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Modern Clinical Research on Acupuncture Treatment for Infertility

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Abstract: ***Infertility has become a significant global reproductive health issue, with its incidence rate showing an increasing trend with advancing age. Although modern medicine has made certain progress in treating etiological factors such as ovulation disorders, fallopian tube abnormalities, and endometriosis, challenges remain including suboptimal therapeutic outcomes in some patients, high treatment costs, and adverse drug reactions, necessitating the exploration of safe and effective alternative or complementary therapies. Acupuncture, as a traditional therapy with a millennia-long application history, demonstrates unique advantages in infertility treatment. This article systematically reviews the modern clinical research progress on acupuncture for infertility, summarizing clinical applications and efficacy evidence from various acupuncture modalities, including simple needling, electroacupuncture, warm needle therapy, moxibustion, and combined acupuncture with traditional Chinese or Western medicines. Modern studies indicate that acupuncture exerts therapeutic effects through multiple mechanisms, including modulation of hypothalamic-pituitary-ovarian axis function, improvement of sex hormone levels, enhancement of uterine and ovarian blood perfusion, optimization of endometrial receptivity, inhibition of granulosa cell apoptosis, and reduction of oxidative stress damage. Clinical studies further confirm that acupuncture, either used alone or in combination with drugs such as clomiphene citrate or gonadotropin-releasing hormone agonists, can effectively improve ovulation rates and pregnancy rates, enhance endometrial thickness and morphology, and exhibit favorable safety profiles. Despite limitations such as small sample sizes, insufficient mechanistic exploration, and non-unified operational standards, acupuncture has emerged as a crucial adjunctive therapy for infertility due to its safety, cost-effectiveness, and ease of administration, providing novel insights and directions for integrated traditional Chinese and Western medicine approaches in infertility treatment. Future research should further conduct high-quality, large-sample randomized controlled trials, combined with modern molecular biology techniques to thoroughly investigate its mechanisms of action, in order to provide more robust evidence-based support for the application and promotion of acupuncture in the field of reproductive medicine.***

Keywords: Acupuncture, Infertility, Electroacupuncture, Moxibustion, Assisted Reproduction, Endometrial receptivity, Hypothalamic-Pituitary-Ovarian axis**.**

1. Introduction

Infertility refers to the inability to conceive after 12 months of regular sexual intercourse. According to statistics, the prevalence of infertility is approximately 13% among women and 10% among men [1]. In women, the incidence of infertility increases with advancing age. A study revealed that 12% and 21% of women aged 32 and 38 years reported infertility, respectively [2]. The primary causes of female infertility include ovulation disorders, fallopian tube diseases, pelvic adhesions, endometriosis, and unexplained infertility. For women with infertility caused by ovulation disorders, interventions to improve conception rates include weight optimization and ovulation induction therapies. For patients with distal fallopian tube diseases, effective treatment measures include in vitro fertilization (IVF) or laparoscopic salpingectomy. For couples with unexplained infertility, effective treatment options include clomiphene combined with intrauterine insemination (IUI), gonadotropin combined with IUI, and IVF. Most infertile women can achieve pregnancy through fertility treatments [3].

Traditional Chinese medicine and other therapies may provide alternative approaches to improve fertility. Acupuncture-assisted conception, as an adjunctive treatment for in vitro fertilization, is gaining increasing recognition. Herbal medicine and dietary therapy have been used in China for centuries and can now be employed either alone or as adjunctive measures to Western medical methods. Traditional Chinese medicine diagnosis comprehensively evaluates overall health status, pulse diagnosis and tongue examination results, menstrual health conditions, including blood color, texture and flow, duration and frequency of menstruation, body temperature changes, and pain manifestations [4]. However, a significant proportion of infertility cases, such as certain ovulation disorders, endometriosis, and unexplained infertility, still show unsatisfactory outcomes with modern medical interventions, indicating substantial unmet clinical needs.

2. Modern Medical Mechanisms of Infertility

2.1 Pelvic Factors

2.1.1 Fallopian tube lesions

Approximately 30% of infertile women worldwide exhibit fallopian tube pathology. Regrettably, this cause of infertility has long been overlooked due to the availability of in vitro fertilization as a viable alternative. The anatomical structure of the fallopian tubes is highly complex, encompassing embryonic development initiation, vascular supply, and ciliary microstructure—all of which play critical roles in oocyte transport to the fertilization site. Numerous well-established etiologies of tubal infertility have been identified, including infections, intrauterine devices, endometriosis, and complications following abdominal surgeries. Although controversies persist regarding the pathogenesis of tubal infertility, advancements in molecular diagnostic techniques for infections have elucidated the

mechanisms by which infections induce tubal obstruction through endometriosis or ciliary motility disorders [5].

2.1.2 Uterine body lesions

Uterine fibroids, the most common uterine tumors in women of reproductive age, affect 20% to 50% of females. Although their association with infertility remains controversial, they continue to be a critical concern for clinicians and patients. During the early follicular stage, uterine contractions exhibit an increasing frequency from the fundus toward the cervix; however, during ovulation and the luteal phase, the contraction direction reverses from the cervix toward the fundus. Current studies indicate that uterine fibroids can impair the contractility of the myometrium and induce chronic inflammatory responses, both of which may potentially hinder embryo implantation [6].

2.1.3 Cervical factors

One of the most common issues associated with female infertility is cervical disease. As a critical component of the sperm passage, any structural or functional abnormalities in the cervix may lead to infertility. The most prevalent cervical conditions are cervical polyps and cervical stenosis. Polyps can be easily diagnosed through routine gynecological examinations and ultrasound imaging. Polyps can be removed via polypectomy, after which patients may achieve natural conception. For cervical stenosis, two treatment options are available: dilation and cervical dilation or intrauterine insemination (IUI). Dilation procedures are recommended for young patients without male factors in their partners. When a woman presents with both cervical stenosis and male factors, intrauterine insemination (IUI) is advised. Treatment outcomes for cervical-related conditions vary in success rates but generally demonstrate favorable efficacy [7].

2.1.4 Endometriosis

Endometriosis is characterized by the presence of endometrial glands and stroma outside the uterine cavity. It is estimated that 5% to 15% of women of reproductive age suffer from endometriosis. Dysmenorrhea, deep dyspareunia, chronic pelvic pain, abnormal uterine bleeding, intestinal disorders, and infertility are the primary symptoms of endometriosis. The prevalence of endometriosis is higher in women with chronic pelvic pain or infertility compared to those without these symptoms. Although the pathogenesis of endometriosis and its associated pain and infertility remains incompletely understood, therapeutic approaches targeting progesterone resistance and systemic immune dysfunction have been proposed, along with interventions addressing angiogenesis, inflammation, neurochemotaxis, and pain transmission [8]. Intrauterine adhesions (IUA) are one of the major reproductive system disorders affecting women globally. The fusion of damaged contralateral uterine walls can lead to partial or complete occlusion of the uterine cavity or cervical canal. The main clinical manifestations of IUA include menstrual irregularities, cyclical pain, and reproductive dysfunction. Compared to women without IUA, IUA patients still experience limited reproductive outcomes and suboptimal outcomes even after adhesiolysis. IUA interferes with sperm transport, causes endometrial vascular defects and reduced responsiveness, leading to decreased endometrial receptivity and thickness. Abnormal decidualization and trophoblastic infiltration result in abnormal placental attachment. Additionally, IUA increases the risk of preterm birth, intrauterine fetal growth restriction, and fetal malformations [9].

2.1.5 Abnormal development of reproductive organs

The fertility of patients with congenital uterine anomalies depends on the severity of the condition. Congenital uterine anomalies are primarily caused by embryonic developmental abnormalities of the paramesonephric duct and are associated with pregnancy complications, reduced fertility, and other adverse fetal outcomes. Congenital uterine anomalies may also coexist with other abnormalities, which can affect adjacent organs and lead to further complications. Congenital uterine malformations are linked to poor reproductive outcomes, with specific impacts varying depending on the type of malformation and the outcome being evaluated. Modern clinical understanding and advanced imaging technologies have enabled more precise identification of congenital uterine anomalies. As affected women approach reproductive age, the impact of these conditions on sexual function and fertility becomes increasingly prominent [10].

2.2 Ovulation Disorders

Ovulation disorders constitute a primary factor in the three-category classification of infertility by the World Health Organization (WHO). Category I ovulation disorders include gonadotropin deficiency caused by hypothalamic dysfunction, accounting for approximately 10% of all ovulation disorders. This category specifically encompasses hypogonadotropic hypogonadism, total hypopituitarism, autoimmune or infectious pituitary encephalitis, pituitary adenoma, and histiocytosis. Category II disorders involve dysfunction of the androgen-silence axis, which accounts for 85% of ovulation disorders caused by polycystic ovary syndrome (PCOS) and is associated with abnormal body mass index (BMI) and endocrine pathologies. Finally, Category III refers to ovarian insufficiency, previously termed ovarian failure, which significantly impacts oocyte depletion [10].

Ovulation disorders manifest as menstrual cycle irregularities and account for approximately 25% of infertility cases among couples struggling to conceive. Hyperprolactinemia and thyroid disorders are unequivocally associated with menstrual cycle disturbances and ovulation dysfunction, and to some extent, also linked to ovulatory infertility. However, given the relatively high natural conception rates observed during these pathological processes, these conditions have not yet been confirmed as direct causative factors of ovulatory infertility. Furthermore, compared to healthy individuals, women with infertility who concurrently exhibit hyperprolactinemia and thyroid disorders demonstrate more pronounced insulin resistance. It is well-established that insulin resistance may constitute a critical factor contributing to ovulatory infertility [11].

2.3 Senescence of Ovary Reproductive Function

With advancing age, ovarian follicles sensitive to FSH in

women aged 35–37 and older are progressively depleted, while aging follicles insensitive to FSH become relatively more abundant, leading to a reduction in the number and quality of oocytes.

3. Multiple Acupuncture-related Methods for Treating Infertility

3.1 Simple Acupuncture

Traditional acupuncture involves inserting needles into specific acupoints that have been locally sterilized, followed by manipulation techniques to enhance the sensation of needle penetration through the skin and to the target area [12]. The fundamental theory of acupuncture is based on the premise that the body contains energy flow patterns (qi), which are crucial for maintaining health. Disruptions in these energy flows are considered primary causes of disease. Acupuncture can correct imbalances of qi and blood at identifiable acupoints near the skin surface [13]. To amplify therapeutic effects, practitioners often employ auxiliary techniques such as repeated lifting, inserting, and rotating of needles. Manual manipulation of acupuncture needles effectively regulates activity in both peripheral and central nervous pathways. When needles are inserted into specific locations, meridian conduction facilitates systemic coordination and balance of qi and blood, thereby triggering a series of physiological and psychological responses [14].

Acupuncture can elevate serum estradiol (E2) and progesterone (P) levels while reducing the incidence of ovarian hyperstimulation syndrome. This demonstrates that acupuncture improves clinical pregnancy rates in in vitro fertilization-embryo transfer (IVF-ET) patients by modulating sex hormone levels and optimizing endometrial status. Additionally, acupuncture may mitigate the occurrence of ovarian hyperstimulation syndrome and alleviate patient anxiety to some extent [15]. The peripheral effects of acupuncture on improving uterine artery blood flow and endometrial thickness provide valuable data supporting its potential positive impact on embryo implantation. Given its non-toxic and relatively cost-effective characteristics, acupuncture can serve as an adjunctive therapy in assisted reproductive technology or as an alternative treatment for women with intolerance, non-compliance, or contraindications to conventional hormone-induced ovulation. Furthermore, substantial evidence highlights the clinical value of acupuncture, enabling its application in traditional medicine and the treatment of female infertility [16].

3.2 Electroacupuncture Therapy

According to the International Acupuncture Terminology proposed by the World Health Organization in 1991, the meridian system consists of 20 meridians interconnected by approximately 400 acupoints. These acupoints correspond to specific regions on the body surface, which exhibit higher conductivity due to dense gap junctions at cellular boundaries. These areas serve as focal points for electromagnetic fields. Elevated metabolic rates, temperatures, and calcium ion concentrations have also been observed at these sites. In principle, positive (anodal) pulse stimulation inhibits organ function, while negative (cathodal) pulse stimulation enhances it. This constitutes the foundation of electroacupuncture, where electrical needles are inserted into specific acupoints [17].

Studies have demonstrated that acupuncture shows promising clinical applications in the treatment of nausea and vomiting, postoperative pain, addiction, and various pain syndromes. Additionally, acupuncture is widely utilized for gynecological and obstetric disorders such as amenorrhea, pregnancy-related nausea and vomiting, and complications during childbirth. Electroacupuncture can normalize hypothalamic – pituitary - ovarian axis function by modulating the expression of specific genes in the brain. Acupuncture administered on the day of embryo transfer significantly improves pregnancy outcomes in infertile patients undergoing in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI). The mechanism may involve acupuncture-induced central β-endorphin release, which subsequently promotes gonadotropin-releasing hormone (GnRH) secretion. GnRH exerts positive regulatory effects on pituitary gonadotropin secretion, ovarian follicular development, and ovulation. Following a series of acupuncture treatments, the uterine arterial pulsatility index decreases, likely due to reduced activity of uterine sympathetic vasoconstrictor fibers and overall sympathetic nerve outflow inhibition mediated by central mechanisms. Electroacupuncture also contributes to reduced uterine arterial blood flow resistance [18].

Electroacupuncture can reduce follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels and increase estradiol (E2) levels in cyclophosphamide-induced premature ovarian failure (POF) rats by inhibiting the expression of p38MAPK protein in ovarian tissues. Simultaneously, electroacupuncture therapy can improve ovarian function and alleviate oxidative stress damage caused by declining ovarian reserve function (DOR) by suppressing the expression of microRNAs (miRNAs) such as bta-miR-7857-3p_R-1, mdo-miR-26b-5p_R+1_1ss10TC, and RNO-miR-92b-3p in ovarian tissues. Additionally, acupuncture intervention can target miR-21-3p via LncMEG3 to inhibit early and late apoptosis of ovarian granulosa cells in polycystic ovary syndrome (PCOS) rats. In a mouse model of premature ovarian failure, electroacupuncture can effectively suppress ovarian oxidative stress and Fe^{2+} accumulation by modulating gut microbiota composition, thereby increasing the number of mature follicles and improving sex hormone levels [19].

3.3 Warm Needle Acupuncture

As a traditional therapeutic approach, warm needle acupuncture emphasizes holistic concepts and individualized treatment principles, focusing on eliminating the root causes of infertility and creating an ideal internal environment for conception. This constitutes a key characteristic of Traditional Chinese Medicine (TCM) in treating infertility. Acupuncture or electroacupuncture stimulation applied to lower abdominal acupoints can enhance blood perfusion to the uterus and ovaries. Adequate blood supply helps improve oocyte quality and endometrial receptivity, facilitating sperm-egg union and embryo implantation, thereby increasing pregnancy rates. Additionally, acupuncture at spleen meridian and stomach meridian acupoints can strengthen the digestive functions of the spleen and stomach. As the source of qi and blood

production, a healthy spleen and stomach nourish the uterus, not only improving pregnancy rates but also providing novel therapeutic strategies for TCM and integrated Chinese-Western medicine approaches in infertility treatment and assisted reproductive technology [20].

3.4 Moxibustion Therapy

Moxibustion, as a therapeutic modality of acupuncture, refers to the application of burning or fumigation using ignited moxa wool or moxa sticks to corresponding acupoints, achieving disease prevention and treatment effects through the combined action of thermal and pharmacological forces. Traditional Chinese Medicine (TCM) theory posits that moxibustion possesses the effects of warming and unblocking meridians, harmonizing qi and blood, dispelling cold and relieving pain, preventing and treating diseases, and enhancing physical constitution. It is commonly employed for gynecological conditions such as infertility, dysmenorrhea, and metrorrhagia caused by cold-induced uterine stagnation [21].

Modern medical research indicates that moxibustion can improve ovarian function by inhibiting apoptosis events in naturally aging ovaries and enhancing antioxidant defense capabilities. Improving ovarian arterial blood supply and increasing diastolic blood perfusion can significantly increase ovulation rates and pregnancy rates [22]. Additionally, moxibustion reduces the expression of p-PI3K, p-Akt, and p-mTOR in rat ovaries. Moxibustion has been widely used to treat female infertility caused by polycystic ovary syndrome (PCOS), premature ovarian failure, and fallopian tube obstruction. Moxibustion may improve ovarian hormone levels and inflammatory responses by inhibiting the PI3K/Akt/mTOR signaling pathway [23]. Thunderfire moxibustion combined with ovulation monitoring demonstrates definitive efficacy for infertility associated with adenomyosis (AM). This method can increase pregnancy rates in AM patients and alleviate dysmenorrhea and related Traditional Chinese Medicine (TCM) syndromes. During application, thunderfire moxibustion is performed at acupoints such as Guanyuan and Qihai, which exerts warming and therapeutic effects through meridian and neural heat conduction. This generates thermal stimulation that inhibits uterine smooth muscle and vascular contraction, improves local microcirculation, thereby alleviating AM-related symptoms and enhancing pregnancy rates. Thunderfire moxibustion combined with ovulation monitoring is an effective treatment strategy for AM-associated infertility, and its underlying mechanisms warrant further in-depth research [24].

3.5 Acupuncture Combined with Traditional Chinese Medicine Therapy

The combined therapy of acupuncture, herbal medicine, and clomiphene citrate effectively improves daily cervical mucus HCG levels, endometrial thickness, and morphology, thereby enhancing pregnancy rates and reducing early miscarriage rates. Its therapeutic efficacy is significantly superior to simple medications containing clomiphene and the combined application of acupuncture with herbal medicine [24]. Studies indicate that compared to conventional Western medicine alone, the integrated use of Traditional Chinese Medicine (TCM) and acupuncture can markedly improve clinical outcomes, elevate sex hormone levels, increase ovulation and pregnancy rates, enhance maximum follicular diameter (MFD) and endometrial thickness, alleviate patient symptoms, and ultimately boost conception success rates. In terms of safety, the adverse reaction incidence in the combined treatment group was significantly lower than that in the control group. In summary, acupuncture combined with Chinese herbal medicine represents a potentially effective approach for treating ovulation disorder-related infertility. This regimen not only improves therapeutic efficacy, pregnancy rates, ovulation rates, and endometrial thickness but also optimizes sex hormone levels and enhances follicular development quality, creating a favorable internal environment for conception [25].

3.6 Acupuncture Combined with Western Medicine

Studies have shown that acupuncture combined with letrozole may be more effective than letrozole alone in the treatment of polycystic ovary syndrome (PCOS) [26]. Electroacupuncture combined with clomiphene intervention can effectively promote ovulation and pregnancy in PCOS patients, significantly increase serum estradiol (E2) and progesterone (P) levels, enhance endometrial thickness and the incidence of type A endometrium. Its therapeutic efficacy is markedly superior to that of clomiphene monotherapy, with good safety profile and mild, tolerable adverse reactions. The mechanism of action of this combined intervention may be closely related to the improvement of estrogen and progesterone levels as well as endometrial receptivity [27]. The combined use of acupuncture and gonadotropin-releasing hormone agonists can improve endometrial receptivity in patients with recurrent implantation failure or those undergoing in vitro fertilization-embryo transfer, thereby enhancing clinical pregnancy rates and improving pregnancy outcomes [28].

4. Summary

In summary, acupuncture, as a traditional therapy with thousands of years of application history, has a broad clinical basis and its therapeutic efficacy has been supported by extensive research evidence. Traditional acupuncture primarily involves inserting fine needles into specific acupoints after local disinfection, followed by manipulation techniques such as lifting, plucking, and twisting to stimulate “Qi acquisition” induction, thereby achieving therapeutic goals. With advancements in science and technology, a series of modified therapies have been developed to enhance acupuncture’s clinical effects and prolong its duration of action, including electroacupuncture, acupoint embedding, and transcutaneous electrical stimulation [29-31].

Modern studies indicate that acupuncture can influence the secretion of gonadotropin-releasing hormone and menstrual cycles, as well as improve uterine blood flow. Previous systematic reviews have demonstrated that acupuncture can reduce the rate of miscarriage, while other studies suggest its potential to enhance reproductive outcomes and mental health in both men and women. Due to a series of adverse events, unexplained recurrent implantation failures, or the high costs of assisted reproductive technologies, more patients prefer

acupuncture as a conservative treatment option [32]. As a safe, cost-effective, and easily administered alternative or complementary therapy, acupuncture not only addresses the limitations of modern medicine in treating certain infertility cases but also provides new insights and directions for integrated traditional Chinese and Western medicine approaches to infertility management. Current clinical observations suggest that acupuncture may positively affect menstrual status and stress regulation in women preparing for pregnancy. Experimental evidence indicates that acupuncture can modulate female reproductive function, though its underlying mechanisms remain to be elucidated. As a composite intervention, the research design and outcome evaluation of acupuncture must balance its complexity with generalizability; a clinical efficacy-oriented research approach may offer viable pathways for addressing such challenges. Future studies should build upon the rich practical experience of acupuncture while incorporating rigorous evidence-based medical methodologies. Current research still faces limitations, including small sample sizes, insufficient mechanistic exploration, and lack of standardized clinical protocols. The next step requires focused efforts to advance high-quality, large-sample randomized controlled trials, combined with modern molecular biology techniques to thoroughly elucidate the biological basis of acupuncture, and to continuously optimize clinical treatment protocols. This aims to provide more robust evidence-based support for the promotion of acupuncture in the field of reproductive medicine [33].

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