

# Research progress of Chinese medicine in the treatment of HyCoSy diagnosis of infertility

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**Abstract:** Infertility is defined as having sex without contraception for more than 12 months without becoming pregnant. The incidence of infertility is high. Once the disease occurs, it will not only affect the physical and mental health of women, but also affect the harmony of their families. Fallopian tube obstruction is the main factor causing infertility. In the past, X-ray hysterosalpingography was used to evaluate the patency of fallopian tube. In recent years, contrast-enhanced ultrasound technology has become more and more mature. It has the advantages of safety, accuracy, non-invasive, and reproducibility in evaluating fallopian tube patency, and is conducive to real-time observation of uterine cavity morphology, which has been widely used in the diagnosis and treatment of infertility. To evaluate the efficacy of Hysterosalpingo contrast sonography (Hysterosalpingo contrast sonography, hysterosalpingo contrast sonography, hysterosalpingo contrast sonography, hysterosalpingo contrast sonography, The improvement of adverse reactions such as pain caused by HyCoSy) in the diagnosis of infertility, and whether there are significant differences in the benefits brought by Hycosy compared with single moxa salt pack hot compress and conventional drugs for pain relief. This article reviews the research progress of Chinese and western medicine related to HyCoSy in the diagnosis of infertility in recent years, so as to provide some reference for clinicians.

**Keywords:** Hysterosalpingography; Infertility; Etiology and pathogenesis; Traditional Chinese and western medicine; Review

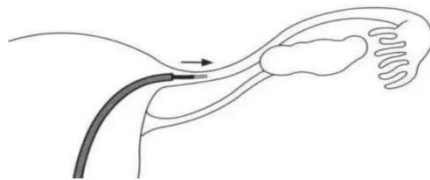
## 1. Introduction

Infertility is one of the common diseases in gynecology, which refers to the couple who have normal sex one year after marriage and cannot get pregnant without taking any contraceptive measures<sup>[1]</sup>. The incidence of this disease has gradually increased in recent years. In addition to pathological reasons (such as ovulation dysfunction, pelvic inflammation, pelvic tumor and genital deformity, etc.), this result is on the other hand attributed to the increasing employment pressure, fierce survival competition, deterioration of living environment and common individual sub-health state in today's society<sup>[2]</sup>. The functions of ovum uptake, mirror transport and fertilized ovum transport based on the fallopian tube to the uterine cavity are affected by many diseases, 8%-17% of women of childbearing age suffer from infertility, and 30%-35% of these patients fall into the above salpingal infertility<sup>[3]</sup>. Infertility will bring anxiety and depression to most patients to varying degrees, indirectly affecting the physical and mental health of patients, and further causing social burdens and family conflicts<sup>[4]</sup>. Even in the mental health assessment of infertility patients, the statistical existence rate of anxiety can reach 31.92 %<sup>[5]</sup>, so it is quite necessary to improve the diagnosis and treatment effect of infertility and regulate the psychological emotions of infertility patients. The traditional medicine of Zu described infertility as follows: the female married couple cohabited for more than two years, the reproductive function of the spouse is normal, without contraception and not pregnant, or have been pregnant, not contraception and more than two years not pregnant again, called "infertility", the former is called "primary infertility", the latter is called "secondary infertility". In ancient times, the former was called "Quanfu" and the latter "Dixu". Both men and women in the kidney qi sheng, Tiangui to, Ren Tong Chong sheng conditions, women's month to the present, men's qi overflow diarrhea, gender, coitus pregnancy, which can be seen the emergence of infertility and kidney qi deficiency, Chong Ren Qi and blood disorders are closely related. The common clinical types include kidney deficiency, liver depression, phlegm dampness and blood stasis. For the differentiation of infertility, women mainly according to the changes of the monthly events, the characteristics of the disease and the mixed

systemic symptoms combined with the tongue and pulse, syndrome differentiation and treatment. According to the Zang fu organs, Qi and blood, cold and heat, deficiency and actual situation of the following treatment key points: warm and nourishing kidney qi, regulating Qi and blood, correcting the month, exorcism and Fuzheng, Qi and blood shunhe, the pregnancy can become. In addition, it is also necessary to be comfortable in love, orderly in sex, and combine Yin and Yang in order to facilitate pregnancy<sup>[6]</sup>.

One of the criteria for the diagnosis of tubal infertility is to evaluate the patency of fallopian tubes, which is one of the reference conditions for clinical treatment decisions<sup>[7]</sup>. Some scholars have suggested that salpingography may have a certain dredging effect on fallopian tubes while helping the diagnosis of the disease, so that infertile patients may benefit from it<sup>[8]</sup>. In addition to evaluating the patency of fallopian tubes, contrast-enhanced ultrasound should also evaluate the status of pelvic cavity and uterus, which can be used as an auxiliary recommendation for reproductive programs. Of course, this is based on its simple operation, safety and practicality compared with other examination methods, and its role in dredging mild obstruction of some fallopian tubes<sup>[9]</sup>. Patients with completely blocked fallopian tubes screened by salpingography can choose assisted reproductive technology to avoid overtreatment.

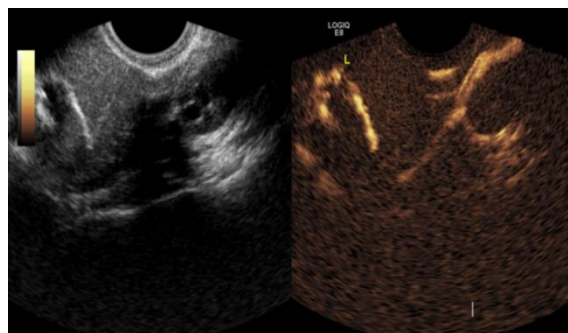
Commonly used to assess uterine tubal patency of checking method has the following kinds: fallopian tube commune fluid (hydrotubation, HDT); Hysteroscopy, laparoscopy, X-Hysterosalpingography (XHSG) and Hysterosalpingo contrast sonography (HyCoSy) were performed. (See Figure1-3)



*Figure 1: Hydrotubation, HDT*



*Figure 2: X-Hysterosalpingography (XHSG)*



*Figure 3: Hysterosalpingo contrast sonography (HyCoSy)*

HDT is the earliest clinical examination method used to determine the patency of fallopian tubes. Simple and easy to use. Doctors judge the degree of fallopian tube patency according to the resistance

of liquid injection, the presence or absence of reflux and the degree of pain response of patients, which has a certain subjectivity. Because this operation is blind, it cannot distinguish one time or bilateral fallopian tube patency, nor can it determine the specific site of obstruction.

XHSG is a common method to determine the patency of the fallopian tube. This method is to inject contrast agent into the uterine cavity through the cervical canal. Under the X-ray film, the contrast agent can not only improve the patency of the fallopian tube, obstruction site, but also can observe the shape of the uterine cavity, but the disadvantage is to accept ionizing radiation, and pregnancy is not recommended within 3 months after the examination, radiation and increase the occurrence of fetal malformation. The commonly used contrast agents iodized oil and iodized water require allergy tests, which are forbidden for those with iodine allergy. There are also risks of iodine allergy and pulmonary embolism in the examination<sup>[10]</sup>.

With the rapid development of ultrasound medicine, Hysterosalpingo contrast sonography (HyCoSy), a safer, real-time and convenient imaging technique, has been gradually used to evaluate the patency of fallopian tubes. HyCoSy has been gradually upgraded from 2D to 4D imaging mode under the continuous update of imaging technology mode<sup>[11-12]</sup>. HyCoSy is a transvaginal ultrasound guided injection of contrast agent into the uterine cavity, and the patency of the fallopian tube is determined by observation of the flow of contrast agent in the uterine cavity and fallopian tube and the diffusion after entering the pelvic cavity. It can not only show the uterine cavity, fallopian tube and pelvic cavity, but also find the disease of uterus and ovary. One examination can make a comprehensive understanding of the patient's condition. HyCoSy has the advantages of high diagnostic accuracy, no radiation, simple operation, safety and non-invasive, and has gradually become the main imaging screening method to evaluate the degree of fallopian tube patency<sup>[13]</sup>.

Among them, HyCoSy has gradually become the main imaging screening method to evaluate the degree of fallopian tube patency due to its advantages of high diagnostic accuracy, no radiation, simple operation, safety and non-invasive<sup>[14]</sup>. However, pain is the most common adverse reaction in the examination of fallopian tube patency, whether it is HDT, XHSG or HyCoSy<sup>[15]</sup>. Secondly, anxiety and depression caused by pain cannot be ignored in the diagnosis and treatment of tubal infertility.

## 2. Etiology and pathogenesis of TCM

According to the clinical manifestations, the disease belongs to the categories of "infertility", "late menstruation" and "less menstruation" in traditional Chinese medicine. The etiology and pathogenesis of infertility were discussed in details in "All Diseases Source and Syndromes of Women Miscellaneous Diseases and Syndromes": "Women with diseases have no children, all of which are caused by labor, the blood qi is damaged, the cold and heat are not controlled, and the wind and cold are affected in the uterus, resulting in the disease in the cell, or the menstruation is closed, or the blood is crushed under the body, causing the qi of Yin and Yang to be inconsistent, and the menstruation is good, so there is no child." Chen Shi-duo's "Stone Chamber Secret Record: On Children" cloud: "A woman who cannot bear children has ten diseases. What are ten diseases? One baby is cold, two spleen and stomach are cold, three belt pulse is acute, four liver qi is stagnant, five phlegm qi is abundant, six phases of fire are prosperous, seven kidney water failure, eight governor and ren disease, nine bladder gasification cannot, ten qi and blood deficiency and cannot be taken." Doctors of past dynasties believed that this disease was both deficiency and excess. The deficiency was mainly kidney deficiency, blood deficiency and spleen deficiency, and the solid was mainly blood stasis, phlegm and liver depression.

### 2.1. Kidney deficiency

The kidney stasis essence, is THE congenital ORIGIN, DOMINATES THE HUMAN body's growth and DEVELOPMENT AND reproduction, THE FEMALE MENSTRUATION and THE PREGNANCY fundamental lies in the kidney - TianyuI-chong Ren - UTERUS reproductive axis normal. If congenital endowment is insufficient, or sexual misconduct, or long illness can cause kidney deficiency, affecting the thoroughness of the two vessels, causing menstrual disorders or infertility. The main reference is Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease 2021 report<sup>[2]</sup> and Guidelines for the Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease (2013 Revision)<sup>[3]</sup>.

## ***2.2. Kidney deficiency and liver depression***

Women with liver as the congenital, liver blood, the main catharsis, love to get evil depression, and liver and kidney as the mother of the viscera, if the woman's sexual depression, or seven feelings caused by liver disorders, but the child disease and mother involved in the kidney, liver and kidney hidden excretion disorders, affecting ovarian reserve function infertility.

## ***2.3. Both spleen and kidney are deficient***

Spleen is the origin of acquired nature, the source of qi, blood and biochemistry, and the transport of water and grain essence to nourish the five zangfu organs. If the spleen is deficient, the source of qi, blood and biochemistry is insufficient, and the inability to transport water and grain is insufficient. Therefore, the innate essence is lost to the acquired essence and nourishment, resulting in the nourishment of Chong and Ren, the sea of blood is not abundant, and the reproductive ability is decreased.

## ***2.4. Heart and kidney do not cross***

The heart is the official of the sovereign, the master of the viscera, the master of the development of the kidney essence and the storage and discharge of the uterus. If the emotional injury, or excessive exertion and annoyance, can consume the blood, deficiency and the heart Yin, the heart fire is more vigorous on the top, cannot lower the kidney water, the kidney water is not solid, the blood sea is not full, so the inability to have a son.

## ***2.5. Both heart and spleen are deficient***

"Jingyue Quanshu ·Woman rule" cloud: "All desire does not follow, meditation accumulation, heart temper knot, the source of injury chong Ren, and kidney qi disappear, light or early or late, heavy gradually become dry closed." Spleen deficiency is lack of qi and blood biochemical source, Chongren uterus lost in Ruyang, the cell vein belongs to the heart and collateral cells, heart and spleen injury can affect the normal menstruation, day long cannot take sperm coagulation pregnancy.

## **3. Advances in the application of contrast-enhanced ultrasound**

### ***3.1. Three dimensional ultrasound***

Three-dimensional ultrasound is a new examination technology with the rapid development of computing technology, which integrates contrast-enhanced ultrasound, transvaginal ultrasound and three-dimensional technology. By injecting contrast agent into the uterine cavity, the process of diffusion of contrast agent from fallopian tube to pelvic cavity is dynamically observed by real-time three-dimensional technology, so as to evaluate the degree of fallopian tube patency according to the fluency of contrast agent through. In the process of examination, this technology can reflect the course and distortion of the oviduct three-dimensional, intuitive and real-time, which provides an important reference for clinical diagnosis of infertility. At the same time, 3D ultrasound can optimize the application of contrast agent through low sound pressure, so that the time of contrast agent in the body is prolonged, so as to ensure that the ultrasound beam is transmitted outward at a specific frequency, and it is easy to accept the signal of the imaging agent in the narrow segment to avoid overlapping contrast effects, and thus improve the diagnostic accuracy of fallopian tube obstruction.

### ***3.2. Four-dimensional ultrasound***

Four-dimensional ultrasound adds a fourth dimensional time vector on the basis of three-dimensional, which can obtain three-dimensional images in real time, make up for the shortcomings of traditional ultrasound, provide rich imaging information for clinical diagnosis, greatly reduce the rate of missed diagnosis of lesions, and enhance the quality of diagnosis. Its application in the diagnosis of infertility can more clearly show the shape of the uterus and fallopian tube, observe the diffusion of the contrast agent in the pelvic cavity and ovary, so as to obtain more abundant diagnostic information and further improve the accuracy of clinical diagnosis. 4D-HyCoSy has high specificity and sensitivity in the diagnosis of fallopian tube patency in infertility. In addition, this method is simple

and repeatable, so it has high clinical application value.

#### 4. Integrated traditional Chinese and western medicine treatment methods

The common western medicine treatment is atropine sulfate injection 0.5mg, three times a day intramuscular injection. The common traditional Chinese medicine treatment method is to pack moxa salt for 30 minutes, twice a day. Or hot compress with moxa salt package for 30min combined with acupoint application with traditional Chinese medicine for 2h, twice a day. Methods Acupoint application: according to the "Traditional Chinese Medicine Nursing Routine Technical operation Specification" issued by the Chinese Medicine Association, continuous application for 2 hours, with an interval of 6 hours between the two times. Hot compress of moxa salt package: heat the moxa salt package to the appropriate temperature through the microwave oven, and heat compress the lower abdomen about 40-45 degrees Celsius, each hot compress for 30 minutes, and the interval between the two times is 9 hours. Selection of TCM acupoint application drugs: Pinellia, Yuan Hu so, frankincense, myrrh, cinnamon to salad oil to grind the end and blend. Acupoint selection: Guanyuan (CV 4), Sanyinjiao (SP 6), Shenshu (BL 23), Dachangshu (BL 23) and Zusanli (ST 36). Making moxa salt bag: Mix the ground moxa and kosher salt (straight diameter 4 mm) according to the weight ratio of 1:3, mix evenly and place in a square canvas bag of 20 cm×20 cm. (See Figure4-5)



Figure 4: Acupoint application



Figure 5: Hot pack of moxa salt

Modern medical treatment of this disease mostly uses individualized hormone replacement therapy combined with ovulation induction, growth hormone, coenzyme Q10, assisted reproductive technology, etc. After treatment, the hormone level and follicular development of patients are improved significantly, but the long-term safety of medication needs to be studied. Integrated traditional Chinese and western medicine treatment integrates the advantages of traditional Chinese medicine and western medicine, shortens the treatment cycle of traditional Chinese medicine, and reduces the adverse reactions of western medicine treatment, which is the current clinical treatment trend.

Zhang Xinxin<sup>[16]</sup> treated 30 patients with this disease with the addition and reduction of traditional Chinese medicine Guisen pill (Codonesia radix, Euphorbiae officinalis, Cuscutazi, Salvia miltiorrhiza, Yuzhu, Liguzi, Wolfberry, Baipeony, Ripeness, fried licorice, Radix bupleurum, Angelica sinensis)

combined with progesterone capsules. The total effective rate was 86.67%, the ovulation rate and pregnancy rate were 53.33% and 36.67%, respectively. The indexes of sex hormones were significantly improved, and the results showed that the combined treatment of traditional Chinese and western medicine improved the clinical treatment effect compared with western medicine alone. Wang Dailin et al.<sup>[17]</sup> concluded through clinical observation that: Self-made Bushen Tongluo decoction (Ziheche powder, Cuscutazi, processed Rehmanniae, Dendrobium, raspberry, Epimedium, Lutong, Sinensis sinensis, Ligusticum chuangxiong, Xiangfu, Yam, Jixueteng, Huangjing, mulberry, Salvia miltiorrhiza) combined with "estradiol valerate + progesterone" in the treatment of 30 patients with this disease, the total effective rate was 96.7%, and the pregnancy rate was 40%. The combination of the two has a synergistic effect and significantly improves the probability of pregnancy.

## 5. Discussion

Infertility is more common in modern medicine and traditional Chinese medicine, among which tubal obstruction is more common in patients with infertility in modern medicine. Therefore, it is particularly important to screen patients with different degrees of tubal occlusion in infertility, which has great significance both for the diagnosis and treatment of the disease. At present, the mainstream contrast-enhanced ultrasound examination often brings pain and different degrees of discomfort and anxiety to patients after examination, so it is particularly important for the relief of pain and other symptoms after examination. The use of conventional analgesics is not ideal, and it will bring more or less various side effects and adverse reactions to the body. Compared with oral drugs, traditional medicine such as acupoint application and hot compress not only have quite definite curative effect, but also bring little side effects. Based on the dialectical treatment of pain in traditional medicine, traditional Chinese medicine plays the role of relieving pain, dispelling cold, warming meridians, dispelling cold and removing dampness, which not only relieves the pain caused by examination. The extremely high acceptance also eliminates the anxiety of the vast majority of patients, and there is considerable acceptance in the patient population.

The combination of traditional Chinese medicine and western medicine can take advantage of each other and obtain better curative effect. Now it has been recognized and respected by most scholars and has broad prospects. However, the differentiation and treatment of integrated traditional Chinese and western medicine is mainly based on the experience of doctors, which lacks objectivity, and the combination and dosage of drugs are lack of unity. The clinical research on the treatment of this disease with traditional Chinese and western medicine is mainly based on the summary of personal experience of doctors. The sample size of clinical research is small and there is a lack of scientific data analysis. Therefore, in the future research, we should expand the sample size, make full use of modern science and technology and means, and believe that with more and more in-depth research, the standardization of clinical treatment can enter a new stage.

## References

- [1] Liu Li, Zhao Junli. *Emotion and coping style of infertility patients of different genders [J]. Chinese Journal of Mental Health, 2011, 25(11):806-809*
- [2] Zhang H, Wang S, Zhang S, et al. *Increasing trend of prevalence of infertility in Beijing[J]. Chin J Med (English edition), 2014, 127(4).*
- [3] Zhou L, Zhang X, Chen X, et al. *Value of three-dimensional.hysterosalpingo-contrast sonography with SonoVue in the assessment oftubal patency[J].Ultrasound Obstet Gynecol. 2012, 40 (1) : 93-98.*
- [4] Zhang X, Li Y F, Cui C Y,etal. *Relationship between fertility stress and general self-efficacy and anxiety in female infertility patients [J]. China Public Health,2019: 807-809.*
- [5] Newton CR, Sherrard W, Glavac I. *The Fertility Problem Inventory: measuring perceived infertility-related stress[J]. Fertil Steril, 1999, 72(1): 54-62.*
- [6] Lian Fang, 2017.6, *TCM Gynecology, Science Press,336 pp.*
- [7] Giuseppe Lo Monte, Gianpiero Capobianco, Isabella Piva, Donatella Caserta, Salvatore Dessole, Roberto Marci.,*Hysterosalpingo contrast sonography (HyCoSy): let's make the point! [J]. Archives of Gynecology and Obstetrics,2015,291(1):*
- [8] Qiang Ye,Mao Shu Xia,Wu Yi Yun,Li Hong Bo,Cai Ting.*Effect of transvaginal real-time three-dimensional hysterosalpingo-contrast-enhanced ultrasound in the treatment of infertility [J]. Chinese Journal of Family Planning and Obstetrics and Gynecology, 2019,11(10):68-70+83.*
- [9] Cui Qi,Liang Xi,Li Ying.*Clinical value of four-dimensional hysterosalpingo-contrast-enhanced*

*ultrasound in pre-pregnancy screening of assisted reproductive technology [J]. Chin J Medical Ultrasound (Electronic Edition), 2020: 1103-1107.*

[10] Salata I, Gottwald L, Sobkiewicz S. *[Comparison of assessing the patency of the Fallopian tubes during laparoscopy and during hysterosalpingography on television in infertile women with endometriosis]. [J]. Ginekologia Polska, 2003, 74(9):1014.*

[11] Jain T. *Socioeconomic and racial disparities among infertility patients seeking care [J]. Fertility & Sterility, 2006, 85(4):876-881.*

[12] F Chen, Quan J, Huang P, et al. *Hysterosalpingo-Contrast Sonography With Four-Dimensional Technique for Screening Fallopian Tubal Patency:.,Let's Make an Exploration [J]. Journal of Minimally Invasive Gynecology, 2016, 24(3):407-414.*

[13] Wang W, Zhou Q, Gong Y, Li Y, Huang Y, Chen Z. *Assessment of Fallopian Tube Fimbria Patency With 4-Dimensional Hysterosalpingo-Contrast Sonography in Infertile Women. J Ultrasound Med. 2017. Oct; 36(10):2061-2069. doi: 10.1002/jum. 14244. Epub 2017 May 24. PMID: 28543598.*

[14] Xiang Yuting, Bai Wenpei. *Clinical application of ultrasound imaging in diagnosis of tubal patency [J]. International Journal of Reproductive Health/Family Planning, 2016, 35(2):4.*

[15] Wang Xiaoqian, SUN Zhiwei, Wang Lin, et al. *Analysis of the tolerance and pain factors of transvaginal real-time three-dimensional hysterosalpingo-contrast-enhanced ultrasound [J]. J Clinical Ultrasound Med, 2018, 20(6):417-419.*

[16] Zhang Xinxin. *Effect of modified Guishen pill on infertility with decreased ovarian reserve function of kidney deficiency [J]. Chinese Medicine Guide, 2018, 16(14):2.*

[17] Wang Zhuan, Lin Kuang-Jilin. *Self-made Bushen Tongluo decoction combined with artificial cycle in the treatment of infertility caused by decreased ovarian reserve function [J]. Chin J Clin Med, 2020, 32(3):486-489.*