Advances in Clinical Diagnosis and Treatment of Intrauterine Adhesions

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Abstract: Intrauterine adhesion is a kind of high incidence disease caused by many pathogenic factors, which damages the endometrial basal layer and affects the menstruation and fertility of women. In recent years, due to artificial abortion and other types of increased uterine cavity surgery, the incidence of the disease gradually increased. Hysteroscopy is the main method to diagnose intrauterine adhesion. Combining with ultrasound, it can determine the range and degree of intrauterine adhesion and guide the choice of treatment. But it cannot find small changes in the uterine cavity, and for serious adhesions and endometrial injury in patients, hysteroscopy examination results are not good. Accurate assessment of recurrence risk and individualized diagnosis and treatment are important prerequisites to reduce the high recurrence rate and improve the low pregnancy rate. This article reviews the research on clinical diagnosis and treatment of intrauterine adhesions in order to enhance and improve the understanding of the disease and provide a new clinical thinking.

***Keywords*:** intrauterine adhesion, hysteroscopy, postoperative recurrence diagnosis and treatment

1. Introduction

Under normal physiological conditions, endometrial tissue is periodically stripped and repaired under the hormonal regulation of the thalamus-pituitary-gonad axis[1] . Damage to the endometrial basement caused by multiple factors can lead to abnormal or even irreversible regeneration of the endometrium, leading to intrauterine adhesions (IUA) [2]. Hysteroscopy plays an important role in the diagnosis and treatment of intrauterine adhesions. It can not only identify the location of the lesions, but also perform precise surgical procedures. Among them, transcervical resection of uterine adhesions (TCRA) under hysteroscope is the main method to treat intrauterine adhesions in clinic, and its curative effect is definite. However, its therapeutic effect is also influenced by many factors, including operation method, degree of damage of endometrium and patient's own situation[3]. At present, the high recurrence rate of intrauterine adhesions is still a problem to be solved. This article reviews the diagnosis and treatment of intrauterine adhesions in order to improve the understanding of the disease and provide some clinical reference for the diagnosis and treatment of the disease.

2. Diagnosis of intrauterine adhesions

2.1 Hysteroscopy

Hysteroscopy is the most valuable diagnostic method at present, which can accurately evaluate the thickness, shape, presence of abnormal bleeding and damage of endometrium. Studies have shown that patients can be comprehensively evaluated under hysteroscopy based on their clinical symptoms and endometrial thickness [4].

2.2 Transvaginal ultrasound (TVS)

Ultrasound has a high diagnostic rate for intrauterine adhesions. Ultrasonic examination is simple, convenient, non-invasive and non-radiative. It can be used as the first choice in diagnosing uterine cavity adhesion and is worthy of wide clinical application. A small clinical trial of Jiang et al [5]found that the sensitivity, specificity and accuracy of 3D-TVS in detecting intrauterine adhesion were 98.8%, 90.8% and 91.4% respectively.

2.3 MRI examination

MRI can be used to observe the relationship between endometrium and myometrium, help to assess the severity of intrauterine adhesions. The study shows that the combination of MRI and ultrasound has high accuracy in diagnosis of intrauterine adhesion and can improve the ability to judge the severity and prognosis[6].

2.4 Hysterosalpingography

Through this examination, it can help to check up the diseases such as oviduct obstruction, uterine cavity adhesion, etc. However, for the patients with cervical adhesion and severe abnormal shape of uterine cavity, its diagnosis is more difficult.

At the same time, because the diffusive degree of contrast medium itself and the influence of air bubbles and mucus in uterine cavity may lead to false positive signs of filling defect, the accuracy rate of clinical diagnosis is only about 50% [7].

3. Treatment of intrauterine adhesions

3.1 Transcervical resection of uterine adhesions (TCRA)

TCRA is the most important therapy for IUA. In recent years, with the continuous development and maturity of hysteroscopic surgery technology, the therapeutic effect of intrauterine adhesions has been greatly improved. TCRA has many unique advantages in the treatment of IUA: ① less bleeding during operation, patients recover quickly after operation; ② clear surgical field, accurate separation of intrauterine adhesions; ③ small injury to endometrium, can be carried out in the outpatient department. Although TCRA can effectively separate the adhesion tissue of uterine cavity, it has limited effect in preventing adhesion recurrence and preserving fertility.

3.2 Drug therapy

3.2.1 Estrogen drugs

Estrogen drugs are the most used drugs after uterine cavity adhesion operation. It achieves the treatment goal mainly through the promotion endometrium's repair and the regeneration, has the good security. Studies have shown that estradiol can promote endometrial self-repair by up-regulating estrogen receptors on the endometrial surface and regulating the expression of various fibrosis factors in endometrial tissue [8].

3.2.2 Vasodilator

Aspirin is widely used in clinical practice, mainly through inhibiting platelet aggregation and increasing local tissue perfusion. Clinically, it is commonly used in combination with estrogen. In a clinical study, aspirin combined with estrogen was used to treat patients with moderate and severe intrauterine adhesions. Through the follow-up treatment effect, it was found that the combination of aspirin and estrogen can effectively improve the symptoms of patients with hypomenorrhea and infertility, and the difference was statistically significant[9].

3.2.3 Gonadotropin releasing hormone agonist

The mechanism may be that GnRH-a regulates GnRH/FSH and LH levels. It can directly inhibit the growth of endometrium, affect estrogen metabolism to improve the patient's menstrual volume is too little, infertility and other symptoms. However, GnRH-a has some side effects, such as nausea, vomiting, abdominal pain, and long-term use can lead to premature ovarian failure. Therefore, its clinical application is limited, and there is no routine clinical application in intrauterine adhesion.

3.3 New treatment methods

3.3.1 Mesenchymal stem cells(MSCs)

MSCs are multipotent stem cells that are highly capable of self-renewal and differentiation and secrete a variety of cytokines to participate in tissue repair and regeneration. Mesenchymal stem cells can induce endometrial tissue to differentiate into stem cells and secrete a large number of cytokines, which are involved in the repair of endometrial injury [10]. Liu et al.[11]successfully constructed the intrauterine adhesion model of rats by means of mechanical injury and infection and injected mesenchymal stem cells into the adhesion model of mice in the experimental group. The results showed that the glandular tissue of the endometrial group was significantly increased, and the degree of intimal fibrosis was significantly reduced compared with the control group, and the endometrial group's endometrial tissue approximated that of the blank control group (normal endometrial).

3.3.2 Platelet -rich plasma(PRP)

Platelet rich plasma is obtained from human whole blood after centrifugation, with high concentration of platelets (2-7 times the basic value), which are rich in growth factors and cytokines and are rich sources of bioactive factors [12]. When activated, platelets in platelet-rich plasma release a large amount of growth factor, which is about 3 to 5 times the normal concentration in the body. In addition, it can also release platelet derived antimicrobial peptides, chemokines and other active factors . The above bioactive factors act synergistically on endometrium and promote the repair of endometrium.

3.3.3 Amniotic membrane transplantation

The amniotic membrane of other biological tissue is transplanted to the site of uterine cavity adhesion, thereby improving endometrial receptivity, and increasing pregnancy and live birth rates. Because of its good histocompatibility

and low immunogenicity, it is widely used in postoperative treatment of intrauterine adhesions. It has been found that the transplantation of amniotic tissue into the endometrium can induce the formation of local endometrial stem cells and further differentiate into endometrial tissue[13].

4. Summary and outlook

With the development of hysteroscopy, the diagnostic accuracy of hysteroscopy is increasing. Hysteroscopy is the most accurate method to diagnose intrauterine adhesions. TCRA is the most widely used method to treat intrauterine adhesions. It can resect the intrauterine adhesions visually and effectively restore the normal anatomy and function of uterus. Looking to the future, we believe that more new technologies, new drugs and new therapies will be applied to the postoperative treatment of intrauterine adhesions, bringing hope to the patients.

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