

Research Progress on the Treatment of Uterine Bleeding by Traditional Chinese Medicine

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Abstract: *Uterine bleeding refers to heavy vaginal bleeding during a woman's abnormal menstruation, The onset of more acute blood storm is called avalanche, and the disease is slower and less dripping blood is called leakage. Often secondary infection anemia infertility and even shock and other complications, it belongs to severe and urgent gynecology. In this paper, the pathogenesis, etiology, pathogenesis, dialectical treatment and clinical research of caving leakage in recent years were reviewed, with a view to providing references for clinical treatment and basic research.*

Keywords: Uterine bleeding, Traditional Chinese medicine, Treatment, Research progress.

1. Introduction

Disintegrating leakage means that the menstrual blood does not fall from time to time, or the sudden heavy bleeding does not stop, or the bleeding is not dripping. The main manifestations are severe disturbances in menstrual volume, menstrual period and menstrual cycle [1]. In Western medicine, abnormal uterine bleed-ing-ovulatory dysfunction (AUB-O) can be referred to this disease [2]. According to statistics, about 1/3 of women will have abnormal uterine bleeding (AUB) at some time in their life, among which AUB-O is the most common, accounting for about 50% of AUB [3], and with the development of social environment, it has a trend of increasing year by year, bringing serious burden to patients and families. In Western medicine, sex hormones and surgery are often used for treatment, although it can quickly stop bleeding, but the therapeutic effect is quite limited, the recurrence rate is high, the side effects are large, affecting the medication compliance of patients, and seriously reducing the quality of life of patients. In recent years, the basic and clinical researches related to the treatment of leaky disintegration have also made a lot of progress. Based on the relevant literature in recent years, the pathogenesis, etiology and pathogenesis, syndrome differentiation and treatment, and clinical research of leaky disintegration will be reviewed.

2. Mechanism Study

2.1 Pathogenesis

At present, the specific pathogenesis of AUB-O is not fully understood. Except for abnormal bleeding caused by systemic chronic diseases or organic lesions of internal and external genitals, AUB-O is generally considered to be due to dysfunction of the hypothalamic-pituitary-ovarian axis (HPO). The ovulation function is inhibited, and the endometrium loses the cyclical regulation of estrogen and progesterone, leading to the disease [4]. Age, HPO axis, abnormal structure and function of uterine blood vessels, and abnormal hemostatic mechanism of endometrial blood vessels are all related to the occurrence of this disease [5]. Relevant studies have shown that apoptosis is also related to the occurrence of this disease [6]. When the expression of Bcl-2 gene

(pro-apoptotic gene) is overactive for some reason, cell proliferation and apoptosis are out of balance, and simple or complex endometrial hyperplasia is promoted, irregular vaginal bleeding will occur [7].

2.2 Etiology and Pathogenesis

"Wan's female Branch" believes that the collapse of leakage is related to the inability of Qi deficiency to absorb blood. It is mentioned in Jingyue Complete Book that the etiology and pathogenesis of disintegration are related to spleen and kidney. "Fu Qing main female Branch" put forward the fiery disease. Tang Rongchuan pointed out that blood stasis leads to the occurrence of leakage. "The Theory of Typhoid Fever Ming" mentioned that blood heat is related to the occurrence of hemorrhage.

On the basis of the experience of predecessors, modern doctors have summarized their own opinions on leakages according to clinical practice. Professor Xu Zhihua of Xu's gynecology department put forward the theory of "heat and blood stasis correlation"[8] in the treatment of disintegrating leakage, believing that heat is the initial stage of blood stasis, and blood stasis is the later development of heat. Director Li Chunxiang [9] believes that liver depression and spleen deficiency is the key pathogenesis of leak-collapse, and Qi deficiency is not controlled and becomes blood stasis for a long time. Professor CAI Xiaosu [10] divided the collapse into Yin collapse and Yang collapse, Yin collapse is mostly cold syndrome, Yang collapse is mostly heat syndrome.

To sum up, the cause and pathogenesis of caving leakage are nothing more than deficiency, heat and blood stasis, namely kidney deficiency and spleen deficiency, blood stasis, and heat is divided into solid heat and deficiency heat. The main pathogenesis can be summarized as Chong Ren injury, can not restrict the menstrual blood, resulting in abnormal menstrual blood.

3. Basic Research

In recent years, on the basis of the research results of the pathologic mechanism of leaky disintegration, the basic research work on the mechanism of the curative effect of

traditional Chinese medicine on leaky disintegration has also made great progress.

3.1 Regulate Sex Hormone Levels and Receptor Expression

The imbalance of estrogen and progesterone levels caused by the dysfunction of HPO [11-12] is the main reason for the occurrence of this disease. Li Chunfang et al. [13] observed the effects of Huangbai Baiwei Powder on sex hormone levels in rats with functional blood model, and found that the drug could increase serum estrogen content, reduce progesterone level, down-regulate endometrial receptor expression, block the effect of estrogen, regulate HPO function and treat the disease. Wei Aiwu [14] discussed the mechanism of action of Gongxuening II granules on HPO, and the results showed that Gongxuening II granules could correct the continuously low level of estradiol value, increase the progesterone value, and gradually restore the secretion function of gonadal axis.

3.2 Improve Blood Clotting Function

Endometrial coagulation dysfunction is one of the important pathogenesis of this disease. Li Chunfang et al. [15] showed that Huangbai Baiwei powder could shorten the prothrombin time and thrombin time of model rats (endometrial bleeding), improve platelet adhesion and aggregation, and thus reduce the amount of vaginal bleeding and bleeding time. Wang Ling et al. [16] found in the experimental study of Gongxuening I and II granules of traditional Chinese medicine that Gongxuening I granules could significantly shorten the bleeding and coagulation time, PT and APTT. The results showed that the drug could stop bleeding by promoting coagulation and inhibiting fibrinolytic activity.

3.3 Intervention of Apoptosis

In the normal menstrual cycle, the apoptosis of endometrial cells changes periodically, and the apoptosis rate of endometrial epithelial cells in patients with this disease is higher than that in normal menstrual patients [17]. Professor He Fengjie et al. [18] applied the dying membrane Zhidong prescription to intervene anovulation type dysfunctional uterine bleeding (ADUB) rats, and the expression of bcl-2 decreased and the apoptosis index increased significantly. It is suggested that the formula may reduce the expression of bcl-2 and up-regulate the expression of bax (which plays the role of anti-Bcl-2), and play the role of removing endometrium to treat the disease.

4. Disintegrating Leakage of Chinese Medicine Treatment

Chinese medicine treatment of the disease follows the basic principle of "urgent treatment of its standard, slow treatment of its root", and flexible use of "plug flow, clear source, rehabilitation" three methods. In clinical practice, according to different syndrome differentiation types, different periods to choose the appropriate prescription and method of treatment, but also according to the patient's personal physique and disease differences, such as "three reasons" clinical addition or subtraction of medication.

4.1 Single Traditional Chinese Medicine to Treat Disintegrating Leakage

Studies have shown that a variety of Chinese medicines can play a role in the treatment of disintegrating leakage, among which the core Chinese medicines include angelica sinensis, Astragalus and Paeony [19], Paeoniae alba can achieve hemostasis by increasing the number of platelets and shortening the bleeding and coagulation time. Paeoniflorin contained in Paeoniae has the effect of shrinking capillaries, especially repairing the damaged endometrium and hemostasis [20]. Relevant studies have shown [21] that Angelica sinensis has the function of supplementing blood, promoting blood circulation and regulating menstrual flow. Different parts of Angelica sinensis have different therapeutic effects due to their different chemical components and contents. Among them, Gui-tou is often used for hemostasis, and Gui-tami is strongly used for supplementing blood. Carbon preparation of Angelica sinensis can enhance its hemostatic effect. Astragalus [22] is one of the representative drugs for invigorating qi and stopping bleeding, and can stop bleeding by promoting endometrial vascular contraction.

4.2 Classification of Traditional Chinese Medicine for the Treatment of Caving Leakage

Treatment by type is a common method of syndrome differentiation in clinic. The clinical classification of disintegrating leakage is more complicated, and many doctors have their own emphasis. The common clinical types are blood heat syndrome, blood stasis syndrome, kidney deficiency syndrome and spleen deficiency syndrome. There may also be a combination of multiple methods of syndrome differentiation. Han Xuemei et al. [23] summarized the syndrome and treatment of dissolving leakage in the "Good Prescription" and divided dissolving leakage into three types: Yiwei Shengyang decoction for Chongren Qi deficiency type, Jiajia Cistanza Cutazi pill for adolescent or perimenopausal women with kidney qi deficiency; Yang stroke in Yin type selection of small thistle decoction, amber powder, miracle four things soup; Wind injury Chong Ren type with Schizonepeta, wind, five spirit fat to eliminate chong ren wind evil. He Ruoping [24] divided caving leakage into three types of qi and blood deficiency, Yin deficiency and blood heat, and blood stasis. Guipi Decoction combined with Siwu Decoction, Liuwei Dihuang pill combined with Erzhi pill, Shenghua decoction supplemented with flavor or combined Xiaoyao powder were selected as the treatment respectively. Ding Ning et al. [25] summarized the treatment of leaky heart from the heart, and believed that the pathogenesis of leaky heart was insufficient heart qi, deficiency of heart blood, obstruction of heart meridian, hyperactivity of heart fire, restlessness of heart, and hyperactivity of heart fire.

4.3 Staging Treatment of Disintegrating Leakage with Traditional Chinese Medicine

Professor Xu Jingsheng [26] In the treatment of disintegrating leakage, the bleeding period was mainly stopped by blocking or Tongxia to stop bleeding, and the blood stopping period was used to strengthen the kidney and consolidate the capital, and the menstrual cycle was adjusted. Professor Wang Cuixia [27] treated disintegrating leakage by "blood stasis" and

stages. During the bleeding period, general cause was used to remove blood stasis and hemostasis. After hemostasis, the main principles were "invigorating kidney and spleen, regulating menstruation and promoting ovulation". Zhou Yun [28] treated 60 cases of spleen-kidney qi deficiency type sputtering (spleen-kidney qi deficiency type) according to bleeding stage and blood stasis stage. Zhidong decoction was used in bleeding stage and Tiajing decoction was used in blood stasis stage. The total effective rate was 96.67%. Director Liu Xiaomao applied "Supplementing Qi with Blood Decoction" and "Promoting Tianguai Decoction" prepared by Mr. Liu Maolin to the bleeding stage and the blood cessation stage respectively for treatment, and the clinical effect was significant [29].

4.4 Traditional Chinese Medicine Classic Compound to Treat Disintegrating Leakage

Gum Ai decoction is one of Zhang Zhongjing's representative prescriptions for the treatment of blood syndrome, which is often used for hemorrhagic diseases in obstetrics and gynecology. The formula is composed of dry rehmannia, ejiao, Chuanxiong, Angelica, peony, licorice and mugwort leaves. Modern pharmacological studies have found that the decoction can promote coagulation and hemostasis by activating endogenous and exogenous coagulation pathways, affecting the levels of thromboxane B₂ (TXB₂) and 6-keto-PGF_{1α} (6-Keto-PGF_{1A}), and play a hemostatic function [30]. Huang Qun et al. [31] treated 70 cases of adolescent functional uterine bleeding by Jiao Ai Tang, 45 cases were cured, 18 cases were significantly effective, and the effect was significant.

Guben Zhigong decoction originated from "Fu Qing main female Branch", composed of cooked rehmannia, angelica, black ginger, ginseng, Angelica, white art, with beneficial qi nourishing blood, tonifying kidney and spleen. Cao Yiming et al. [32] explored the targets and potential mechanisms of action of this prescription in the treatment of functional blood, and found that Gubenzhitong Decoction can synergically act on functional blood with multiple components, multiple pathways and multiple targets. Zhou Meiyun [33] treated 28 patients with disintegrative leakage (spleen-qi deficiency type) with Gubenzhitong decoction, with a total effective rate of 96.43% and only one ineffective patient, with no related complications and significant improvement in physical signs.

Taohong Siwu decoction is a representative prescription for promoting blood circulation and regulating menstrual flow. It is composed of Siwu decoction with peach kernel and safflower. It mainly treats diseases of blood deficiency and blood stasis. Pharmacology studies of modern Chinese medicine have shown [34] that Taohong Siwu Decoction can significantly improve microcirculation and increase platelet. Zhu Xiufen [35] treated 280 cases of disintegrative leakage by adding or reducing Taohong Siwu decoction, which lasted for 3 courses in 7 days. The total effective rate was 97.4%.

4.5 Self-prepared Prescription for the Treatment of Disintegrating Leakage

In addition to the classic prescription, modern doctors through summarizing the etiology and pathogenesis, combined with

their own clinical experience, self-made prescription for treatment, and achieved a good effect. Southern section of the pavilion, a professor at [36] combined with more hot wet climate characteristics and dietary habits, hot and humid to ren is put forward, with spleen and dehumidification hemostatic effect of segment's dehumidification party (magnolia bark, patchouli, rhizoma atractylodis, perrin, Fried atractylodes, dangshen, tuckahoe, alisma, herba agrimoniae, madder, cuttlebone, thistle, cohosh, liquorice) treatment of the disease, even served for ten days, The total effective rate of hemostasis was 93.33%. Professor Luo Yuankai [37] believed that hemorrhage hemorrhage was mainly caused by massive or long-term bleeding, resulting in loss of both qi and blood, and deficiency of spleen and kidney, so he took Lingnan's characteristic drugs Gangnium root and Diren root as the main drugs to create Erren Decoction with strong astringent and hemostasis, strengthening spleen and kidney, which was used in hemorrhage hemorrhage period with one dose per day for 7 days. The mean time of hemostasis after treatment was significantly shorter than that of control group (control group was given oral adrenal hydrazone tablets).

4.6 Acupuncture Therapy

Acupuncture therapy is guided by the theory of traditional Chinese medicine, through acupuncture stimulation of specific points on the body surface, with the help of the conduction of the whole body meridians, adjust the functions of qi, blood and zang-fu organs, so as to achieve the purpose of preventing and treating diseases. Dr. Liu Hongmei [38] followed the three principles of treating disintegrating leakage and flexibly applied uterine acupuncture with unique operation and needle feeling, which had remarkable effects on the treatment of disintegrating leakage. Wang Lingmin et al. [39] randomly divided 80 patients with abnormal perimenopausal uterine bleeding (spleen-kidney deficiency type) into 2 groups: control group (oral ethoestradiol cyproterone tablets and mifepristone tablets); treatment group, on the basis of the control group, took oral Jianpibushen styptic prescription, plus acupuncture of uterus points, Baihui, Qihai and other points, and the total effective rate of the treatment group was 95.00%. It was significantly higher than that of control group (80.00%).

4.7 Others

Wu Xueling [40] randomly divided the patients with this disease into two groups: 40 cases in the control group (conventional Western medicine treatment) and 40 cases in the treatment group (Gubenzhitong decoction combined with acupoint application). The results showed that the effect of the treatment group (total effective rate of 95.00%) was more ideal.

Yao Yun [41] discussed the curative effect of acupoint embedding and regulating cycle method combined with oral drug treatment. 36 cases in the control group (oral Fimortone) and 36 cases in the observation group (on the basis of the control group) were treated with acupoint embedding and regulating cycle method. The results showed that patients in the observation group had significant curative effect, which could effectively improve clinical symptoms, anemia and hormone levels.

Xia Wanting et al. [42] randomly divided 160 patients with this disease into two groups: the control group (tranexamic acid); the treatment group, on the basis of the control group, was treated with intramuscular injection of Leonuri injection for 3 days; the total effective rate of the treatment group was 96.00%, which could significantly improve the hemostatic effect.

5. Disintegrating Western Medicine Treatment

The principle of Western medicine treatment is to stop bleeding, regulate the cycle, protect the endometrium, and avoid recurrence and severe bleeding. Oral drug therapy is usually used, including hormonal drugs and non-hormonal drugs.

5.1 Hormone Therapy

Estrogen and progesterone therapy are often used to stop bleeding [43]. Progesterone therapy, also known as "drug curettage". Progesterone and estrogen antagonism, promote the proliferation of endometrium into a secretory phase, after stopping the drug, the functional layer is completely stripped, and then through its own estrogen repair to achieve the purpose of hemostasis. Dedrogestrone and medroxyprogesterone acetate are commonly used in clinical practice. Not suitable for patients with long bleeding time and thin intima. Estrogen therapy, endometrial repair and hemostasis. Hemostasis is achieved by rapidly proliferating the endometrium, covering and repairing the wound. It is only suitable for patients with heavy bleeding with thin intima. Commonly used drugs are estradiol valerate (buxalide), which is only used in patients with heavy bleeding with a thin endometrium. combined oral contraceptives (COC) containing estrogen and progesterone, Eustamine (drospirone ethinylestradiol tablets) and mafuron (desogestrel ethinylestradiol tablets) are used to stop bleeding by inducing periodic shedding of the endometrium. This kind of drug treatment is better than single hormone therapy, and the hemostatic effect is better. Western medicine often adopts artificial cycle therapy to regulate the menstrual cycle by simulating the changes of hormones in the menstrual cycle through sequential therapy of estrogen and progesterone, combined therapy of estrogen and progesterone, and second half cycle - short-term therapy, etc., so as to make menstruation come on schedule [44].

5.2 Non-hormonal Therapy

Non-hormonal treatment with anti-fibrinolytic (tranexamic acid) and non-steroidal anti-inflammatory drugs (NSAIDs), such as methanamine, ibuprofen, naproxen, etc., is available for women who do not want to use hormones or have contraindications. Compared with periodic oral progesterone tranexamic acid therapy, the therapeutic effect of reducing menstrual bleeding is better [45]. NSAIDs play a hemostatic role by inhibiting cyclooxygenase, which can relieve dysmenorrhea when used during menstruation, but should be contraindicated in ulcer patients. Studies have shown that NSAIDs can reduce the amount of menstrual bleeding by about 40%, but the effect is less than that of progesterone [46].

5.3 Surgical Treatment

Hysteroscopy plus diagnostic curettage is suitable for recurrent women of childbearing age and perimenopause to quickly stop bleeding, clarify endometrial pathology, and exclude malignant disease. Hysterectomy, only for repeated bleeding, long-term treatment and no fertility requirements.

6. Chinese and Western Combined Treatment

It is found that the curative effect of the combination of traditional Chinese and Western medicine is more significant than that of traditional Chinese medicine or Western medicine. Liu Erfang et al. [47] observed the combined treatment of Chinese and Western medicine (Ziyin Bushen styptic decoction, estrogen and progesterone) in the treatment of adolescent patients with impaired blood (44 cases), and the total effective rate was 95.45%, which was lower than that of the simple western medicine group. Chen Xiangyan et al. [48] observed that the total effective rate of the western medicine plus Chinese medicine group was 91.30% higher than that of the control group (69.56%) in the treatment of patients with disintegrating leakage (kidney deficiency type) with Bushen Shujing prescription. Zhou Senying [49] Both the control group and the treatment group were given western medicine treatment (desogestrel estradiol tablets), and the treatment group was combined with Shugan Qingre decoction for 3 cycles. The results showed that the treatment group (total effective rate 97.830%) had a significant effect, which could improve coagulation function and control clinical symptoms faster, with high safety.

7. Concluding Remarks

To sum up, traditional Chinese medicine has its own advantages in the treatment of leakage. Its treatment attaches importance to the overall concept, can simultaneously regulate endocrine, blood coagulation and other systems, can cure and slow down clinical symptoms, improve the body's immunity, reduce the recurrence rate, and has a more accurate effect. Western medicine treats the disease quickly, but it is easy to cause the body to produce toxic side effects and drug resistance, clinically effective combination of traditional Chinese medicine and western medicine, draw on each other's strengths, while supplemented by corresponding external treatment to play its unique advantages, will be more conducive to the treatment of such diseases. Traditional Chinese medicine has a broad prospect for treating leakage and has great room for development.

Although many clinical and experimental studies have shown that traditional Chinese medicine is effective in treating disintegrating leakage, there are still some limitations. 1. Lack of high-quality clinical studies such as large sample, double-blind control and multi-center. Second, the specific components and deep mechanism of TCM need to be further explored, and the pharmacological and toxicological effects need to be further clarified. Third, there are few studies on the prevention of traditional Chinese medicine. In view of this, we should adopt large sample, multi-center, double-blind control study in the future; Conduct in-depth basic experimental research, explore the efficacy and pharmacology of TCM monomer, deeply study its pathway and mechanism of action, design more relevant TCM prevention studies, and

make TCM treatment of leakage more standardized and scientific.

Fund Project

- (1) Construction Project of Inheritance Studio of Liu Maolin, the national famous old Chinese medicine expert (Chinese Medicine Education Letter [2018] No.134);
- (2) Construction Project of Regional Diagnosis and Treatment Center of Gynecology of Traditional Chinese Medicine in shaanxi Province (Shaanxi Medicine Letter [2018] No.268);
- (3) Construction Project of Inheritance Work of Huo Liu's School of Gynecology in Yulin City (Shaanxi Medicine Letter [2018] No.337);
- (4) Yulin City "Young Talent Lifting Program" project (20220473).

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