

Discussion on the Treatment of Ovulatory Dysfunction Infertility with Kidney Deficiency and Blood Stasis Based on the Theory of "Tian Gui"

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Keywords: Tian Gui; Kidney deficiency and blood stasis; Ovulation disorders; Infertility

Abstract: The theory of “Tian Gui” originated from “Huangdi Neijing”, in which it is written that a woman can only get pregnant when her internal organs are full of qi and blood, and her reproductive function is normal, and its research significance and clinical practical value have far-reaching impacts. Infertility is a common intractable disease among women of childbearing age, and its incidence rate is as high as one sixth. Ovulation dysfunction has become one of the main causes of infertility in women. Kidney is the master of reproduction, the lack of kidney essence, stagnation of blood stasis in the uterus, the follicle development and maturation of obstacles and difficulties in discharging, kidney deficiency and blood stasis is an important mechanism of ovulatory dysfunction infertility (ODI). According to Chinese medicine, the occurrence of this disease is closely related to the reproductive axis of “Kidney-Tianguai-Chongren-Cystic uterus”, and the treatment can be based on tonifying the kidney and activating the blood, supplemented by strengthening the spleen and dredging the liver, promoting the flow of qi and resolving phlegm. By analyzing the relationship between “Tian Gui” and female reproduction, this article explores the pathogenesis of ODI with kidney deficiency and blood stasis, with a view to providing more ideas for the clinical diagnosis and treatment of ODI with kidney deficiency and blood stasis.

1. Introduction

Infertility is a common reproductive disorder in women and is associated with a variety of disorders such as reduced ovarian function, polycystic ovary syndrome, luteal insufficiency, hyperprolactinemia, and tubal obstruction [1]. The hypothalamic-pituitary-ovarian axis affects the secretion of follicle stimulating hormone and regulates ovulation, with abnormal follicular development or difficulty in ovulation, resulting in ovulatory disorder infertility (ODI) [2]. According to the analysis of the World Health Organization report, about one in seven couples of childbearing age worldwide suffer from infertility, and in recent years it has even risen to one in six [3]. The causes of infertility include ovulatory dysfunction, abnormal tubal patency and immunologic factors, and lifestyle and environmental factors can also adversely affect reproduction, with ovulatory dysfunction

being the most significant factor leading to infertility [4]. Currently, western medicine mainly uses drugs to induce ovulation and assisted reproduction technology to treat this disease, but there is a high ovulation rate but low pregnancy rate in drug ovulation promotion, and assisted reproduction also requires huge financial and human resources. There is no such disease name as “Ovulation Disorder Infertility” in ancient literature, but according to its clinical characteristics, Chinese medicine categorizes this disease as “broken threads”, “childlessness”, “infertility”, “infertility”, “infertility”, and so on. Infertility”, “total infertility” and other diseases [5]. According to Chinese medicine, this disease is mainly caused by stagnation of blood stasis and phlegm-dampness in the uterus due to insufficiency of kidney essence, stagnation of liver qi, and failure of the spleen to regulate its movement, etc. Clinical diagnosis and treatment centered on the “holistic concept” has unique advantages [6]. Now, we analyze the physiological characteristics of the kidney-tianguai-chongren-cystic uterus axis with the theory of “Tian Gui” in “Huangdi Neijing” as the core, in order to provide more ideas for the diagnosis and treatment of renal deficiency and blood stasis type of ODI.

2. Huangdi Neijing of Internal Medicine on “Tian Gui” and Female Reproduction

2.1. Traditional understanding of “Tian Gui”

Ancient scholars had different understandings of the term “Tian Gui”, including “male essence and female blood”, “dynamic qi between the kidneys”, “originating from the mind”, and “inherent in the body”. There are “male essence and female blood”, “dynamic qi between kidneys”, “from the mind”, “true water”, etc. Ancient people interpreted “Tian Gui” as congenital essence, and modern people think that Today, it is also believed that “Tian Gui” is a kind of Yin attribute substance, which dominates menstrual flow and is of great significance to human fertility and reproduction [7]. Xia Guicheng believes that Tian Gui has a close relationship with the heart and kidney, is to maintain sexual physiology and function of the important water-like substances, kidney qi full of influence on decanter full of kidney qi full of organs and organs, Tian Gui can be secreted to promote menstruation, reproductive reproduction [8].

2.2. The modern understanding of the “Tian Gui”

Traditional Chinese medicine believes that after the fullness of Tian Gui nourishes the essence of reproduction, women from the state of yin and yang decline to the state of heavy yin and must be transformed into the state of yang, yang qi growth to the heart and brain, regulation of ovulation, meridians through the fullness of the month to the ovary that is, the ovary normal ovulation. Modern life sciences pointed out that the female Tian Gui is the hypothalamus - pituitary - ovary axis of the basis of the gonadal tissue function and the regulation of the reproductive axis of the strong and weak decision of the surplus and deficit of Tian Gui, indicating that estrogen and progesterone secretion is a material basis of Tian Gui [9]. This indicates that the secretion of estrogen and progesterone is the material basis of Tian Gui. The arrival and exhaustion of Tian Gui depends on the strength of the kidney function, the normal secretion of hormone with sufficient kidney essence, the normal growth of follicle and endometrium. Therefore, Tian Gui can be regarded as a substance with reproductive significance.

2.3. Interpretation of Female Reproduction Based on the Theory of “Tian Gui”

According to Zhang Dengben, in the word “Tian Gui”, “Tian” refers to the kidney and kidney essence, and “Gui” is the end of the ten heavenly stems, and the month of Gui in the October Solar Calendar corresponds to the kidney, which is why it is also known as “Gui” [10]. Kidney qi is

sufficient, yin and yang coordination, Tian Gui overflow, Chongren vigorous qi and blood, the uterus in order to regularly hide diarrhea, the overall conditions to meet the normal ovarian ovulation, menstruation, women's conception is possible, and “kidney - tiangui- Chongren - cystic uterus,” the axis of any of the links in the abnormalities can lead to a state of postponement, the real water is damaged or even disappeared, thus triggering infertility [11]. Thus, Tian Gui is the material basis of ovulation, Tian gui on time to urinate, smooth ovulation is a woman's sex hormone levels normal direct response, but also the seed into the core of pregnancy.

3. The relevance of the “Tian Gui” theory to ODI

3.1. Pathogenesis of ODI

Modern medicine believes that the hypothalamus releases gonadotropin-releasing hormone through positive feedback, after which the pituitary gland releases luteinizing hormone and follicle-stimulating hormone to reach the peak, and the ovary functions normally to be discharged after the follicle develops and matures smoothly. If progesterone is not sufficiently secreted from the corpus luteum, endometrial tolerance will be unsatisfactory and fertilization will be difficult; if too much estrogen is secreted, it will easily affect ovulation and lead to irregular menstruation, and even breast hyperplasia or increase the risk of endometrial cancer, etc, and will cause infertility [12]. On the other hand, ovarian angiogenesis also affects follicular development and expulsion. If angiogenesis is abnormal, insufficient blood flow to the ovary will result in insufficient nutrients to the follicle, and the follicle will not be able to ovulate normally due to the defective internal environment, which will ultimately lead to infertility.

3.2. Changes in the “Tian Gui” affect the growth of follicles

“Kidneys hide essence, the main reproduction”, oocytes can be considered to belong to the essence of reproduction, when the kidney qi is abundant, qi and blood regulation, Tian gui accumulation and then to, the woman menstruation can come, and has the ability to reproduce, just as the follicle's development, maturation and normal discharge is the prerequisite for a successful pregnancy [13]. Normal transformation of yin and yang, the fullness of Tian gui, Chong Ren blood sea full of heavy yin, into the state of follicle rupture, egg discharge. Various dynamic changes of yin and yang in “Tian Gui” can cause follicular developmental retardation, ovulation after abnormal maturation of eggs, and thus lead to different diseases. This can lead to different diseases, such as luteinized follicle failure syndrome, polycystic ovary syndrome, Silkman's syndrome, and hyperprolactinemia, all of which ultimately cause ODI [14]. When the follicle develops to maturity, it can unite with the sperm to conceive an embryo; if the kidney essence is deficient and the kidney qi is insufficient, the follicle does not develop properly, so there is no child [15]. If Tian Gui is insufficient, the Chong Ren Qi and blood cannot nourish the follicles, and premature ovarian failure occurs when the yin fluid is not nourished. The invisible water of Tian Gui is similar to estrogen-like substance in modern medicine in one aspect, therefore, taking Tian Gui as the starting point to think about the growth and change of follicles is the trend of ODI diagnosis and treatment.

3.3. The heart and mind regulate “Tian Gui” and ovulation

The heart hides the spirit and is the master of the blood, while the brain is the house of the spirit. The heart and brain affect the growth of follicles, and Tian Gui is the key to the heart and brain's regulation of the kidney's essence. The essence of female reproduction, is dependent on the Tian Gui for its growth and nourishment; and the maturation of the development of the ovum as well as its

ovulation is subject to the control of the heart and brain. Studies have shown that depression, stress and anxiety problems have a significant impact on female hormone balance, quality of ovulation, and account for a greater proportion of infertility factors [16]. If the heart and mind are restless, the liver loses detachment and excretion, the pivot of qi elevation and drainage is abnormal, and the blood flow is not smooth, and the mature egg cannot be discharged normally, then ovulation disorder or no ovulation will be caused [17]. Therefore, the heart and brain affect the emotions, the qi is not smooth, the blood stasis is blocked, and the Chong Ren and the uterus are not nourished, which will cause the end of pregnancy difficulties.

3.4. Pathogenesis of kidney deficiency and blood stasis type of ODI

Kidney deficiency is the root cause of follicular ovulation difficulties and is the determining factor of ODI, while blood stasis is always present in the course of the disease. Ma Kun pointed out that the key pathogenesis of ovulatory dysfunction infertility is kidney deficiency and blood stasis, while depression and phlegm also lead to meridian obstruction and congestion, and the disease is attributed to the liver, spleen and kidney, and is also influenced by the heart [18]. Infertility occurs if congenital insufficiency, insufficiency of kidney qi or injury to kidney qi by repeated pregnancies and births, surgical history, gradual decline of kidney qi in old age, deficiency of Chong Ren, etc. leading to deficiency of essence and blood, and inability to nourish and nourish the essence of procreation; blood stasis is the pathological product of renal deficiency, kidney essence loss, will inevitably lead to the lack of source of blood production, blood and fluid withered, lack of renal essence, yuan qi deficiency and weakness, the blood line is powerless and stagnant, stagnant veins can not be blocked, will lead to infertility. Modern medical research shows that the kidney is closely linked to many endocrine glands such as the pituitary gland, the thyroid gland and the gonads, and endocrine disorders in women directly affect ovulation, and the prevalence of infertility increases with the degree of renal function damage [19]. If blood stasis forms and blocks the cellular channels for a long period of time, infertility can also occur in severe cases of premature exhaustion of Tian Gui. Symptoms of blood stasis resemble the pre-thrombotic state in modern medicine, which is considered by Western medicine to affect uterine arteries and endothelial growth, which may further lead to infertility [20]. In women, the kidney is the root and blood is the use, long-term kidney deficiency and blood dysfunction will result in blood stasis, which will affect the production of kidney essence and aggravate the deficiency of the kidney, and both of them will affect each other, ultimately leading to the occurrence of ODI.

4. Treating Kidney deficiency and Blood stasis type ODI based on the theory of “Tian Gui”

4.1. Nourish the kidney and fill in the essence, and nourish the Tian Gui

According to “Huangdi Neijing”, “Tian Gui is the essence of yin, which belongs to water in the kidney and also belongs to water in the kidney, and is born from the accumulation of innate qi”, which reveals that Tian Gui is produced from the essence of the kidney, and therefore, the most fundamental cause of ovulatory disorders is the insufficiency of the essence of the kidney [21]. The five human organs, kidney failure is the earliest, if the kidney yin is insufficient, blood biochemistry lack of source, the uterus no blood can be down, the follicle will be due to the lack of moistening material and the development of maturity difficulties; if the kidney yang is insufficient, the cold stagnation of blood stagnation will lead to follicle initiation obstacles, or the egg discharged difficult, difficult to conceive. Kidney is a water organ, which is the origin of phlegm. Kidney deficiency leads to abnormal gasification, phlegm-dampness, and phlegm-saliva injected into Chongren, which can easily cause infertility; at the same time, phlegm-dampness can also be intermixed with qi stagnation, blood stasis,

and other real evils, which can lead to abnormal function of the reproductive axis of “Kidney-Tianguai-Chongren-Cystic Uterus”, and obstruction of the cytosolic vein and thus cause infertility [22]. When treating the disease, the kidney essence can be replenished to nourish Tian Gui, so that qi, blood, yin and yang can be regulated to prevent the pathological products from affecting ovulation.

Zhu Nansun believes that the cause of ODI is mainly kidney deficiency, lack of kidney yin, lack of essence and blood, the eggs are not nourished by the lack of source of growth; kidney yang drumming powerlessness is cold and weak Chong Ren, regaining the sperm, treatment focuses on the “Chong Ren as the basis, the liver and kidney as the outline” of the ideological guidance, the use of medication to warm the kidneys to fill the essence of the main, Zhu's menstruation and fertilization formula for tonifying the kidneys to invigorate the blood, menstrual stimulation to help conception. Its Zhu's formula for regulating menstruation and promoting pregnancy tonifies the kidney and activates blood, regulates menstruation and helps pregnancy. Wan Yiting et al randomly divided 150 ODI patients into three groups, group A received conventional ovulation-promoting treatment, group B received Zhu's menstruation regulating formula combined with conventional ovulation-promoting treatment, and group C received oral aspirin combined with conventional ovulation-promoting treatment, and after three menstrual cycles of continuous use of medication, the pregnancy rate of group B who received Zhu's menstruation regulating formula was higher than that of group A and group C, which proves that Zhu's menstruation regulating formula helps follicle development by strengthening the kidney and yang, while nourishing and tonifying the kidney [23]. It proves that Zhu's Menstruation Regulation and Fertility Promotion Formula helps follicle development by strengthening kidney yang, and at the same time nourishes kidney yin, tonifies qi and passes through the collaterals, promotes endometrial hyperplasia, elevates sex hormone secretion, improves blood rheology and increase the rate of ovulation in patients with ODI, and the clinical pregnancy rate is also effectively improved. Nourishing the kidneys is the way of seeds.

4.2. Promoting blood circulation and removing blood stasis, and promoting drainage through the veins

If the evil qi is invaded during menstruation, or if the house is not properly maintained, the evil will enter the uterus and cause blood stasis; dampness will be attached to the lower jiao for a long time and become stasis over time, which will block the cell veins; insufficient qi and blood or qi is weak, which will cause stasis in the Chongren, and the blood supply to the uterus and ovary will be insufficient, and the endothelial lining will grow abnormally, so that follicles can't be discharged normally and lead to infertility. Blood stasis affects the “hypothalamus-pituitary-ovary-uterus” axis, leading to dysfunction, especially in hypopituitary women, due to insufficient production of gonadotropins and follicle stimulating hormones, abnormal ovarian development and follicular growth, amenorrhea and even infertility [24]. In the treatment, while nourishing kidney yin and warming kidney yang, the addition of medicines that activate blood circulation and remove blood stasis to improve blood circulation around the ovaries can enhance the blood supply to the ovaries and promote follicular discharge.

Xiao Chengzong believes that infertility is mostly attributed to insufficient kidney qi and stagnation of the cytosolic veins, and often uses the empirical formula of Er Bu Zhu Yu Tang to tonify the kidney and activate blood circulation, and dredge the cytosolic veins. Liang Jialing et al reported that in 32 cases of infertility patients with kidney deficiency and blood stasis, Er Bu Zhu Yu Tang was effective in improving the clinical symptoms of kidney deficiency and blood stasis and endometrial tolerance, and was able to promote a good pregnancy outcome [25]. Clinical studies have shown that traditional Chinese medicines that warm and tonify kidney yang can stimulate ovarian function, and traditional Chinese medicines that tonify blood and activate blood circulation can

enhance uterine blood supply to improve the internal environment, and regulate endocrine and metabolism related to ovulation as a whole [26]. When the blood stasis is removed, new blood is generated, and when the stagnant blood in the flushing period is dispersed, the blood flow is smooth, and the endometrium and ovaries are nourished normally, and the ovulation function can be restored.

4.3. Harmonizing the internal organs and regulating the menstrual cycle to help conception

Fu Shan suggested that female menstrual regulation is a necessary condition for seed, menstrual cycle disorders will affect the conception, more than the use of fixed menstrual soup to tonify the kidney essence to dredge the liver, nourish the blood and soften the liver in order to help conception. Luo Yuankai believed that by tonifying the kidneys can promote ovulation and later adjust menstruation to help conception [27]. Imbalance of yin and yang in the kidneys, or the phase shift of the other four organs, kidney-liver, kidney-spleen interactions can affect the kidneys, leading to disordered transformation of qi and blood between menstruation, dysfunction of the ovaries, and ultimately the inability to ovulate normally for infertility to occur [28]. Zhang Jingyue attached importance to the function of the spleen and stomach on female reproduction, the later treatment of infertility with warm medicines, such as Luo's "ovulation soup", by warming the spleen and stomach, tonifying the kidneys and nourishing the liver, especially kidney yang deficiency ovulation disorders, and more use of blood and flesh with sentient products to regulate the Chongren to help conception and fertilization. Jiang Zhuojun et al found that the treatment of ODI with the formula of regulating menstruation and promoting pregnancy by tonifying the liver and kidney can improve pregnancy outcome by tonifying the kidney and activating the blood and facilitating the meridians to adjust the patient's menstrual cycle [29]. Therefore, in the clinical treatment of ODI, not only should we pay attention to the leading role of the kidney in the regulation of the reproductive axis, but we should also make clear the influence of the internal organs, qi and blood on the regulation of the reproductive axis, and we should pay special attention to the regulation of the kidney, the liver, the spleen, and the heart, and we should also comply with the women's menstrual cycle, so as to benefit Tian Gui and regulate the rushing period, and realize qi and blood, and the regulation of internal organs and organs, so as to promote the development of the follicle normally and the smooth discharge of the ovum. The follicles will develop normally and the eggs will be discharged smoothly.

Xia Guicheng often treats ODI with kidney deficiency with his empirical formula Tonic Heavenly Seed Jade Dan, which is based on the method of adjusting the rhythm of the menstrual cycle, and consists of the formula of Four Substance Soup, Six Flavors of Dihuang Soup, and Five Sons Diffractive Pill, which promotes yin and yang to promote yin and yang, and achieves nourishment for Tian Gui, vitality of qi and blood, and the development of follicle maturity and normal discharge [30]. In the treatment of ODI, Tan Yong often used the empirical formula Zi Yin Fang to nourish blood and nourish yin, while *Cornus officinalis* and *Semen cuscutae* played the role of nourishing the liver and kidney, and seeking yin in yang, to regulate the function of the ovaries, and help to nourish the follicles to achieve a successful pregnancy [31]. Ma Kun's team used 100 cases of infertility patients as research subjects, the test group was treated with the formula of tonifying the kidney and activating the blood to promote ovulation, and the control group was given Clenbuterol combined with clomiphene, and finally the test group had a higher total effective rate, and the test group was more effective in improving the patients' Chinese medicine symptoms and pregnancy outcomes compared with the control group [32]. Li Liyun's treatment of ODI follows the principle of "the way of conception is to regulate the menstruation, to regulate the menstruation, to regulate the period, to regulate the successive heavens, to strengthen the spleen and tonify the kidneys, to regenerate the vital essence", follow the rationale and method of dispensing the medicines to achieve the goal of balance of yin and yang, harmony of internal organs and restoration of the balance of the heavenly

decadal and the normal ovulation [33]. Chen Xia believes that the treatment of ODI should be tonifying the kidneys and adjusting the weekly treatment, menstruation overdue amount is small, accompanied by lumbar and knee pain, fatigue, mostly for kidney qi deficiency; menstruation in advance amount is small, accompanied by dizziness, tinnitus, thirst and dry throat, mostly kidney yin deficiency; menstruation is pushed back, the menstrual blood is light in color, accompanied by fear of cold limbs cold, cold abdomen, mostly for kidney yang deficiency, by regulating yin and yang in the kidneys, it can make the Chong Ren qi and blood vigorous, the follicle can be mature and ovulate smoothly then The follicle can be developed and matured, and then ovulate smoothly and become pregnant.

5. Summary

To summarize, when treating ODI with kidney deficiency and blood stasis, TCM practitioners select formulas and medicines that mainly benefit the kidney and fill in essence, regulate qi and blood, and supplement them with strengthening the spleen and detoxifying the liver, dispelling dampness and resolving phlegm, etc. Through various special therapies such as herbal tonics as well as acupuncture and moxibustion, they can promote the sufficiency of kidney essence and kidney qi, the sufficiency of ”, the harmony of meridian and water, and the exuberance of Chongren and blood qi, so as to improve the function of the ovaries, guarantee the endometrium's tolerability, and assist in ovulation to improve the pregnancy rate. Tianjie is not only a substance with reproductive function, but also a material basis for normal ovulation. Based on the theory of Tianjie, adjusting the qi, blood, yin and yang of internal organs through traditional Chinese medicine can realize normal secretion of Tianjie, and the uterus will be full of fluid on time, which can broaden the idea of clinical treatment of kidney deficiency and blood stasis type ODI. It can broaden the idea for clinical treatment of ODI with kidney deficiency and blood stasis.

Acknowledgements

National famous old Chinese medicine expert Liu Maolin inheritance studio construction project (National TCM human education letter [2018] No. 134); Yulin Huo Liu's gynecology school inheritance work construction project (Shaanxi TCM letter [2018] No. 337); Yulin “young talent support program” project (20220473); Yulin famous Chinese medicine Liu Shiaomao studio (Yu zheng health and fitness issue [2024] No. 157).

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