Acupuncture Enhances Fertility Treatment, Lowers Adverse Effects

Published by HealthCMI on 08 January 2018.

Acupuncture boosts the efficaciousness of fertility treatments. Three independent studies confirm that acupuncture increases positive patient outcome rates. Two studies find acupuncture effective for increasing the efficacy of clomifene for the treatment of infertility due to ovulatory dysfunction. Another study finds acupuncture effective for reducing the adverse effects caused by bromocriptine treatments for hyperprolactinemia related infertility. The study also confirms that acupuncture balances hormone levels.

**Ovulatory Dysfunction**

Ovulatory dysfunction accounts for approximately 25–30% of female infertility. The root of ovulatory dysfunction is related to disorders of the hypothalamic–pituitary–gonadal axis (HPG axis) because it is closely related to the uterine and ovarian roles in menstruation cycles. The hypothalamus secretes gonadotropin-releasing hormone (GnRH). GnRH stimulates the anterior pituitary to produce two important hormones essential for folliculogenesis and ovulation: luteinizing hormone (LH) and follicle-stimulating hormone (FSH). As a result, dysfunction of the HPG axis may lead to problems in proper follicle development, maturation, and rupture.

Treatment for this type of infertility includes ovulation inducing drugs, surgical intervention, and assisted reproductive technology (ART) including artificial insemination, in-vitro fertilization, etc. Clomifene is often a prescribed drug for ovulation induction, and while it has a high efficacy rate, it also has common adverse effects. It may deleteriously affect cervical mucus or decrease the amount produced. Vaginal dryness due to thicker cervical mucus is a common adverse effect, which impedes sperm transport and is ultimately counterproductive to the drug’s other properties that promote fertility. Anti-estrogenic actions of clomifene reduce uterine vascularization, eventually lowering endometrial receptivity. Therefore, though clomifene helps patients to ovulate, it may not be entirely conducive to the goal of conceiving. It is therefore beneficial to use other treatments with fertility boosting value to complement clomifene ovulation induction.

**Hyperprolactinemia**

Hyperprolactinemia (HPL) is characterized by elevated serum prolactin. The occurrence of HPL in females with reproductive disorders falls between 9% and 17%. Infertility from HPL arises from the
inhibitory effect of prolactin on GnRH secretion. Some HPL patients, despite having elevated serum prolactin, do not show signs of pituitary or central nervous system diseases, nor any other identifiable causes of increased prolactin secretion. In these cases, we term this condition idiopathic hyperprolactinemia (IH).

Bromocriptine is a medication option for IH treatment because it normalizes serum prolactin levels. However, the drug comes with a downside. According to research, approximately 12% of IH patients choose to discontinue bromocriptine intake due to adverse effects such as dizziness, nausea, hallucinations, and uncontrollable movements. It is important for treatments to be tolerable. An effective treatment cannot realize its full potential if patients are unable to comply with treatment regimens. The research reveals that acupuncture is well-suited as a complementary therapy to prevent or attenuate bromocriptine adverse effects.

**TCM**

According to Traditional Chinese Medicine (TCM) principles, hyperprolactinemia is a condition arising from spleen and kidney deficiency, liver qi stagnation, excess dampness, and imbalances in the Chong and Ren channels. Acupoints Qihai (CV6), Guanyuan (CV4), and Zusanli (ST36) are included in primary acupuncture point protocols because they are useful for nourishing the female reproductive system and correcting the aforementioned constitutional imbalances. Qihai and Guanyuan are particularly useful for correcting Ren channel related deficiencies and Zusanli is administered to tonify qi and promote blood circulation. Together, these acupuncture points fortify yuan qi.

**Ovulatory Dysfunction Study #1**

The first study was conducted by researchers Zhong Weihua and Chen Qiuping. Their research finds that acupuncture effectively raises hormone levels and benefits endometrial thickness among ovulatory dysfunction patients taking pharmaceutical drugs. The 2-month clinical trial compared two patient groups, both receiving clomifene and one receiving acupuncture additionally. The results demonstrate that acupuncture creates a more fertile environment for successful conception.

Two indicators were used to evaluate clinical efficacy: hormone levels and endometrial thickness. Before and after treatment, 3 mL of peripheral blood was taken from each patient. Estrogen (E2), FSH, and LH levels were measured via enzyme-linked immunosorbent assay (ELISA). Sonography was used to measure endometrial thickness. In addition to ELISA and sonography, the overall treatment efficacy was also surveyed. With reference to “Guidelines for the Clinical Study of New Drugs of Traditional Chinese Medicine,” the treatment efficacy for each patient was categorized into 1 of 3 tiers:

- **Clinical recovery**: Successful conception.
- **Effective**: Ovulation detected via ultrasound. Basal body temperature (BBT) showed bi-directional trend. Periodical change detected via exfoliative vaginal cytology. No successful conception.
- **Not effective**: No ovulation detected after treatment for 3 menstrual cycles.

The clomifene plus acupuncture group achieved a treatment effective rate of 92.11%. The group receiving only clomifene had a 68.42% rate. The treatment effective rate for each group was derived using the following formula:

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\text{Treatment effective rate} = \frac{\text{Clinical recovery} + \text{Effective}}{\text{Total number of patients in group}} \times 100\%
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The data demonstrates that patients receiving acupuncture in addition to clomiphene have significantly higher positive patient outcome rates. The group receiving acupuncture and clomiphene had a boost in hormone levels:
• E2 (ng/L) was 317.34 ±24.83 before treatment and 418.34 ±27.56 after treatment. For the group receiving only clomifene, E2 was 319.83 ±24.46 before and 367.45 ±25.34 after.
• Interesting numbers for FSH (IU/L) were documented. The acupuncture plus clomiphene group was 7.98 ±1.54 before and 23.42 ±2.75 after. The clomiphene only group was 8.04 ±1.50 before and 15.78 ±1.93 after.
• LH (IU/L) for the clomiphene plus acupuncture group was 13.47 ±1.46 before and 54.84 ±4.50 after. The group receiving only clomifene was 13.42 ±1.50 before and 29.75 ±2.04 after.

The post-treatment levels for clomifene plus acupuncture were all markedly higher than that of standalone clomifene. The difference in post-treatment results indicates that acupuncture promotes the production of E2, FSH, and LH, making the uterine environment more conducive for healthy folliculogenesis and ovulation.

Endometrial thickness results document a similar trend. Before treatment, the mean endometrial thickness for both groups were equivalent, at 6.34 ±0.48 mm for clomifene plus acupuncture and 6.39 ±0.45 mm for clomifene only. After treatment, the results increased to 8.12 ±0.32 mm for clomifene plus acupuncture and 7.31 ±0.37 mm for clomifene only. Both treatments were effective when compared to pre-treatment results, but clomifene plus acupuncture produced greater endometrial thickness than clomifene. The results demonstrate that acupuncture is valuable in maintaining healthy folliculogenesis, ovulation, and endometrial receptivity, which are essential aspects of successful conception.

The study was set up as a comparative clinical trial as described henceforth. A total of 76 patients with ovulatory dysfunction infertility participated in the study. They were diagnosed between September 2014 and September 2016. The following selection criteria were applied in choosing trial participants:

• 18 – 40 years of age and aiming to conceive.
• Male partner had healthy reproductive function.
• Signed informed consent.

The following exclusion criteria were applied:

• Congenital anomalies in reproductive organs.
• Ovulatory dysfunction due to sexual physiological defects.
• Uterine leiomyomas (fibroids) or endometriosis.
• Recently took steroids.
• Premature ovarian failure.
• Severe liver, cardiac, renal, or hematopoietic diseases.

Patients were randomly divided into two groups of 38: treatment and control. Both groups were comprised of equivalent demographics. The treatment group ranged between 23 – 37 years of age, (mean age 30.84 ±1.64), duration of infertility 2 – 12 years (mean duration 7.30 ±1.27 years). The control group ranged between 22 – 39 years (mean age 31.02 ±1.56 years), duration of infertility 2 – 13 years (mean duration 7.23 ±1.31 years). Both groups received drug treatment with clomifene. In addition, the treatment group received acupuncture. Treatment was administered for 2 menstrual cycles. The following primary acupoints were treated for the treatment group:

• Guanyuan (CV4)
• Sanyinjiao (SP6)
• Zhongji (CV3)
• Zigong (extra)
• Zusanli (ST36)
• Taichong (LV3)
Stainless steel filiform acupuncture needles were used to administer acupuncture. For abdominal acupoints, the needles were diagonally inserted facing downwards. After achieving deqi, needles were retained for 30 minutes. Moxibustion was applied to Shenque (CV8) and Sanyinjiao (SP6). Treatment commenced from the 5th day of menstruation, at a rate of once per day. For drug treatment, clomifene was orally administered starting from the 5th day of menstruation. The prescribed dosage was 50 mg each time, once per day, for 5 consecutive days. The addition of acupuncture to clomiphene treatments increased the total effective rate by 23.69%.

**Henan Zhengzhou Huashan Hospital**

The second study was conducted by Sheng et al. from Henan Zhengzhou Huashan Hospital. The team finds that acupuncture increases the conception rate in patients with ovulatory dysfunction. The 5-month clinical trial compared two patient groups, both groups receiving ovulation induction treatment with drugs and one group receiving additional acupuncture treatment. The results show that acupuncture increases fertility rates.

Ovulation and conception rates were used to evaluate clinical efficacy. The rates represented the percentage of patients in each group that successfully achieved ovulation and conception. Ovulation was monitored by ultrasonography. Starting from the 9th day of menstruation, ovarian development was observed via ultrasound and LH tests. Ovulation was confirmed upon detection of ≥18 mm follicles, follicle rupture, and a ≥20 mIU/mL increase in LH levels. The definitive standards for conception were:

- 50 consecutive days without menstruation.
- Subsequent detection of gestational sac via ultrasound.
- Subsequent positive human chorionic gonadotropin (hCG) urine test.
- Subsequent detection of fetal heartbeat.

The data shows that the drugs and acupuncture group achieved an ovulation rate of 67.8% and a conception rate of 52.5%. The drugs only group achieved an ovulation rate of 51.9% and a conception rate of 30.4%. Though the ovulation rate did not differ significantly between both patient groups, the conception rate was much higher for the drugs plus acupuncture group. The data shows that acupuncture effectively creates a healthier internal environment and increases the chances of conception.

The study was set up as a comparative clinical trial as detailed hereafter. A total of 138 patients from the infertility division of Henan Zhengzhou Huashan Hospital, diagnosed with ovulatory dysfunction infertility, participated in the study. The diagnostic criteria for patients were in accordance with “TCM New Medicine Clinical Research Guidelines: 1st Edition” and “Integrative Medicine Diagnosis and Treatment Guidelines for Endometriosis, Gestational Hypertension and Female Infertility,” listed below:

- Menstrual cycle >35 days or <21 days.
- Continuous ultrasonography throughout ≥1 menstrual cycle showing slow follicle growth, absence of dominant follicles, premature follicle shrinkage or termination, no follicle rupture, and abnormally thin endometrium.

For the diagnosed patients, the following selection criteria were applied in choosing trial participants:

- No follicle ruptures.
- No severe complications.
- No response after 2 – 3 cycles of clomifene treatment.

The selected patients were randomly divided into 2 groups: treatment and control. Both groups had equivalent demographics. The treatment group with 59 patients were aged between 20 – 38 years (mean
age 25.00 ±2.37 years), duration of infertility was 2 – 4.5 years (mean duration of fertility 3.00 ±1.37 years). The control group with 79 patients were aged between 19 – 37 years (mean age 25.00 ±2.07 years), duration of infertility was 2 – 4 years (mean duration of fertility 3.00 ±1.09 years).

Both groups received ovulation induction treatment with the pharmaceutical drugs clomifene, menotropins, and hCG (human chorionic gonadotropin). In addition, the treatment group received acupuncture. Both groups received treatment for 3–5 months. All patients were monitored by ultrasound and were advised to have intercourse during ovulation. The following primary acupoints were used:

- Zhongji (CV3)
- Guanyuan (CV4)
- Zigong
- Zusanli (ST36)
- Neiguan (PC6)
- Sanyinjiao (SP6)

Treatment consisted of conventional acupuncture, electroacupuncture, and indirect moxibustion. Hwato brand acupuncture needles (Suzhou Medical Appliances Factory Co., Ltd.) were used. An SDZ-II model electroacupuncture device (Suzhou Medical Appliances Factory Co., Ltd.) was used for electroacupuncture. 10 mm x 200 mm moxa cigars (Nanyang Wolong Hanyi Moxa Factory Co., Ltd.) and single-vent bamboo moxa boxes (Guangzhou Shangguan Beauty Supplies Factory Co., Ltd.) were used for indirect moxibustion.

Conventional acupuncture was applied to Zhongji, Guanyuan, Zusanli, and Neiguan. Electroacupuncture was administered to Zigong and Sanyinjiao. Both acupoints were stimulated until deqi was achieved. Next, the electroacupuncture device was connected to the needles and set to a low continuous frequency (2 Hz) for 30 – 45 minutes. Shenque (CV8) was treated with indirect moxibustion. A lit moxa cigar was inserted, lit side down, into a moxa box. After ensuring that the temperature was warm but not too hot, the moxa box was placed over Shenque and left for 30 – 45 minutes. One treatment cycle was administered per menstrual cycle. A treatment cycle started on the 9th day of menstruation and was comprised of 7 – 10 consecutive treatment days, one session per day.

For both groups, the following protocol was observed for ovulation induction treatment with pharmaceutical drugs. Starting from the 3rd day of menstruation, clomifene citrate capsules (GKH Pharmaceutical Ltd.) were given orally. The prescribed dosage was 50 mg each time, twice per day, for 5 consecutive days. Starting from the 5th day of menstruation, injectable menotropins (Ningbo Renjian Pharmaceutical Group Co., Ltd.) was administered via intramuscular injection. The prescribed dosage was 75 U each time, once per day, for 7 consecutive days. In the event that no ovulation was detected after treatment with 75 U for 2 menstrual cycles, the dosage was increased to 150 U each time. Starting from the 9th day of menstruation, when sonography showed ≥18 mm average follicle diameter, one shot of hCG (Ningbo Renjian Pharmaceutical Group Co., Ltd.) was administered via intramuscular injection. The prescribed dosage was 5000 – 10000 U.

Drugs plus acupuncture achieved an ovulation rate of 67.8% and a conception rate of 52.5%. Drugs without acupuncture achieved an ovulation rate of 51.9% and a conception rate of 30.4%. The data indicates that acupuncture optimizes positive patient outcome rates.

Mawangdui Hospital
The third study was conducted by Hu et al. from Mawangdui Hospital of Hunan. The research finds that adding acupuncture reduces infertility drug adverse effects and improves hormone level regulation in women with idiopathic hyperprolactinemia (IH) infertility. Patients receiving only bromocriptine were compared with patients receiving both bromocriptine and acupuncture in this 1-year clinical trial. The
results highlighted the importance of acupuncture in supporting bromocriptine treatment by reducing adverse effects and balancing hormones.

Referring to the guidelines by the Obstetrics and Gynecology Committee of the World Federation of Chinese Medicine Societies, the study evaluated treatment efficacy by considering hormone normalization time, adverse effects, and conception rates. Before and throughout treatment, hormone levels of prolactin, E2, progesterone (P4), and FSH were measured. The time taken for hormone levels to adjust to normal levels was recorded. The number of patients that did or did not experience adverse effects was also recorded. Finally, the conception rate was recorded. The conception rate for each group was defined as the percentage of patients that successfully conceived within 6 months after the start of treatment.

Similar results were recorded for the acupuncture plus bromocriptine and bromocriptine only groups for some parameters. Both groups took 2 – 3 menstrual cycles for prolactin levels to be normalized. For the bromocriptine group, the longest normalization time was 3 menstrual cycles and the shortest normalization time was 2 menstrual cycles. For the bromocriptine with acupuncture group, the normalization time was 2 menstrual cycles for all. The conception rates varied, acupuncture plus bromocriptine had a 43.3% conception rate and standalone bromocriptine produced a 20.0% rate.

The bromocriptine group had 19 patients who experienced adverse effects during treatment while the bromocriptine with acupuncture group had 7 patients that experienced adverse effects during treatment. The data shows that acupuncture effectively alleviates the adverse effects caused by bromocriptine intake. Considering that many patients discontinue bromocriptine due to adverse effects, acupuncture may be helpful to improve long-term compliance.

The time for hormones E2, P4, and FSH to reach normal levels differed (P < 0.05) between both groups. For the bromocriptine group, the longest normalization time was 6 menstrual cycles and the shortest normalization time was 3 menstrual cycles. For the bromocriptine with acupuncture group, the longest normalization time was 4 menstrual cycles and the shortest normalization time was 2 menstrual cycles. Here, the study shows that acupuncture is advantageous in creating hormonal balance.

The study was designed as a comparative clinical trial as detailed hereafter. A total of 60 IH patients from the gynecological division of Mawangdui Hospital (Hunan) participated in the trial. All 60 patients were recorded in the final results since none were disqualified for failure to complete treatment, failure to follow treatment protocols, adverse effects, or severe complications. The diagnostic criteria for patients were in accordance with the 7th edition of “Gynecology,” by People Health Publishing House and “TCM Gynecology,” listed below:

- Normal sex life.
- No conception for ≥ 2 years without contraception.
- Irregular periods, galactorrhea, amenorrhea or pre-menstrual mastalgia.
- Easily agitated, weakness and soreness in waist/knees, constant thirst, red tongue with thin coating, thin and taut pulse.
- Serum prolactin concentration 40 ng/mL.

For the diagnosed patients, the following selection criteria were applied in choosing trial participants:

- 26 – 33 years of age.
- Male partner with healthy sperm quality.
- The following exclusion criteria were applied:
  - Pregnant or lactating.
  - Taking medication which influences serum prolactin.
  - Pituitary tumors.
• Hyperthyroidism, hypothyroidism, or kidney dysfunction.
• Congenital reproductive anomalies.

Patients were randomly separated into 2 groups of 30: treatment and control. Both groups were equivalent in age, duration of illness, serum prolactin levels, and other hormone levels (E2, P4, FSH). The treatment group had a mean age of 28.77 ±1.74 years, mean duration of illness 4 years, and 24 patients with abnormal hormone levels. The control group had a mean age of 28.47 ±1.72 years, mean duration of illness 4 years, and 20 patients with abnormal hormone levels. Both groups received drug treatment and the treatment group received acupuncture treatment. The treatment period was 1 year. Patients also complied with a 1-year long follow-up after treatment ended. The following primary acupoints were applied to the acupuncture treatment group:

- Qihai (CV6)
- Guanyuan (CV4)
- Zusanli (ST36)
- Sanyinjiao (SP6)
- Taichong (LV3)
- Taixi (KD3)
- Ligou (LV5)

Hwato brand 0.30 x 40 mm acupuncture needles were used. Qihai, Guanyuan, Taixi, and Zusanli were applied with reinforcing needle manipulation techniques. Taichong and Ligou were applied with attenuating techniques. Needles were retained for 30 minutes. One treatment cycle was conducted per one menstrual cycle. A treatment cycle started on the 8th day of menstruation and was comprised of 10 consecutive treatment days, one session per day.

For drug treatment, bromocriptine was administered. Patients were initially prescribed 1.25 mg each time, twice per day, after meals. After the first 7 days, the prescribed dosage was increased to 2.5 mg each time, twice per day, after meals. BBT (basal body temperature) was monitored throughout treatment. If there was no bidirectional trend in BBT after 3 months of treatment, clomifene was prescribed, in ovulation induction dosages. The data indicates that acupuncture reduces infertility drug adverse effect rates and improves hormone level regulation in women with idiopathic hyperprolactinemia (IH) related infertility.

Summary
Acupuncture is a proven complementary therapy for women receiving drug therapy for the treatment of infertility. Acupuncture increases positive patient outcome rates and reduces the adverse effects caused by medications. Patients interested in learning more about acupuncture and herbal medicine for the treatment of infertility are advised to consult with local licensed acupuncturists.
References