

Advances in Chinese and Western Medicine Research on the Treatment of Endometrial Polyps and Postoperative Prevention of Recurrence

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Abstract: Endometrial polyps are benign gynecological lesions caused by localized endometrial overgrowth and have a high incidence and recurrence rate after surgery. The treatment of endometrial polyps can be divided into Western medicine and Chinese medicine. Western medical treatment is divided into expectant treatment, drug treatment and surgical treatment, TCM mainly plays a role in preventing recurrence of polyps after surgery. This article reviews the research progress of Chinese and Western medicine treatment of endometrial polyps and prevention of recurrence after Chinese and Western medicine surgery.

Endometrial polyps are superfluous organisms that protrude into the uterine cavity, with an overall incidence of 7.8%-34.9% [1], mostly in perimenopausal or postmenopausal women. With the change of social environment and life style and the development of medical technology, the incidence of endometrial polyps has increased and the incidence of the population has a tendency to be younger. Most endometrial polyps are clinically asymptomatic and are often detected during gynecological checkups. Some can cause abnormal uterine bleeding, postmenopausal bleeding, pelvic pain, abnormal vaginal discharge, infertility, etc. (see Figure 1).

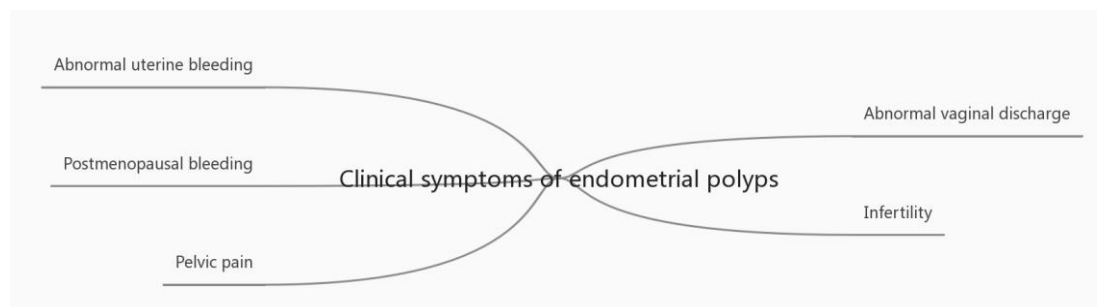


Figure 1: Clinical symptoms of endometrial polyps

1. Western Medicine's Understanding of EP

The current understanding and research on the pathogenesis of endometrial polyps in Western medicine focuses on the expression of hormone receptors and the imbalance between estrogen and progesterone on the endometrium. In addition, there are other theories such as overproliferation of cells, abnormal distribution of endometrial enzymes, abnormal expression of cytokines, and inflammatory stimulation of the endometrium. However, the specific mechanism of the disease pathogenesis is not clear and needs further study. Endometrial polyps consist of endometrial glands, thick-walled blood vessels and fibrotic endometrial mesenchyme and surface-coated epithelium, which are localized benign hyperplasia of the endometrium. They can be classified into 6 types according to their pathological characteristics, namely functional polyps (associated with the menstrual cycle and can shed on their own), nonfunctional polyps (a combination of basal and functional layers in which the functional layer can be hyperstimulated by estrogen and continue to proliferate), adenomyoma-like polyps (interspersed with smooth muscle and posterior vessels in addition to glands), postmenopausal polyps, tamoxifen-associated polyps, and endometrium-endocervical canal polyps(see Figure 2).The diagnosis is not difficult and is mostly made by ultrasound (vaginal ultrasound mainly) or hysteroscopy.



Figure 2: Types of endometrial polyp pathology

2. Western Medical Treatment

2.1. Looking Forward to Treatment

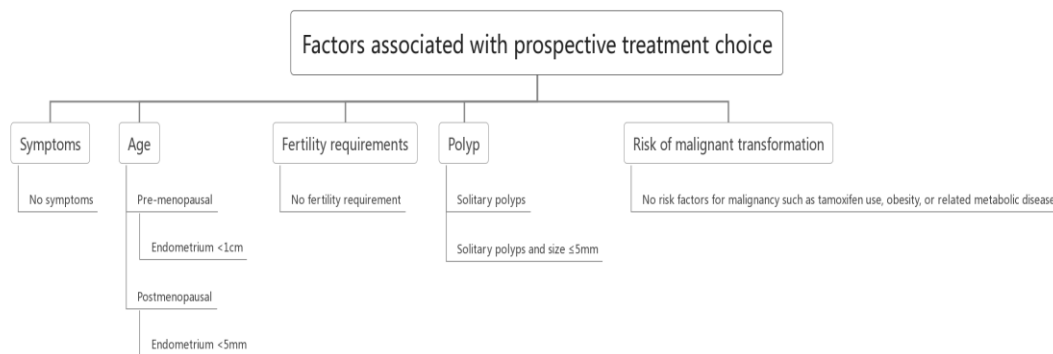


Figure 3: Factors associated with prospective treatment choice

The choice of prospective treatment should take into account the patient's symptoms, age, fertility requirements, polyp size, and risk of malignant transformation. Patients with premenopausal endometrium <1 cm, single polyp, asymptomatic, without fertility requirements, and without risk factors for malignant transformation can be treated expectantly. In postmenopausal patients with EP, treatment can be expected after ruling out the risk of endometrial malignancy if they are asymptomatic, have an endometrial thickness ≤ 5 mm, have polyps ≤ 8 mm in diameter, have solitary polyps, have no history of taking drugs such as tamoxifen, and have no obesity or

related metabolic diseases(see Figure 3).Patients with unexplained infertility, as their endometrial polyps often cannot be expected to disappear within a short period of time, in which case they can be actively treated with surgery. Many studies have confirmed that removal of endometrial polyps improves the natural pregnancy rate in infertility patients. This may be related to the change in the internal environment of the endometrium due to EP.

2.2. Medication

Drugs are generally used for adjuvant treatment of TCRP, which can prevent recurrence of EP and malignant transformation of EP after surgery, and can be used for preoperative pretreatment, etc. They can also relieve clinical symptoms of EP, prevent the occurrence of EP, improve the pregnancy rate of EP infertility patients after surgery, and eliminate single <1 cm polyps, etc. The current study focuses on LNG-IUS-based anti-estrogenic drugs, they are intrauterine placement of LNG-IUS, progestins (didrogestrel, progesterone), oral short-acting contraceptives, GnRH-a analogues, hemostatic analogues, progesterone, letrozole, mifepristone, tibolone, etc. These drugs vary and can be selected according to clinical symptoms, fertility needs, length of treatable cycles, perimenopausal stage, and whether the drug is administered pre or post TCRP [2], LNG-IUS is indicated for patients without fertility requirements and requiring long-term treatment to prevent postoperative recurrence, may prevent the occurrence of EP due to high-risk factors such as TAM treatment for breast cancer[3], Treatment of low to moderate risk hyperplastic endometrial polyps[4], also treats premenopausal patients without risk factors for malignancy who have symptoms of excessive menstruation caused by smaller polyps[5]. LNG-IUS has the advantages of low systemic side effects, high patient compliance, high efficacy, ease of operation, and high safety[6]. Progestins are mainly oral dydrogesterone tablets and subcutaneous progesterone injections, which are generally used for patients with fertility requirements who receive short-term treatment, mainly to prevent the recurrence of EP after surgery, relieve the symptoms of excessive menstruation caused by EP, and eliminate or reduce the size of small polyps in premenopausal patients.In summary, although progestins and short-acting progestins are far less effective than LNG-IUS in preventing recurrence, they offer a highly viable option for preventing postoperative recurrence in patients with fertility requirements. The gonadotropin-releasing hormone agonists GnRH-a mainly refers to goserelin, leuprolide, treprostin and other drugs, although the efficacy is better, but after taking the drug is easy to cause hypoestrogenic reaction and easy to relapse after stopping the drug, generally do not advocate the application of premenopausal women. It can be used in perimenopausal or postmenopausal patients for recurrence prevention after surgery. Hemostatic drugs are used as an adjunct to control the symptoms of abnormal uterine bleeding caused by EP. Others such as pregnenolone, letrozole, mifepristone, and tibolone have been shown to prevent the development of E, However, because of its disadvantages of poor efficacy and side effects, it is generally not a preferred choice for the treatment of EP.

2.3. Surgical Treatment

2.3.1. Non-Energy Systems

Non-energetic systems commonly used include the new hysteroscopic shaving (IBS) system, cold knife excision, and mechanical removal. Cold knife resection refers to the removal of polyps with microscopic scissors or grasping forceps under direct hysteroscopic view, and is good for removing single, small (≤ 5 mm diameter) polyps. Mechanical removal refers to the use of small oval forceps to remove the lesion after hysteroscopic localization, usually in conjunction with full-scale curettage. The advantage of this procedure is that it is simple for the operator to perform,

but the disadvantage is that blind pulling tends to fracture and break the polyp tissue, which is not conducive to pathological diagnosis and has a high recurrence rate due to the inability to effectively remove the base[7, 8], In addition, the recovery in one piece significantly reduces the number of trips to and from the uterine cavity, protecting the cervix and the uterine cavity with high safety [9, 10]. The high recurrence rate after scraping alone may be due to the inability of the surgeon to locate the polyp during blind scraping with experience, which may easily miss the location of the uterine fundus and both uterine horns, resulting in a high recurrence rate, therefore, it is not used alone in clinical practice nowadays, and is mostly used as an adjunct to different surgical operations under hysteroscopy, for example, some studies have confirmed that for multiple endometrial polyps with a high risk of recurrence, hysteroscopic electrosurgery with scraping has a lower recurrence and bleeding rate than electrosurgery alone, and enhances the patient's immune function.

2.3.2. Energy System

Hysteroscopic endometrial polyp electrosurgery (TCRP), which is divided into monopolar electrosurgery and bipolar electrosurgery, i.e., the use of an electrosurgical ring that combines electrical cutting and electrocoagulation. TCRP as a conventional procedure without clear surgical guidelines. Several clinical studies comparing the postoperative clinical outcomes of TCRP, hysteroscopic post-localization polyp clamping, and hysteroscopic curettage have shown that TCRP is more effective in improving menstrual flow and endometrial thickness, reducing recurrence rates, increasing pregnancy rates, and improving immune function [11-13], its disadvantage is heat damage. In clinical practice, TCRP is not only suitable for complex cases, such as polyps with multiple occurrences, large size and special location, such as polyps located at the fundus and horn of the uterus, but it can also be used flexibly according to the patient's specific condition, for example, simple endometrial polypectomy for women with fertility requirements, resection to the myometrium for patients without fertility requirements, recurrent recurrence and contraindications to medication, and resection of the functional layer for endometrial polyp-like hyperplasia.

Hysteroscopic endometrial surgery is relatively easy, it is advocated that single, small polyps can be done on an outpatient basis without anesthesia or with local anesthesia. The author believes that the existing dual hysteroscopic surgery system combines the advantages of non-energy system and energy system, and the clinic can make cold and hot knives cooperate with each other and play their respective advantages, which can realize both traditional hysteroscopic cold cutting surgery and cold cutting technology, which can be converted at will between electric cutting and cold cutting, thus completing hysteroscopic surgery with less bleeding, better effect and shorter time, which is now a better choice for all kinds of hysteroscopic surgery.

2.3.3. Endometrial Removal and Total Hysterectomy

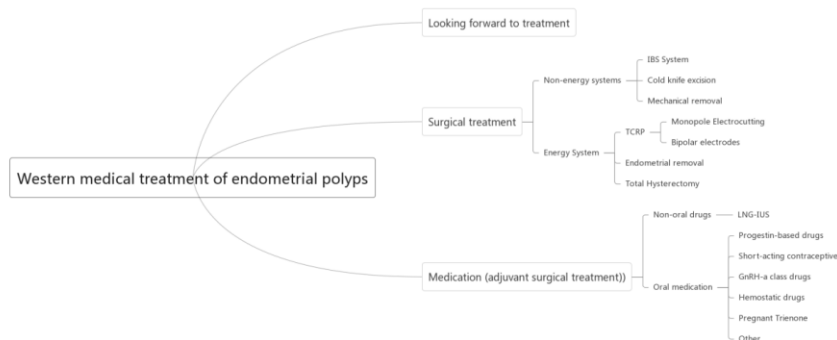


Figure 4: Western medical treatment of endometrial polyps

TCRP plus endometrial debulking is an effective alternative surgical procedure for patients with recurrent endometrial polyps, severe symptoms, risk factors for malignancy and inability to receive progestin therapy. For surgical treatment of endometrial polyps alone, total hysterectomy is generally not recommended (see Figure 4).

3. Chinese Medicine Treatment

There is no record of the name "endometrial polyp" in Chinese medicine. According to the characteristics of endometrial polyp as a mass in the lower abdomen of women, which can be accompanied by abnormal vaginal bleeding, it belongs to the category of "obstruction" in Chinese gynecology, and can also be classified as "excessive menstruation", "prolonged menstruation", "infertility", etc. Jing Yue Quan Shu - Women's Rules" said: "The evidence is either from menstruation, or from the postpartum period, where the internal injury of cold, or external wind and cold, or rage and anger injury to the liver, Qi rebellion and blood retention, or worry and thought injury to the spleen, Qi deficiency and blood stagnation, or accumulation of labor and weakness, Qi weakness and not work. Always by the time the blood is moving, the remaining blood is not yet pure, and a rebellion, the stagnation of the day accumulates and gradually to become the symptoms [14]." The Chinese Organ Classic states, "The accumulation of zhengzheng is caused by the loss of true qi in the five viscera and six internal organs and the combination of evil qi." The Treatise on the Origin of the Diseases states, "Zhengzheng is born from unregulated cold and warmth, unchanged diet, and the fight with dirty qi." The invasion of external evil is also one of the important factors in the development of obstruction in women. Thus, the formation of obstruction in women is due to carelessness during menstruation or after childbirth, weakness of the internal organs, disharmony of emotions and will, poor diet, and internal invasion of wind, cold, dampness and heat, resulting in Qi stagnation and Qi deficiency or accumulation of phlegm and dampness or imbalance of the flushing mechanism, resulting in blood stasis. Blood stasis is not only a pathological product caused by phlegm-dampness and Qi disorder, but also a pathological factor leading to endometrial polyps, which become blood obstruction and accumulate in the lower abdomen and uterus, and accumulate over time to become obstruction. Blood stasis is the main pathological factor, and treatment is based on resolving blood stasis (see Table 1).

Table 1: Chinese medical evidence and treatment of endometrial polyps

| | Chinese medicine evidence type | Chinese Medicine Treatment |
|---|---|--|
| Chinese medicine evidencetype and treatment | Qi stagnation and blood stasis evidence | Removing blood stasis and clearing the channels, dispersing nodules and eliminating symptoms |
| | Qi deficiency and blood stasis evidence | Generating new blood stasis |
| | Phlegm and Blood Stasis | Warming phlegm and dampness, invigorating blood circulation and removing blood stasis |
| | Cold clotting and blood stasis evidence | Warming the meridians and dispersing cold, resolving blood stasis and clearing the channels |
| | Dampness and heat stasis | Clearing heat and dampness, promoting circulation and dispersing stagnation |

3.1. Relieving Blood Stasis and Clearing the Channels, Dispersing Nodules and Eliminating Symptoms

Blood stasis is the main pathological factor of endometrial polyps, at the root of which, treatment cannot be separated from activating blood stasis and eliminating the symptoms. Wang Xinmei [15] gave 62 post-EP patients in the Chinese herbal medicine group the combination of oral administration of the formula for activation of blood circulation and elimination of blood stasis and external application of anti-inflammatory powder, and the recurrence rate of endometrial polyps was 4.8% after 1 year, which was much lower than that of 16.4% in the Western medicine group, and the expression of PR was higher than that of the Western medicine group ($P < 0.01$), and Survivin and Bcl-2 in the Chinese herbal medicine group were lower than that of the Western medicine group, and it was speculated that Chinese herbal medicine could regulate The expression of PR, Survivin and Bcl-2 in the herbal medicine group was lower than that in the western medicine group. Similarly, in Zhang Weiling [16], the Chinese herbal medicine group used the internal treatment method of chemotherapy and elimination of stasis combined with the external application of anti-Zheng San, and the comparative results of inhibiting the expression of Bcl-2 in the endometrium were observed after 3 months as Chinese herbal medicine group > western medicine group > control group, indicating that Chinese herbal medicine down-regulated the expression of Bcl-2. Jiang Ying [17] collected 147 patients after EP and randomly divided them into 49 cases each in the Chinese medicine group, Western medicine group and control group, among which, the Chinese medicine group was given staging treatment together with the external application of Zingzheng San. Sun Shuyun et al [18] treated the herbal group with the same method as Jiang Ying, and after 3 months of continuous treatment, the herbal group showed an increase in PR level 3 expression and a decrease in Ki-67 level 3 expression, which were significantly better than the other two groups. It was hypothesized that herbal medicine could increase endometrial PR expression and decrease Ki-67 expression, which could achieve the therapeutic effect of preventing recurrence of endometrial polyps.

3.2. Generating New Blood Stasis

The hysteroscopic operation of EP patients can damage the cellular ligaments, resulting in postoperative stasis, thus easily causing recurrence of endometrial polyps, and postoperative deficiency, resulting in Qi deficiency and blood stasis, so the treatment is appropriate to both attack and supplementation, to produce new and eliminate stasis. Gong Wei [19] et al. divided 194 patients with endometrial polyps after EP into a control group and a treatment group of 97 cases each, and the treatment group was treated with biochemical soup plus reduction for 3 courses, and the recurrence rate in the treatment group (6.19%) was lower than that in the western medicine group (18.56%) after 6 months of follow-up, $p < 0.05$, while showing no significant changes in serum estrogen and progesterone in more patients with endometrial polyps, so it was concluded that local ER and PR level abnormalities may be the main factor of endometrial polyps. Hu Ping [20] treated 134 post-EP patients in the treatment group (with biochemical soup) and 67 patients in the control group (without any treatment), and after 3 months of treatment, the recurrence rate of EP in the treatment group was 4.48%, which was significantly lower than that in the control group of 19.40%, $P < 0.05$. This indicates that biochemical soup can reduce the recurrence of endometrial polyps.

3.3. Warming Phlegm and Dampness, Invigorating Blood Circulation and Removing Blood Stasis

Emotional and moral disharmony, unclean diet, and external sensation of the six sexes can easily lead to dysfunction of the internal organs, loss of spleen and kidneys, Yang deficiency and failure to transform water and fluid, thus generating internal phlegm and dampness, thus blocking the qi flow and causing the accumulation of phlegm and stagnation in the ramus and uterus. Chen Yanxin [21] et al. treated post-EP patients by oral administration of Chinese herbs for 3 months, treating them with strengthening the spleen and warming the kidney, drying dampness and resolving phlegm, and activating blood stasis, and the recurrence rate after 1 year of EP was lower than that of the control group without treatment and the Western medicine group, $P < 0.05$. Zeng Yuanling [22] showed a recurrence rate of 2.50% at 6 months postoperatively in the Chinese herbal medicine group ($P < 0.05$), which was significantly lower than the 17.50% recurrence rate in the Western medicine group of oral ethinylestradiol cyproterone tablets, in patients with EP.

3.4. Warming the Meridians and Dispersing Cold, Resolving Blood Stasis and Clearing the Channels

External evil wind, cold, dampness and heat invade internally, of which, cold is the main attraction and will contract and stagnate, which can lead to loss of harmony between qi and blood and cause blood stasis. For the evidence of blood clotting and stasis, the treatment is to warm the meridians and disperse cold, resolve blood stasis and open the channels. Liu Na et al [23] divided 147 postoperative patients with TCRP into observation group and control group, the control group did not use any intervention after surgery, the observation group was given Shao Abdominal and Yu Tang to warm the meridians and disperse cold, resolve blood stasis and open the ligaments, all completed 12-month follow-up after surgery, the recurrence rate in the control group was more than 4 times than the observation group, indicating that Shao Abdominal and Yu Tang can reduce the recurrence rate of endometrial polyps.

3.5. Clearing Heat and Dampness, Promoting Circulation and Dispersing Blood Stasis

After menstruation and childbirth, when the cell veins are empty and the remaining blood is not yet exhausted, it is easy to be infected with damp-heat evil toxins, which can lead to the disorder of the internal organs, loss of harmony between qi and blood, and the formation of zhengzheng, stasis of blood, blood does not return to the menstruation, resulting in prolonged periods and excessive menstruation. Xiang Lijuan [24] selected 80 postoperative EP patients, and 40 patients in the observation group were treated with topical enema of elimination of dampness and dissipation of stasis after surgery, while 40 patients in the control group were treated with medroxyprogesterone acetate tablets after surgery, all for 3 months, and after 6 months there was no recurrence in the observation group and 3 cases (7.5%) in the control group, and the observation group was significantly lower than the control group. Xue Qinmei [25] selected 121 post-EP patients, and the TCM group was given Qingjing San plus reduction to clear heat and cool blood, and the follow-up after 2 years showed that the recurrence rate of 3.13% in the TCM group was significantly lower than that of 17.86% in the control group and 3.45% in the Ma Fu Long group.

Western medicine and Chinese medicine have made outstanding contributions to the prevention and treatment of EP. At present, for EP with surgical indications, Western medical surgical treatment can achieve good results, but the high postoperative recurrence rate of 2.5% to 13.3% remains a problem in gynecology. For patients without fertility requirements, long-term treatment with intrauterine placement of LNG-IUS is generally advocated to prevent postoperative recurrence.

For patients with fertility requirements, oral anti-estrogen drugs are mostly considered as an option, but the side effects of long-term medication are high and often lead to poor patient compliance, which in turn is detrimental to postoperative management of EP. Chinese medicine provides a new way of thinking for postoperative prevention of EP, reflecting the advantages of holistic and physical improvement, but there are problems of strong individualization and lack of uniform standards for quantifying its evidence and efficacy.

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