Progress in Traditional Chinese Medicine Syndrome Differentiation and Treatment of Premature Ovarian Failure

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Abstract: Premature ovarian failure has directly or indirectly caused unspeakable physical and mental suffering to many women because of its increasing incidence. People of all ethnic groups in the world are actively seeking the best method, but the results are only basically satisfactory. As far as treatment is concerned, Chinese and Western medical treatments have their own advantages and disadvantages. However, because of the variety of syndrome types in traditional Chinese medicine, there are many descriptions of a single disease syndrome, and there are few systematic generalizations and classifications. Therefore, the experience of traditional Chinese medicine in the treatment of premature ovarian failure in recent 10 years is classified and summarized. Traditional Chinese medicine believes that the root cause of premature ovarian failure is the disorder of viscera, and the pathological sign is phlegm dampness and blood stasis. Therefore, the treatment should be based on kidney, syndrome differentiation and treatment of multiple viscera, taking into account phlegm dampness and blood stasis, combined with periodic therapy and acupuncture treatment, striving to nourish the kidney, regulate the heart, liver, spleen and lungs, and smooth phlegm dampness and blood stasis, so as to achieve the effect of prevention and treatment.

Keywords: Premature ovarian failure, Syndrome differentiation and treatment, Traditional Chinese medicine syndrome type, Traditional Chinese medicine treatment, Syndrome and treatment ideas

Premature ovarian failure refers to a phenomenon in which women's ovarian function fails prematurely due to various causes. Menstrual amenorrhea, infertility, genital atrophy, and regression in female patients before age 40, with varying degrees of hypergonadotropin and hypoestrogenic syndromes, such as mood disorders, facial flushing, hot flashes, and night sweats and osteoporosis. Chinese medicine belongs to the category of "amenorrhea" [1-2].

Epidemiological studies have shown that the incidence of premature ovarian failure in women is 0.9 to 1.2% at or before the age of 40 [3], and the prevalence has declined approximately 10-fold in each decade before that [4]. Due to racial differences, the prevalence of women in China and Japan is also different, 0.5% and 0.1%, respectively [5]. It is true that the etiology and pathogenesis of premature ovarian failure are complex and unclear, but most of them are genetic and immune factors, and are also related to medical, environmental, personal behavior and emotional factors [6-7]. In terms of treatment, Western medicine currently uses hormone replacement therapy, ovarian transplantation, immunotherapy, stem cells and gene therapy, etc. [8], which have indeed alleviated the disease. Eastern medicine regulates the internal organs through syndrome differentiation and treatment, taking into account both the symptoms and the symptoms, and has outstanding curative effects [9-10]. According to the clustering analysis of Chinese medical evidence of premature ovarian failure and the identification of internal organs and the eight syllabuses in the literature, the distribution pattern of the evidence types is shown in Figure 1 and Figure 2 [11-12].
Figure 1: The distribution pattern of TCM evidence types of premature ovarian failure under cluster analysis

Figure 2: The distribution pattern of TCM evidence types of premature ovarian failure under the identification of internal organs and the eight syllabuses

1. Treating from the perspective of the viscera

Since ancient times, Eastern medicine has viewed the human body and even all things in the world in a unified way. Chinese medicine believes that the five internal organs of the human being are independent and unified and cannot be separated. The normal operation of the body not only requires each viscera to function independently, but also needs to work together in coordination to support the normal cycle of nature. Therefore, as far as the treatment of premature ovarian failure is concerned, this principle should also be followed, and the method of cure should be explored based on the harmony of viscera.

1.1 Treating from the kidney

"Menstruation comes from the kidneys". The yin essence of the kidney is not filled, the source of essence and blood is lacking, the kidney yang is not filled, and it is lost in warmth. Kidney essence is difficult to transform, there is no source of metaplasia, such as water without source, Tiangui are difficult to reach, Chong Ren is difficult to adjust, the uterus is difficult to overflow, and menstruation is difficult to come on time. Therefore, looking back to the source, premature ovarian failure should first be based on strengthening the kidney.
1.1.1 Invigorating the kidney and filling essence

Traditional Chinese medicine believes that the function of kidney essence is related to the process of human growth, development and aging. Fu Yanjin et al. combed the role of kidney-tonifying method and bone marrow mesenchymal stem cells in the treatment of premature ovarian failure, and confirmed that kidney-tonifying method has the ability to promote the proliferation, differentiation and migration of bone marrow mesenchymal stem cells [13]. Wang Hui et al. have concluded that Bushen Tiaojing Decoction combined with estrogen and progesterone replacement in the treatment of premature ovarian failure can effectively relieve clinical symptoms and improve the blood flow of the ovary and its interstitial arteries, with good safety [14].

1.1.2 Warming the kidney and helping the yang

Lu Xiaonan and others used Bushen Erxian Decoction to treat premature ovarian failure of kidney-yang deficiency type, and the symptoms were relieved obviously, and the actual curative effect was 72.5% [15]. The combination of movement and stillness, complementing yin and yang, stimulates the development of follicles and induces ovulation through the immune regulation mechanism, and has the effect of restoring ovarian function. It has been reported in the literature that the improvement rate of clinical manifestations of kidney-yang deficiency type premature ovarian failure is as high as 88.30% by using Wenshen Zhiyang Yiqi Yangxue Recipe combined with western medicine [16]. It can improve the main complaints and accompanying symptoms to a large extent, can awaken and reshape part of the ovarian function, and improve the sensitivity to gonadotropins, with better curative effect.

1.1.3 Complementing the yin and yang

Mr. Xiao Chengcong believes that the main cause of premature ovarian failure is the deficiency of both yin and yang of the kidney, the difficulty in regulating the Chong pulse, and the difficulty in filling the sea of blood [17]. Therefore, Yishen is mainly used, Yin and Yang are supplemented, and Qizi Yishen Lichong Decoction is formulated to treat premature ovarian failure. This recipe is made on the basis of Wuzi Yanzong Pills, which has the effects of nourishing kidney yin, warming kidney yang, and absorbing astringency and solidifying essence. The whole formula is matched with various medicines to supplement the double deficiency, and the essence can be replenished, so that the supplement is not stagnant. The essence and blood are both complete, the kidney qi is filled, the yin and yang are reconciled, and the functions of benefiting the kidney are played together, all diseases can be cured, and the curative effect is remarkable [18].

1.2 Treating from other viscera

For the treatment of premature ovarian failure, the clinical academia presented a star-studded academic feast. From the treatment of the spleen and stomach, the insight is clear and fundamental, treat from the liver, size up the situation and guide according to the situation; explore the treatment from the heart, and complement each other from top to bottom; from the treatment of the lungs, the views are original and the viewpoints are novel. Through the treatment of multiple viscera, the intertwined premature ovarian failure is gradually clear and easy to solve.

1.2.1 Treating from the spleen and stomach

Professor Luo Songping pointed out that the essence of premature ovarian failure is the deficiency of yin and essence, and the lack of yang, especially spleen yang [19]. Therefore, under the basic principle of invigorating the kidney and replenishing the essence, attention should be paid to the adjustment and replenishment of the spleen and stomach, so that the essence and chemical production have a source, the blood has a root, and the acquired and innate are replenished [20]. Luo Yuxue et al believe that the spleen and stomach are the foundation of the day after tomorrow, and should be based on regulating the spleen and stomach, choosing Shengmai Decoction to improve qi and nourish yin, strengthen the spleen and kidney to treat premature ovarian failure, and advocate eating more beans containing protein and soy isoflavones phytoestrogens. Because it has the effect of anti-aging [21].

1.2.2 Treating from the liver

Professor Zhang Yuzhen believes that, caused by emotion or inherent weakness, kidney qi is weak, liver qi is stagnant, and Tiangui loses its source and cannot arrive on schedule [22]. Chong Ren is not full, it fails to adjust and dredging, the sea of blood is not full, it is difficult to overflow. Menstruation can not come on time, resulting in infertility or premature ovarian failure. Therefore, an empirical prescription plus Chinese patent medicine Liuwei Dihuang Pill and Xiaoypao Pill are formulated to treat
premature ovarian failure, and the curative effect is definite. Some literatures explore that the important pathogenesis of premature ovarian failure is that the liver loses its dredging function [23]. Therefore, to regulate and nourish the liver and kidney, soothe the liver and relieve stagnation is the way to cure, so that the yin and blood are sufficient, the qi machine is smooth, and the combination of medicine and syndrome can be effective [24]. Du Changyan and others found that Bushen Yanggan Decoction can continuously and effectively improve ovarian function gradually, and achieve the effect of moderate adjustment and awakening, thereby curing premature ovarian failure [25].

1.2.3 Treating from the heart

Xia Guicheng, a master of Chinese medicine, believes that "if the heart is calm, the kidney is strong" [26]. It should focus on regulating the heart, and regulating the heart is beneficial to the kidney, so as to achieve the effect of promoting the kidney water and lowering the heart fire. He formulated Qingxin Zishen Decoction to assist Western medicine in the treatment of premature ovarian failure, and the curative effect was satisfactory. The whole prescription can nourish the kidney and calm the heart, and the heart and kidney are in harmony [27]. At the same time, Xia Lao pointed out that the pathogenesis of premature ovarian failure should be that the heart and kidney cannot work together. Exhausted water is difficult to fish. Therefore, it is necessary to nourish the kidney yin, clear the heart fire, and communicate with the heart and kidney [28].

1.2.4 Treating from the lung

Professor Chai Songyan believes that for menstruation to be on schedule, the uterus needs to be full [29]. However, the foundation of menstruation is menstrual blood, and the foundation of menstrual blood is the essence of water and grain. The metaplasia of essence and blood has a source, the transportation path is smooth, and menstrual blood can be sufficient. The lungs are directed towards the various channels, and they control the flow of qi and water. Under the action of the lungs, the essence of water and grain is like nectar moisturizing the earth, turning red into the lungs, and then entering the uterus, and menstruation is smooth. Therefore, lung gold produces kidney water, and when the source is open, water is prosperous. Lung qi is prosperous, kidney essence is prosperous, essence qi is prosperous, and menstruation returns. Governance should be based on the lungs, open the lungs and open the kidneys. The two flavors of lily and northern ginseng are mostly used in the medicine, and the curative effect is remarkable [30].

2. Treating from the phlegm dampness and blood stasis

Prolonged illness leads to blood stasis. Therefore, stagnation of blood stasis is the state of the disease from time to time, and it is an important cause of its course and treatment stages, and it is especially important to pay attention [31]. Kidney deficiency is the root cause of the disease, and blood stasis is the manifestation of the disease. Therefore, we should search for its root, identify its symptoms, and briefly treat its symptoms [32]. The foundation of invigorating the kidney, promoting blood circulation and removing blood stasis, making Qi and blood smooth. When the blood phase is in harmony, Chong Ren is regulated, the sea of blood is full, the uterus is overflowing, and menstruation can come on time every month [33].

2.1 Treating from the phlegm-dampness

Obese people have a lot of phlegm and dampness. Or due to the imbalance of the spleen and stomach, the spleen loses its health, the dampness is not transformed, and the phlegm-dampness is endogenous. Relevant studies have shown that internal resistance of phlegm-dampness is the most critical pathogenic factor and pathogenic mechanism of premature ovarian failure [34]. Modified Wendum Decoction can effectively improve its clinical symptoms, and can significantly reduce FSH and LH, with a total effective rate of 73.33% [35].

2.1.1 Invigorating the spleen and removing phlegm

The main clinical symptoms of spleen deficiency and phlegm type include: sparse menstruation, amenorrhea, irregular menstruation, infertility, wide body and fat body, swollen face and swollen limbs, and excessive vaginal discharge. Professor Li Liyun believes that "fat people have more phlegm and dampness" [36]. Phlegm-damp occupies the uterus and blocks the uterus, resulting in premature ovarian failure. Therefore, the treatment is to strengthen the spleen and stomach, remove phlegm and dispel dampness [37].
2.1.2 Invigorating the spleen and removing dampness

Chief Physician Xia Tian adopts the idea of combining Chinese and Western medicine in stages and steps to attack and treat the disease. Firstly, western medicine is used to reconstruct the menstrual cycle, secondly, traditional Chinese medicine is used to regulate ovarian function, and finally, ovulation and pregnancy are aided by integrated traditional Chinese and western medicine. He believes that only when the spleen rises and the stomach descends, the qi is in harmony, and the meaning of nourishing is reconsidered, can we achieve twice the result with half the effort. It mostly uses medicines that nourish qi, invigorate the spleen and dispel dampness, clear dampness and turbidity, and then nourish the liver and kidney. This method can prevent the nourishing products from stagnant dampness, which is wonderful.

2.2 Treating from the blood stasis

"Long illnesses enter the meridians and become stasis". If blood is blocked and stasis is stagnant, it will be difficult for Tiangui to arrive. Chong Ren fails to regulate, the sea of blood is not full, cannot overflow, and menstruation is difficult to come on time. Therefore, the treatment should be based on promoting blood circulation and removing blood stasis. Ye Yiping, a famous old Chinese medicine doctor, believes that it is necessary to pay attention to promoting blood circulation and removing blood stasis, nourishing deficiency and eliminating blood stasis in order to be effective. Zedoary turmeric, Sanleng, etc. are used to treat premature ovarian failure, but the dosage should be light and not excessive, so as to avoid breaking blood and hurting qi and seriously hurting the sea of blood. Professor Chai Songyan believes that in order to avoid fishing in depleted ponds, the drugs for promoting blood circulation and removing blood stasis should be used at the right time when the effect of nourishing the kidney and nourishing blood is effective. It promotes blood circulation but not break blood, avoid excessive dosage, which is not worth the loss.

2.2.1 Invigorating the kidney and activating blood

Relevant experiments show that Bushen Huoxue Recipe can significantly reduce FSH and LH in patients with premature ovarian failure, and increase E2, while PRL does not fluctuate significantly. It wakes up part of the ovarian function by sorting out the disordered endocrine system. Cai Lirong et al. conducted research on the prevention and treatment of experimental premature ovarian failure in mice through Bushen Huoxue Recipe, and concluded that this recipe is expected to awaken some of the remaining ovarian follicles, so that their functions can be repaired and resuscitated accordingly.

2.2.2 Invigorating the spleen and activating blood

Professor You Zhaoling pointed out that premature ovarian failure should be mainly due to kidney deficiency, as well as other visceral dysfunction. But blood stasis is one of its states. Therefore, the treatment is based on tonifying the kidney, taking into account other internal organs, promoting blood circulation and removing blood stasis, in order to achieve the meaning of cure. Premature ovarian failure prescription has obvious curative effect, this prescription is tonic but not stagnant, the way of dredging, the coordination of movement and stillness, the harmony of yin and yang, the smooth flow of qi and blood, the harmony of ying and wei, the overflow of the uterus, the arrival of Tiangui on schedule, and the return of menstruation.

2.2.3 Nourishing qi and activating blood

It has been reported in the literature that Chinese herbal medicines that nourish qi, activate blood and regulate menstruation have good curative effect on premature ovarian failure of qi deficiency and blood stasis type. Jiang Huizhong treats premature ovarian failure by typing and staging. By nourishing qi and activating qi, promoting blood circulation and regulating menstruation, the curative effect is considerable.

3. Treating from cycle therapy

Zhao Haiyun took anti-aging No. 1 and No. 2 prescriptions in the premenstrual period and the late period respectively, and the full course of treatment was given. The total effective rate was 87.5%, the effect was satisfactory, and there was no significant side effect. The yin and yang are peaceful, the righteousness is improved, and the aging is delayed. Wu Jianlan et al. used Yushen Tongluo Formula to promote ovulation in the postmenstrual period and intermenstrual period, which decreased FSH, increased E2, increased menstrual flow, and decreased the amount of estrogen, and effectively...
improved the symptoms of estrogen deficiency and the main clinical symptoms and ovarian function [47]. Zhou Ruixiu et al. used hormone replacement artificial cycle traditional Chinese medicine therapy to treat premature ovarian failure, which significantly improved hormone levels and clinical symptoms, and helped restore stable ovarian function [48].

4. Treating from acupuncture and moxibustion

Xia Liangjun et al. searched the literature on the treatment of premature ovarian failure with acupuncture and moxibustion in the past 20 years, and showed that traditional acupuncture and moxibustion can regulate and improve ovarian function in a holistic and multi-dimensional, systematic way [49]. Studies by Luo Xi and others have shown that acupuncture in the treatment of premature ovarian failure can restore menstruation and regulate FSH levels [50]. Xu Donghan's research shows that acupuncture therapy can effectively reduce the clinical symptoms and complications of patients with premature ovarian failure, and regulate hormone levels [51].

5. Conclusion

To sum up, the root cause of premature ovarian failure should be the disorder of the viscera, and the phlegm-dampness and blood stasis are the signs of its pathological essence. Therefore, the treatment should be mainly based on the kidney, and the multiple viscera should be treated based on syndrome differentiation, taking into account phlegm-dampness and blood stasis. Combined with periodic therapy and acupuncture treatment, it strives to nourish the source of the kidney, regulate the heart, liver, spleen and lung, and smooth phlegm and blood stasis, so as to achieve the effect of prevention and treatment. With the continuous development of Chinese medicine, its advantages and prospects are gradually emerging: 1) Dialectical treatment from multiple perspectives to formulate more targeted for individual diagnosis and treatment plan; 2) Based on extensive clinical experience, it is easy to know that the adverse effects caused by TCM are minimal; 3) Chinese medicine can effectively reduce the time and economic costs associated with laboratory and imaging diagnosis by means of "looking, smelling, asking and cutting"; 4) Chinese medicine has the unique idea of "treating diseases before they happen", thus preventing diseases before they happen. However, there are several issues that remain a major concern for the further promotion of our TCM [52]: 1) Failure to have a unified classification of TCM evidence types, a mature clinical prescription system and clear criteria for evaluating efficacy; 2) Relatively mature pharmacological support for Chinese medicine needs to be further developed; 3) There is a large research gap on factors related to the impact of the disease, such as the impact of work, living environment, geographical differentiation and individual differentiation on the disease; 4) The clinical treatment of premature ovarian failure has fewer proprietary Chinese medicines, and it is difficult to meet the different needs of individual differences with a single evidence and dosage form.
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References

[24] Han YH, Geng TT and Han YG. Experience of Han's gynecology in the treatment of premature
