiotensin I secreted by adrenal glands, thus affecting electrolyte metabolism and causing water and sodium retention. However, some studies have found that PMS patients have unstable vascular regulation function. Capillary permeability increases, leading to fluid redistribution in the body, causing abdominal distention, breast pain.[14]

#### **4.2.4 Spiritual factors:**

According to the etiology theory of Parker, personality and environmental factors are very important to the occurrence of PMS symptoms, and the appearance of symptoms reflects the unresolved conflicts in the patient's heart. Tracing back to the patient's life history, there are often more obvious mental stimulation experience, such as childhood unfortunate experience and mental trauma, parents and family discord, poor academic performance, love, etc., may be an important factor to produce premenstrual mood changes. Some of the patients have prominent mental symptoms, and the tension of the tang aggravated the original symptoms.[15]

### **5. The treatment of premenstrual syndrome**

#### **5.1. Medication**

Western medicine generally uses drugs to adjust the activity of central nervous system neurotransmitters, in order to subside psychological and emotional disorders, or the application of hormones to inhibit ovulation, in order to eliminate breast pain and other serious pre-menstrual symptoms. And can take appropriate amount of sedative, diuretic, progesterone, androgen according to different manifestations. Currently, prozac (fluoxetine hydrochloride) has been proven to be one of the most effective drugs in the treatment of PMS.

(1) Diuretic application. To relieve the water and sodium retention in the premenstrual period, start a low-salt diet 10 days before menstruation, and for those with obvious symptoms, take diuretics,

oral dihydrogram urusea 25mg each time, 3 times a day. In order to avoid hypokalemia, 10% potassium chloride 10ml can be added, 3 times a day, or Gasonolysis 20mg each time, 3 times a day.

(2) Hormone therapy. Premenstrual tension syndrome may be caused by excessive estrogen, progesterone deficiency or deficiency, so progesterone replacement and complementary therapy can be given. Such as progesterone 20mg intramuscular injection, every other day, a total of 5 times. Starting from the 16th day of menstruation, oral norethinnes 5mg or megestrel 5mg daily can also be taken 14 days before menstruation. Androgen has estrogen effect and can inhibit gonadotropin secretion, indirectly achieve the reduction of estrogen level. Therefore, starting from the 15th day of menstruation, 5-10mg methyltestosterone was taken orally daily for 10-14 days.

(3) Aoyinting treatment. Symptoms of breast tenderness may be related to increased secretion of prolactin, which can be administered with the antagonistic prolactin drug Aoyinting 2.5mg, twice a day, from 12 to 26 days of menstruation. If nausea, headache and other side effects occur, the dosage can be reduced as appropriate, 1.25mg each time, 1-2 times a day.

(4) Vitamin B6 treatment. It has certain effect on regulating the relationship between plant nervous system and hypothalamus - pituitary - ovary. Vitamin B6 can also inhibit xlactin. Patients with severe vitamin B6 deficiency can take vitamin B620-40mg orally from the 10th day of menstruation, 3 times a day.

(5) Antiprostaglandin drug therapy. Methanic acid, sodium methoxypropionate 275mg oral every 4-6 hours.

(6) Choose appropriate painkillers and sedatives when necessary.

## 5.2. Psychotherapy

The main psychological treatment for premenstrual syndrome is cognitive behavioral therapy, or CBT. It includes coping skills training, biofeedback, relaxation training and rationalized emotional therapy. This is proposed by Zhang Li, Yuan Haolong and others in their research. However, there are few researches on the psychological treatment of premenstrual syndrome at present.

Among them, relaxation training is relatively simple and easy, and is similar to the "three-line relaxation exercise" in traditional Qigong. It requires the patient to sit in a chair, with the limbs and body in a relaxed state, or lie flat on a bed. The training environment should be quiet and maintain a certain comfortable temperature. Noisy and cold environments can cause muscle tension and the inability to relax. Then follow the guidance of the psychologist for training. Start with your scalp, eyes, lips, face, neck muscles and work your way up to your extremities. In order for patients to fully experience relaxation, they can first experience tension. For example, clench your right fist, then release it and allow the fingers to relax naturally. Experience how the blood rushes from the upper limb to the fingers. The fingers become hot, heavy and almost impossible to control. This is the end of a 15-20 minute relaxation session.

We also found that PMS patients had obvious negative emotions, such as anxiety, depression and somatization. Stress factors will cause physical and mental diseases, one of the important mediators is emotion, so through the cognitive evaluation of patients, stress factors can be transformed into emotional responses. Researchers at home and abroad have concluded that mood disorders are a related risk factor for PMS onset and repeated somatization. Li Hengfen, He Tea et al.'s research suggests that PMS can be treated through psychological counseling, emotional adjustment and seeking support and help from relatives. Psychological counseling is to help PMS patients adjust their psychological state, so that they can fully recognize the disease and build courage and confidence in such a process.

## 6. Summary of problems encountered in the study of premenstrual syndrome

The exact cause of PMS is unknown: There are currently no studies to determine whether PMS is caused by hormonal and neuroendocrine factors that increase sensitivity to progesterone, or by 5-hydroxytryptamine deficiency, so the exact cause of PMS is unknown.

It is difficult to unify the diagnostic criteria and the diagnostic process: as the premenstrual syndrome is greatly affected by personal characteristics, regional environment and living environment, and the clinical manifestations are personalized, it is difficult to form a unified and standardized diagnostic standard. Due to the lack of distinct symptoms in clinical premenstrual syndrome, there are many similarities with other emotional disorders, so it is difficult to judge the process.

Treatment is not targeted and has yet to be proven experimentally: as the factors affecting PMS are diverse and change rapidly, it is difficult for the same treatment to continue to work, but there is currently no one-to-one treatment for each stage of the syndrome. The effectiveness of current treatments has not been fully validated by large-scale clinical trials.

Single investigation method: In the current investigation, due to the problems of funds and emphasis, questionnaires and tests are basically used for experimental subjects, and there is a lack of clinical trial data and results of large-scale testing of progesterone and hormones on experimental subjects.

Low popularity of treatment methods: At present, most women's treatment of PMS is still in the stage of medication, the surrounding mental support system is not perfect, biofeedback relaxation training, essential oil therapy and other methods have not been popularized.

## 7. Discussion on future research

Necessity: The clinical manifestations of premenstrual syndrome are varied and individual. At the same time, in previous studies, PMS has neither prescribed symptoms for diagnosis, nor provided accurate laboratory diagnostic indicators, and there is still no unified diagnostic standard established internationally. From the statistics of PMS, the disease mainly occurs in women of childbearing age. Qiao Mingqi et al. [16] conducted an epidemiological investigation on PMS and pointed out that the incidence of the disease accounted for 41.9% of adult women. As the incidence of PMS varies according to different diagnostic criteria, and the research objects and living environments reported in relevant literatures are different, the subjectivity of the research cannot be ruled out. Therefore, all the epidemiological research results are only for reference.

Future research direction: With the transformation of medical model from bio-medical model to bio-psycho-social medical model and the rise of medical psychology, research should gradually pay attention to the influence of psychological aspects on diseases. Xia Guicheng [17] found that women's diseases, especially premenstrual syndrome and menopause syndrome, are related to this. Therefore, future research should focus on the use of psychological modulation therapy for PMS patients as an adjunct to drug therapy. In addition, most studies on premenstrual syndrome only describe clinical manifestations and observation of efficacy, reflecting only the subjective feelings of patients before and after treatment, which cannot guarantee the repeatability and effectiveness of the test. Therefore, future studies should pay more attention to objective laboratory testing and experiments.

## 8. The theory of TRADITIONAL Chinese medicine should be introduced into the study of premenstrual syndrome in the future

Currently, the treatment theory of premenstrual syndrome is still in the exploration stage, and there is still a gap in international research. For this disorder in the future, not only the participation of

modern medicine, but also the multi-dimensional diagnosis and treatment combined with traditional Chinese medicine theory should be carried out.

The doctor of traditional Chinese medicine thinks, the occurrence of the disease is due to the women in the early stage of the menstrual blood except nourishes the zang-fu organs, but also bet on blood, fancy is fully prepared for next time menstruation, so at this time the whole body blood, organs, tissues and organs needed blood is that much more scarce, qi and blood deficiency, will further lead to internal organs function imbalance temporarily, A number of symptoms followed. Some scholars believe that liver depression, qi stagnation, kidney water deficiency is the root cause of this disease, because of the liver and kidney, combined with the adjustment of zang-fu qi and blood for dreading, will achieve good curative effect. (Chinese Medicine therapy PMS) [18]

TCM treatment is mainly aimed at the etiology of the syndrome in the early stage of the syndrome, dialectical treatment, the establishment of the liver and qi, in addition to distension and pain, with the treatment of the stomach and other criteria, to paeony, xiangfu, neem, Bupleurum and other traditional Chinese medicine as the main prescription, also can often achieve very good results. In addition, can also be taken according to the specific situation of some Chinese patent drugs, such as liver qi stagnation patients can take Danzhi Xiaoyao pills, spleen kidney Yang deficiency patients can take Zhidai pills, Jisheng Shenqi pills, liver and kidney Yin deficiency patients can take Qiju Dihuang pills and tiaojing granules, blood deficiency patients can take Funing capsules, Women's health tablets, etc.

The development of psychology industry in China is in full swing. We should also combine the physiological and psychological characteristics of Chinese women and combine TCM with psychosomatic diseases to better explore the physical and mental health of human beings.

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