SOUTH BAYLO UNIVERSITY

The Effectiveness of Acupuncture and Herbal Medicine Combined Treatment for Female Infertility with Polycystic Ovary Syndrome: A Narrative Review

by

Zhengjie (Jane) Zhou

A RESEARCH PROJECT SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE

Doctor of Acupuncture and Oriental Medicine

December 2022

DISSERTATION OF ZHENGJIE ZHOU APPROVED BY RESEARCH COMMITTEE

Won Foo Din

Won Z. Shin, DAOM, L.Ac.

malle

Hanok Lee, DAOM, L.Ac.



Shan Qin Cui, OMD, L.Ac.

Anne Ahn, OMD, L.Ac.

Joseph H. Suh, Ph.D, OMD, L.Ac.

South Baylo University Los Angeles, California December 31, 2022 Copyright

by

Zhengjie (Jane) Zhou

The Effectiveness of Acupuncture and Herbal Medicine for Female Infertility with Polycystic Ovary Syndrome: A Narrative Review

South Baylo University

Research Advisor: Junfeng Xi, OMD, L.Ac.

ABSTRACT

The prevalence of Polycystic Ovary Syndrome (PCOS)-induced infertility in the US has been increasing in recent years. Medication, such as Clomiphene Citrate (CC) and Letrozole (LE), is the main treatment method for restoring fertility for women at reproductive age. Acupuncture and herbal medicine treatments have been used in China and received remarkable results for infertility due to PCOS over decades. There are sufficient studies demonstrating either acupuncture or herbal medicine improves female fertility due to PCOS. However, there is insufficient systemic research that examines the efficacy of acupuncture in combination with herbs for infertility due to PCOS. A narrative review in this field is needed. This article reviews protocols of 30 related research of combining acupuncture and herbal medicine in treating PCOS-induced infertility. By analyzing the synergic effects of the combined method, it concludes that the combined treatment receives better results in having a higher ovulation rate, increasing the chance of pregnancy, and relieving PCOS symptoms significantly, compared to the conventional western medical method. The details of acupuncture points selections and herbal ingredients are also summarized in this paper. Hence, it is promising for Eastern medicine practitioners in the U.S. to apply on a larger scale to help more women and families to have babies.

i

TABLE OF CONTENTS

ABSTRACT

I.	INTRODUCTION	1
	OBJECTIVES	3
	LITERATURE REVIEW	4
II.	MATERIALS AND METHODS	6
III.	RESULTS	8
IV.	DISCUSSION	11
V.	CONCLUSION	22

REFERENCES

LIST	OF	TABI	LES
	·		

Table 1. Comparison of Ovulation Rate, Pregnancy Rate, LH, FSH between Control Group and Acupuncture+ Herb Intervention I	9
Table 2. Comparison of Ovulation Rate, Pregnancy Rate, LH, and FSH between Control Group and Acupuncture+ Herb Intervention II	10
Table 3. The Most Chosen Acupuncture Points	12
Table 4. The List of Herbal Formula Ingredients	14
Table 5. Property of the Top 17 Herbs	16

Table 6. Top 17 Herbs Entered Meridian

LIST OF FIGURES

Figure 1. The Flow Chart of Research Articles Selection	7
Figure 2. The Occurrence of Acupuncture Point Selection among 18 Protocols	11
Figure 3. Top 17 Repeated Herbs	15
Figure 4. Analysis of the Top 17 Herbs' Properties	16
Figure 5. Analysis of the Top 17 Herbs Entered Meridians	17

I. INTRODUCTION

Female infertility is common in the United States. The CDC defines an individual's inability to conceive and become pregnant after one or more years of unprotected sex (Centers for Disease Control and Prevention, 2019). Around 6% of married American women, ages 15 through 44, have been affected by this ailment (Centers for Disease Control and Prevention, 2019). Among female reproductive disorders, Polycystic Ovulatory Syndrome (PCOS) is a leading cause of infertility in the US. PCOS affects anywhere between 6% and 12% of the women of reproductive age in the US (Centers for Disease Control and Prevention, 2019) and is the cause of up to 75% of the anovulatory type of infertility.

The main symptoms of infertility caused by PCOS are amenorrhea, irregular menstruation, and anovulation. A regulated and healthy ovulation schedule is the key for PCOS patients to conceive. An increased Gonadotropin-releasing hormone has been observed in infertility patients with PCOS. The endocrine abnormality causes the excessive secretion of luteinizing hormone (LH) compared to follicle-stimulation hormone (FSH). A high LH level disturbs the development of the follicle.

Moreover, the higher level of LH also leads to hypersecretion of testosterone. The increasing testosterone further impairs follicular development, which causes ovulation disorders and reduces the possibility of pregnancy. Usually, the ratio between LH and FSH lies between 1 and 2 in healthy women. For women with PCOS, the LH/ FSH ratio can reach 3 (Saadia, 2020). Testosterone level for PCOS patients ranges from 70-150 ng/dL. Therefore, maintaining a stable

LH/FSH ratio and testosterone level is crucial to help PCOS patients restore ovulation and get pregnant successfully.

Conventional western treatment highly relies on medication to restore ovulation for conceiving. For infertile PCOS patients, regulating menstruation and inducing ovulation are the key to restoring fertility. Oral contraceptive pills are commonly used for decreasing LH and antiandrogen. The androgens are a group of sex hormones that testosterone is the primary hormone in the group. Clomiphene Citrate (CC) is the most common medication for regulating menstruation and restoring ovulation, which aims to increase the possibility of pregnancy. However, these medications may have undesirable side effects on both the patient and their children. The adverse effects may include abnormal vaginal bleeding, disturbed gut flora, hypertensive disorders, perinatal mortality, and congenital abnormality (Lee et al., 2021). Studies also show the usage of CC thins the lining of the uterus, which decreases the chance of embryos staying. (Wu et al., 2020) Therefore, the Eastern medicine combining treatment will be a valuable method for practitioners to help the community of infertility women caused by PCOS.

OBJECTIVES

This paper is to study the effectiveness of acupuncture and herbal medicine combined treatment for female infertility with Polycystic Ovary Syndrome (PCOS) as a Narrative Review.

The detailed objects for this study are as follows.

- To analyze qualified RCTs protocols that combine acupuncture and herbal medicine for PCOS-induced infertility.
- To compare the differences in pregnancy rate, ovulation rate, and LH/FSH ratio between Western medical treatment and the combined Eastern treatment among the qualified RCTs, for seeking the method receive higher successful rate.
- Discuss the synergy of combining acupuncture and herbal medicine in treating infertility due to PCOS.

LITERATURE REVIEW

Studies show that the combined treatment of acupuncture and herbal medicine are beneficial to females with PCOS in terms of increasing pregnancy and ovulation rates, regulating menstruation, and even weight loss. Among the studies, most of them have the premise of using Western medications as a primary treatment. On top of Western medication, acupuncture, and herbal medicine work as adjunctive interventions to treat patients. According to Yan, an RCT with 120 samples divided into three groups, with all applying Letrozole, the 3rd group with Letrozole, herbal formula, and electroacupuncture received the highest pregnancy and ovulation rates. The combined treatment with Letrozole remarkably improves the menstrual cycle, and decreases the level of LH/FSH ratio, as well as Body Mass Index. (Yin et al, 2018) Another RCT conducted by Yu in China also shows that on the precondition of taking Clomiphene, the therapeutic effects of the combined intervention are remarkably better than those of the simple application of Clomiphene (Yu, et al. 2018). Even though Western medication is a precondition, Eastern medicine combined modalities receive higher efficacy on helping PCOS patients to conceive. This indicates the combined treatment is effective in improving infertility on PCOS patients.

Acupuncture and herbal medicine are safe methods for increasing the chance of getting pregnant among PCOS patients. A systematic review investigates the efficacy of acupuncture or herbal medicine in receiving a higher successful pregnancy rate. On the one hand, this systematic reviewed two systematic reviews and meta-analyses to see the efficacy of herbal medicine for infertile women with PCOS. The control group is using clomiphene, while the intervention group applies the exact dosage of Clomiphene as the control group and herbal medicine. The

combination of herbal medicine and Clomiphene has significant improvement in pregnancy rate. Moreover, herbal medicine also assists women who are undergoing In Vitro Fertilization (IVF) in receiving higher pregnancy rate.

On the other hand, thirteen meta-analyses have been reviewed to see acupuncture's efficacy for infertile women with PCOS. Although there are contradictory results among all analyses, major of the studies support that acupuncture has significant effects on improving PCOS-induced infertility. There are no adverse or harmful events reported among all the systematic reviews and meta-analyses. Hence, acupuncture and herbal medicine are safe for infertile PCOS women and help them increase the possibility of pregnancy.

Many studies show the combined treatment of acupuncture and herbal medicine is beneficial to infertile women and infertility caused by PCOS. It will be valuable to dig deep into the protocols of combining acupuncture and herbal medicine modality, passing the protocol on to practitioners in the US to help females suffering from infertility due to PCOS.

II. MATERIALS AND METHODS

This study was performed by searching the following databases: PubMed, Wan Fang Database, ResearchGate (researchgate.net), and Google Scholar. The articles are filtered to include only those written in English or Chinese and published from 2010 to 2021. The keywords "female infertility," "Polycystic Ovulatory Syndrome," "PCOS," "acupuncture combined with herbal medicine," "herbal medicine," and "acupuncture" were used to find the relevant articles. After compiling a published paper catalog, the author scanned through each article's title, abstract, and introduction.

Inclusion criteria: The articles must follow studies that use randomized controlled trials (RTCs) that make the following three comparisons:

1. Comparing a combination treatment using acupuncture and herbal medicine to treatment using the conventional western medicine Clomiphene Citrate (CC) 2. Comparing a combination treatment using acupuncture and herbal medicine to treatment using Letrozole (LE).

3. Comparing acupuncture treatment with herbal medicine and Lapascopic Ovarian Drilling surgy. Only full-length texts were selected. Patients in the studies are clinically diagnosed with infertility due to PCOS, ages 20 to 41 years old, and whose male partners' sperms are healthy.

Exclusion criteria: This narrative review excludes papers that solely study the effects of acupuncture or herbal medicine on PCOS-induced infertility.

Search results: There are 30 relevant articles. Nine articles are from English databases, and the other 21 papers are from the Chinese database. One of them is systematic reviews. Four of the articles are not in full-text length. Two out of 30 articles are about infertility issues not due to

PCOS. One out of the 30 used herb only, and another four pieces used acupuncture solely.

Therefore, there are 18 articles meet the inclusive criteria of this narrative review. (See Figure 1.)

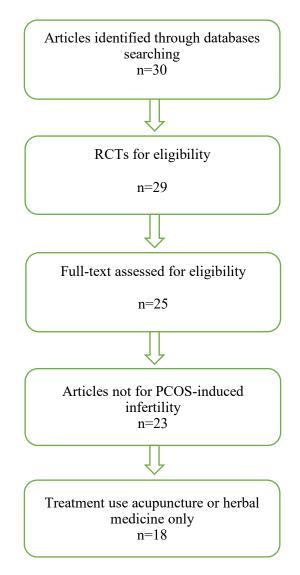


Figure 1. The Flow Chart of Research Articles Selection

Statistical Tool: Microsoft Excel is the tool for statistical comparison.

III. RESULTS

Characteristics of Included Studies

All 18 RCTs research performed and published in China. The published year ranges from 2013 to 2018, with sample sizes between 42 to 128. Only one study with 86 participants compares manual acupuncture and sham-acupuncture with the same herbal formula applied to both groups. The outcome measurements are pregnancy rate, ovulation rate, LH level, and FSH level. The analysis shows a significant difference in lowering LH level and increasing FSH level, which generally decreases the LH/FSH ratio. Hence, it improves the symptoms of PCOS patients.

One research out of 18 compares Eastern medicine combining treatment with medication, the medication itself, and the combined treatment solely. With a total sample size of 92 participants, it compares birth control pills (Diane-5, China) plus CC and acupuncture with herbal formula treatment. The participants have divided into three groups: Diane-5 with CC, Diane-5 with CC plus the Eastern medicine combined treatment, and the Eastern medicine combined treatment only. The outcome measurements are LH level, FSH level, and Testosterone level. The results (P-value) show a significant decrease in LH levels in all three groups. Moreover, there is no significant difference in p-values among the three groups. Therefore, the TCM combined treatment can achieve the same effect of restoring ovulation as the western medication.

One study compares acupuncture treatment combined with herbal medicine and moxibustion versus acupuncture with herbal formula. The sample size is 86 participants, and the study shows both groups significantly increase pregnancy rates (P-value <0.05). However, treatment with moxibustion has a higher successful pregnancy rate.

The Main Findings:

Four authors, Xue H, Zhang J, Xu, and Yang, conclude that no statistical significance has been found between acupuncture combined with herbal medicine and Western Medicine in helping women ovulate and getting pregnant. Because the three studies receive relatively similar results in restoring ovulation. (see Table 1.) However, Xu considers acupuncture and herbal medicine combined treatment receive better effects on lowering LH/FSH ratio than western medicine.

Author	Size		Ovulation Rate	Pregnancy Rate	LH(IU/L)	FSH (IU/L)
	n=80	Control Group	10/40	28/40		
Xue, H	11=80	Intervention	9/10	23/40		
	P value		P=0.677	P=0.065		
	n=80	Control Group	13/40	22/40		
Zhang,JH	11=80	Intervention	14/40	25/40		
	P value		P>0.05	P>0.05		
	n=86	Control Group	3/43	12/43	2.37±0.88	1.52±0.42
Xu, J	11-00	Intervention	6/43	23/43	2.53±0.86	1.03±0.21
	P value		P>0.05	P>0.05	P<0.05	P<0.05
	n=72	Control Group	12/31	15/31		
Yang, G	11-72	Intervention	11/31	23/31		
	P value		N/A	N/A		

Table 1. Comparison of Ovulation Rate, Pregnancy Rate, LH, FSH between Control Group and Acupuncture+ Herb Intervention I

*Intervention: Acupuncture and Herbal Combining Treatment *Control Group: Western medication

Thirteen authors conclude that combined Eastern medicine treatment versus CC results are statistically significant. The combination treatment of acupuncture and herbal medicine receives a significantly higher success rate in pregnancy in PCOS female patients. Among the authors, 2 out of 13 authors, Yu and Zhou, have the conclusion that there is no difference in ovulation rate between the combined treatment and CC. Both the Eastern medicine combined treatment and CC could restore ovulation at a similar level; however, CC does not increase the fertility rate as the combined treatment does. The reason may be because CC increases the secretion of progestogen

that lead to insufficient production of cervical mucus, which will fail to provide the environment

for embryos to stay in the uterus, according to Wu (Wu, etc)¹ (See Table 2.)

Author	Size		Ovulation Rate	Pregnant Rate	LH(IU/L)	FSH (IU/L)
	n=68	Control Group	17/34	8/34		
Yu, Z	11-00	Intervention	18/34	13/34		
	P value		P>0.05	P=0.03		
Zhong, C	n=92	Control Group	13/46	5/46	1.02±0.21	
Zhong, C	11-52	Intervention	21/46	13/46	1.52±0.43	
	P value				P<0.05	
Xiao, H	n=84	Control Group	5/42	17/42	30.2±0.31	11.5±1.6
лао, п	n=64	Intervention	10/42	31/42	25.4±2.8	9.8±1.3
	P value		P<0.05	P<0.05	P<0.05	P<0.05
01 ' D		Control Group	N/A	N/A	25.5±2.9	11.6±1.5
Shi, P	n=82	Intervention	N/A	N/A	30.3±3.1	9.8±1.3
	P value				P<0.05	P<0.05
6 N	60	Control Group	14/30	19/30	7.45±2.12	5.39±1.57
Guo, M	n=60	Intervention	17/30	23/30	8.98±2.82	5.48±1.62
	P value			,	P<0.05	P<0.05
		Control Group	15/26	8/36	1 10100	
Li, Y	n=72	Intervention	33/36	28/36		
	P value	intervention	33,30	P<0.05		
		Control Group	9/23	8/23		
Zhang, C	n=46	Intervention	12/23	10/23		
	P value	intervention	12/25	10/25		
71 0	0.5	Control Group	20/43	14/43	7.26±2.51	14.26±1.71
Zhu, C	n=86	Intervention	15/43	24/43	6.14±2.41	13.41±1.71
	P value		17	P<0.05	P=0.046	P=0.016
71 1	420	Control Group	14/64	25/64		
Zhou, L	n=128	Intervention	16/64	39/64		
	P value			P<0.05		
Deng, Z	n=90	Control Group	11/45	17/45	9.2±1.2	31.2±3.0
Delig, Z	11-50	Intervention	13/45	30/45	11.1±1.4	26.1±2.2
	P value			P<0.05	P<0.05	P<0.05
Shuai,Y	n=65	Control Group	71.00%	38.70%		
e.ruui, r	11=05	Intervention	93.50%	64.50%		
	P value		P<0.05	P<0.05		
Pan	N/A	Control Group	45.47%	18.42%		
		Intervention	58.14%	46.43%		
	P value		P<0.05	P<0.05		
Ding, ZP	N/A	Control Group	N/A	N/A		
5116, 21	19/5	Intervention	N/A	42/72		
	P value		N/A	N/A		

 Table 2. Comparison of Ovulation Rate, Pregnancy Rate, LH, FSH between Control Group and Acupuncture+ Herb Intervention II

t *Control Group: Western medication

IV. DISCUSSION

Acupuncture and Herbs to Regulate Ovulation and Increase Pregnancy Rate

17 results of the 18 studies show acupuncture combined with herbal medicine is beneficial in improving symptoms, regulating menstruation, restoring ovulation, and increasing pregnancy success rate in PCOS-induced fertility patients. By analyzing the acupuncture protocols and herbal formulas, respectively, this paper aims to decode the synergistic effects of the combined treatment. Below are the most used acupuncture points from the 18 studies. The most commonly used acupuncture points are Ren4 (Guan Yuan), SP6 (San Yin Jiao), UB23(Shen Shu), ST36(Zu San Li), Zi Gong (Extra points) Ren6 (Qi Hai). (see Chart 1) Practitioners can add points based on each patient's differential Eastern medicine diagnosis. For instance, if a patient presents symptoms with Liver Qi Stagnation, LV3 (Tai Chong), UB 18 (Gan Shu), and UB19 (Dan Shu) can be added; for a patient with Dampness Accumulation, add ST40 (Feng Long); if the patient has Blood Stagnation signs, add SP10 (Xue Hai), LV3 (Tai Chong), and LI 11 (Qu Chi), etc.

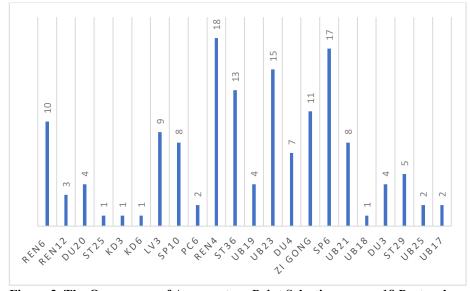


Figure 2. The Occurrence of Acupuncture Point Selection among 18 Protocols

The most commonly used points work in two different levels on helping females regain their fertility. On one hand, the points improve and enhance the functions of the organs. Ren4 (Guan Yuan) and UB23 (Gan Shu) strengthen the Kidney. Ren 4 (Guan Yuan) tonifies reproductive functions in both males and females. Especially, Ren 4 (Guan Yuan) nourishes Kidney Essence, Yin and Yang. UB23 (Shen Shu) is the Back-Shu point that tonifies Kidney Essence, Yin, and Yang. It also strengthens the Kidney's ability to grasp Qi, which benefits the ear and bones.

On the other hand, the point selection works on increasing Qi and Blood. SP6 (San Yin Jiao) is the conjunct point of all three foot-yin meridians. It is known for female health-related issues, including irregular menstruation, abnormal discharge, and infertility. Moreover, SP6 is in the Spleen meridian, nourishing Spleen, an essential organ for the female reproductive system. ST36 (Zu San Li) is the He-Sea point of the Stomach meridian, one of the main meridians controlling Qi and Blood. Ren6 (Qi Hai) is the Sea of Qi; as its name describes, Ren6 tonify Qi all over the body. Qi promotes the formation and circulation of Blood while Blood generates Qi. The location of Zi Gong is where the uterus is. It increases blood circulation in the uterus and ovaries.

The Most Chosen Acupuncture Points						
Acupuncture Points	Frequency Function					
Ren4	18	major point of strengthen the Kidney Essence and reproductive functions for males and females				
SP6 17 major		major points for female reproductive issues				
UB23 15 strengthen Kidney Essence, Yin, and Yang		strengthen Kidney Essence, Yin, and Yang				
ST36	13	tonify Spleen, Qi and Blood				
Zi Gong 11 streng		strengthen uterus, and improve				
Ren6	10	tonify Qi all over the body, especially for Qi in the reproductive system				

Table 3. The Most Chosen Acupuncture Points

Herbal medicine is the other important component of restoring fertility for PCOS female patients. This paper will study herbal formulas from the 17 articles, concluding that acupuncture combined with herbal decoction increases the pregnancy rate in women with PCOS infertility.

There are only two RCTs studies that used classical formulas. In Pan's analysis, applying herbal formula can divide into two phases: during menstruation and not during menstruation. Tao Hong Si Wu Tang applies during menstruation. When patients are not on period, herbal formulas have been applied based on two differential diagnoses. For Spleen and Kidney Yang deficiency, use Bu Shen Tiao Jing Tang; for Liver and Kidney Yin Deficiency, use Gui Shao Di Huang Wan. Li's study has four differential diagnoses: LV Qi Stagnation, Dampness Accumulation, Kidney Deficiency, and Blood Stagnation. Bai Ling Tiao Gan Tang (One Hundred Spirit and Liver Smoothing Decoction), Qi Gong Wan (Arousing the Uterus Pills), Yu Ling Wan (Fertility pills), and Shao Fu Zhu Yu Tang are applied, respectively. Both authors use Blood-moving herbs and formula Tao Ren and Hong Hua to invigorate blood flow and concentrate on strengthening patients' Liver and Kidney.

Three out of 17 research used Shu Gan Yi Shen Qu Tan Tang (Sooth Liver Strengthen Kidney and Expel Dampness Decoction), a modified formula, to help patients improve symptoms and restore reproductive ability. The formula targets soothing Liver Qi, strengthening KD Yin, expelling Dampness, and increasing circulation. The main ingredients are Shu Di Huang, Xiang Fu, Chuang Qiong, Fu Ling, Gou Qi Zi, Yin Yang Huo, Dang Gui, Ban Xia, Shan Yao, Bai Zhu, Dan Shen, Tu Si Zi, and Gan Cao.

The formulas can be divided into five customized herbal formula types. Four of the 17 authors share similar formulas, which can be named formula 1 (see Table 5). Another four use herbal medicine based on formula 2 (see Table 5). 5 authors use formula 3 to treat PCOS patients, while

author Zhang and author Ding use their custom formula, respectively.

	Formula 1	Formula 2	Formula 3	Formula 4	Formula 5
	Gan Cao	Dan Shen	Nv Zhen Zi	Yu Zhu	Xian Mao
	Liu Ji Nu	Tu Si Zi Han Lian	Ji Xue Ten	Dan Shen	Yin Yang Huo
	Shu Di Huang	Сао	Gou Qi Zi	Shu Di Huang	Rou Song Rong
	Dang Gui	Gou Qi Zi	Han Lien Cao	Shan Yao	Huang Jing
	Bai Shao	Ji Xue Teng	Tu Si Zi	Dang Gui	Gou Qi Zi
	Bai Zhu	Nv Zhen Zi	Dan Shen	Yin Yang Huo	Dang Gui
	Bai Jie Zi	Tao Ren	Chai Hu	Zao Jiao Ci	Xiang Fu
	Fu Chao Chang Zhu	E Shu	Bai Jie Zi	Chuan Duan Xu	Ji Xue Ten
	Xiang Fu	San Leng	Chi Shao	Fa Ban Xia	Tu Bie Chon
Ingredients	Duan Xu	Zhi Ke	Bai Shao	Chen Pi	Zhe Bei Mu
-	Dan Nang Xing	Dang Shen	Dan Nang Xing	Ze Xie	Ju Pi
	Chi Shao	Mu Xiang	Shu Di Huang	Tao Ren	Fa Ban Xia
	Chai Hu	Zhi Ke	Duan Xu	Hong Hua	Fu Ling
	Tu Bie Chong	Yu Jin	Dang Gui	Suo Yang	Tian Qi
	Dan Shen	Shi Hu	Liu Ji Nu	Fu Pen Zi	Tao Ren
	Gou Qi Zi		Xiang Fu		Hong Hua
	Tu Si Zi		Fu Chao Cang Zhu		
	Ji Xue Teng		Tu Bie Chong		
	Han Lian Cao		Bai Zhu		
	Nv Zhen Zi		Gan Cao		
Numbers of Author Use	4	4	5	1	1

 Table 4. The List of Herbal Formula Ingredients

Every herb plays a unique and indispensable role in the formula, to have synergic effects with acupuncture to restore fertility for women. Among the 17 studies, there are 40 single herbs involved in total. This session lays out the occurrence of 40 single herbs among the studies and picks the most popular 17 herbs. Data is selected by repetition and more than five times in all formulas. Here are the results:

The most commonly used single herbs are Dang Gui (17), Xiang Fu (16), Shu Di Huang
 (13), Dan Shen (12), Gou Qi Zi(11), Tu Si Zi (11), Gan Cao (10), Shan Yao (9), Bai Shao

(8), Yin Yang Huo (7), Bai Zhu (7), Dan Nang Xing (6), Chai Hu (6), Nv Zhen Zi (6), TuBie Chong (6), Bai Jie Zi(5), Xu Duan (5). (See Figure 3.)

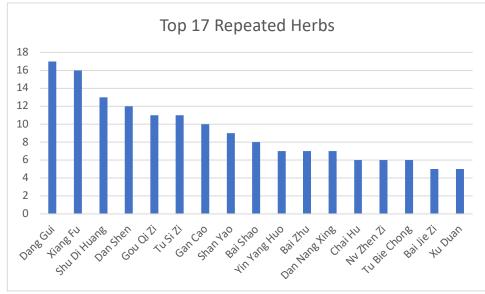


Figure 3. Top 17 Repeated Herbs

- 2) Among these single herbs, there are three Qi-Tonify herbs Gan Cao, Shan Yao, and Bai Zhu. Shu Di Huang, Dang Gui, and Bai Shao are Blood-Tonify herbs. Another three Yang-Tonify herbs are Yin Yang Huo, Tu Si Zi, and Xu Duan. Yin-Tonify herbs include Gou Qi Zi and Nv Zhen Zi. Two Blood-invigorating herbs: Tu Bie Chong and Dan Shen. Two Phlegm-resolving herbs, Dan Nan Xing and Bai Jie Zi. (See Table 6)
- 3) Qi-Tonify herbs, Blood-Tonify herbs, and Yang-Tonify herbs are 17%, respectively. These three herbal categories take up 35% of the herbal formula for PCOS infertility patients. They are the critical herbs of the herbal formula for infertility patients due to PCOS. Herbs with Yin-Tonify, Phlegm-Resolving, Blood-invigorating, and Qi-Regulating properties take second place in the herbal formula. Each takes up 12%. (See Figure 4.)

Table 5. Property of the Top 17 Herbs

Herbs	Property of the Top 17 Herbs		
Gan Cao	Qi-Tonifying herb		
Shu Di Huang	Blood-Tonifying herb		
Xiang Fu	Qi-Regulating herb		
Gou Qi Zi	Yin-Tonifying herb		
Yin Yang Huo	Yang-Tonifying herb		
Dang Gui	Blood-Tonifying herb		
Shan Yao	Qi-Tonifying herb		
Bai Zhu	Qi-Tonifying herb		
Tu Si Zi	Yang-Tonifying herb		
Dan Nang Xing	Phelm-Resovling herb		
Bai Shao	Blood-Tonifying herb		
Chai Hu	Wind-Heat Releasing and Qi-Regulating herb		
Nv Zhen Zi	Yin-Tonifying herb		
Tu Bie Chong	Blood-invigorating and Stasis-removing herb		
Bai Jie Zi	Phelm-Resovling herb		
Dan Shen	Blood-invigorating and Stasis-removing herb		
Duan Xu	Yang-Tonifying herb		

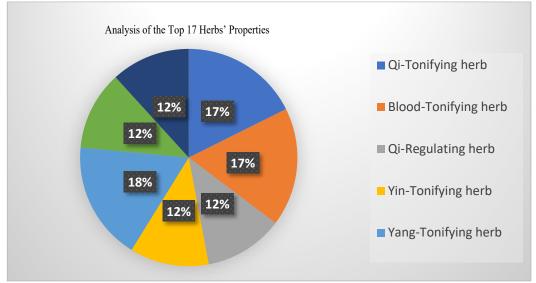


Figure 4. Analysis of the Top 17 Herbs' Properties

4) The 17 herbs' entered channels are the Liver, Lung, Kidney, Heart, Gallbladder,Pericardium, and Stomach. (See Table 7 and Figure 5)

Top 17 Herbs Entered Meridian				
Gan Cao	Heart	Lung	Stomach	
Shu Di Huang	Liver	Kidney		
Xiang Fu	Liver	San Jiao		
Gou Qi Zi	Liver	Kidney	Lung	
Yin Yang Huo	Liver	Kidney		
Dang Gui	Heart	Liver	Spleen	
Shan Yao	Kidney	Lung	Spleen	
Bai Zhu	Spleen	Stomach		
Tu Si Zi	Liver	Kidney		
Dan Nang Xing	Liver	Lung	Spleen	
Bai Shao	Liver	Spleen		
Chai Hu	Liver	Gallbladder		
Nv Zhen Zi	Liver	Kidney		
Tu Bie Chong	Liver			
Bai Jie Zi	Lung			
Dan Shen	Heart	Pericardium	Liver	
Duan Xu	Liver	Kidney		

Table 6. Top 17 Herbs Entered Meridian

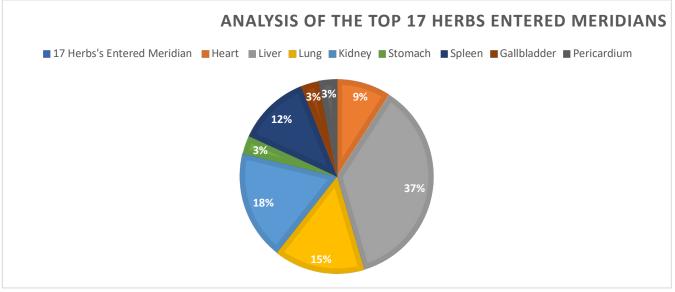


Figure 5. Analysis of the Top 17 Herbs Entered Meridians

The most significant portion of herbs entering in Liver channel (37%), the 2nd most prominent part is the herb goes to the Kidney channel (18%), and the following one is Lung (15%) and Spleen (12%).

Analysis

In Eastern medicine theory, a healthy female reproductive system should have a harmonized foundation of Kidney Essence-Tian Kui (menstruation)-balanced Chong and Ren meridian-Uterus. According to The Yellow Emperor's Classic of Internal Medicine, Tian Kui (menstruation) comes when Kidney Essence is sufficient. Chong meridian and Ren meridian work as a pathway for Tian Kui to pass through and reach the uterus, and then the lady will be ready to conceive. Anything that disturbs the Kidney-Uterus harmony can lead to infertility in the female. PCOS-induced infertility can be categorized under Infertility in Eastern medicine. There are four reasons cause Infertility:

 The influent flow of Chong and Ren Channels due to Kidney Essence Deficiency Kidney essence is crucial to the reproductive system in Eastern medicine. To ensure the female has a healthy and functional reproductive system, Kidney Essence, Blood, Kidney Yin, and Kidney Yang must be sufficient.

Kidney Essence consists of congenital essence from parents and the food essence (水谷

精微) from everyday meals. The healthy Kidney Essence generates Blood, while Blood nourishes the Kidney Essence to continue reproducing. Kidney Essence and Blood ensure Chong and Ren's meridians have ample flow. Under this circumstance, ovulation happens when a woman's Kidney Qi is sufficient. Kidney Qi consists of Kidney Yin and Yang. Kidney Yin is the foundation of the egg cell, while Kidney Yang is the facilitator for the egg cell to growth. Sufficient Kidney Yin and Yang are the keys for healthy egg cells to grow and ovulate. Hence, all four kidney elements must function well for ovulation.

2) Disharmony of Chong and Ren Channels due to Liver Qi Stagnation

Liver stores blood. Its function is to disperse and dredge Chong and Ren meridians. According to TCM's theory, liver Qi flow needs to be smooth, which can be damaged by emotional disorders, including depressed feelings, anxiety, and anger (Liu et al., 2017). The liver delivers nutrients and blood to organs all over the body, including the reproductive system-Bao Gong (胞宮). When enough blood floods to Bao Gong, Chong,

and Ren meridians, menstruation comes, and ovulates. Hence, Liver Qi stagnation will have impacts on menstruation and ovulation.

The explanations resonate with the relationship between the Liver, physiology, and women's reproductive system from Western Medicine's point of view. Hepatic blood usually accounts for ¹/₄ of the cardiac input of a healthy adult. The liver is the biggest organ in the human body, which plays a crucial role in digestion and absorption. Emotional disorders, such as stress, anxiety, depression, and anger, can lead to an abnormal LH/FSH ratio that causes ovulation disorders.

3) Blockage in both Chong and Ren Channels due to Blood Stagnation Nourished Chong and Ren meridians are critical factors for women's ovulation. The Chong channel, also known as the "Sea of Blood, " is a pathway to the uterus and controls the ovulating process. Another essential organ to ensure a smooth path for blood is Lung. Lung rules and regulates all Qi of the body and the blood vessels, especially the Heart's blood flow. Any blood stagnation will block the uterine pathway, impacting the ovulating process. Hence, when blood circulation is improved, it can increase the chance

of getting pregnant.

4) Blocked Chong and Ren channels e to Dampness Accumulation

The functions of Spleen are versatile. The first function is to control the digestion and absorption of the food essence (水谷精微). Secondly, Spleen participates significantly in generating blood for daily activities. As previously discussed, blood is the foundation substance to create and interact with the essence (精). The third function of the Spleen is to transport and transform the food essence, which usually is in fluid-like form, throughout the whole body. It also participates in the transportation of fluid, which prevents the body from getting edema. If there is a dysfunction of the Spleen, it may cause fluid accumulation and insufficient blood flow. Both factors may contribute to dampness accumulation which blocks Chong and Ren meridians and lead to anovulation. The analysis explains the reason why the most common herbs from 17 formulas are mainly

entering to Liver (37%), Kidney (18%), Lung (15%), and Spleen (12%). Liver stores Blood. If the Liver is dysfunctional, it can lead to irregular menstruation and ovulation disorders. The kidney is the source of Blood. If the source is damaged, good-quality Blood will not be created to nourish the uterus. Blood could need a smooth pathway to transport and transform Blood. Spleen transport and transform Blood. The Lung meridian plays a unique role in blood vessels and enormously assists the blood-related function of the Kidney, Liver, and Spleen.

The Synergic Effect of Combing Acupuncture and Herbal Medicine in Treating PCOSinduced Infertility

Acupuncture and Herbal medicine are the two most important means of Eastern medicine to heal patients. Acupuncture works on Qi and Blood levels. As the essence of vital signs, Qi and Blood

runs through the body from Eastern medicine's point of view.

Acupuncture aims to work on the meridian level. According to Yellow Emperor, "meridians internally belong to organs and connect to extremities externally" (内属脏腑,外络枝节).

Acupuncture treatment enhances the flow of Qi and Blood in the body, which unblock and clears obstructions in the meridians. It helps to improve circulation in the local area and nourishes the ovary and uterus to provide a healthy environment for pregnancy.

A healthy body needs homeostasis. In Eastern medicine, smooth meridians without any blockages are the foundation of homeostasis-Yin and Yang balance. The Yin and Yang balance is always dynamic, and the Yin and Yang are complementary and contradictory. Organs also must be taken good care of to reach a dynamic balance. Herbal medicine can significantly help in treating the ailments caused by organs. Herbal medicine works on organs, accelerating the body to restore balance and improve functions. In the 18 RCTs, the top 17 herbs mainly affect Kidney, Liver, Spleen, and Lung to recover and enhance the body's functions. Kidney, Spleen, Liver, and Lung are crucial organs to the female's reproductive system. The efficacy of the combing treatment could reinforce the functions of the reproductive system of PCOS patients and reach the maximum results of helping them conceive.

V. CONCLUSION

Infertility has been bothering most PCOS patients who are of reproductive age. To get pregnant, regulating menstruation, stabilizing LH/FSH and testosterone levels, and ensuring ovulation are critical to reaching the goal. This paper analyzes related studies of acupuncture and herbal medicine verse western medication treating infertility caused by PCOS. Thirty related studies were selected, and 18 fell in the criteria. Among the 18 RCTs, 4 out of 18 show that acupuncture treatment combined with herbal medicine receives the same successful pregnancy rate as the western medication. 14 out of 18 research present a higher pregnancy rate with more remarkable improvement in PCOS symptoms, including lower LH/FSH ratio, compared to patients who are only on western medicine. It concludes that the combined TCM treatment receives a higher pregnancy rate than the conventional western treatment.

Moreover, acupuncture and herbal formula from 18 research have been analyzed. The top 6 acupuncture points and the most frequently used 17 herbs have been selected. The most commonly used points aim to improve Qi and Blood circulation to provide better blood flow for the uterus and ovaries to conceive. The top 17 herbs work on Kidney, Liver, Spleen, and Lung to tonify essence and unblock stagnation to ease symptoms, regulate period, enhance ovulation, and increase the chance of pregnancy.

There is a limitation in this paper. 18 RCTs all happened in China with geodemographic bias. The total sample size involves 1443, which may not be big enough. However, Eastern medicine as the medicine that is based on over-time experience, so it is worth borrowing the treatment experience and protocol to help more PCOS patient to get pregnant in the US.

REFERENCES

- Centers for Disease Control and Prevention. (2019, August 12). PCOS (Polycystic Ovary Syndrome) and Diabetes. Centers for Disease Control and Prevention. https://www.cdc.gov/diabetes/basics/pcos.html
- Centers for Disease Control and Prevention. (2019). Infertility. Centers for Disease Control and Prevention. https://www.cdc.gov/reproductivehealth/infertility/index.htm
- Deng, Z. (2016). 多囊卵巢综合征不孕不育应用中药联合针刺治疗的临床分析. 黑龙江医学 Heilongjiang Medical Journal, 40(4), 347.
- Ding, Z., Yu, Z., Li, M., & Chen, S. (2014). 针药结合治疗多囊卵巢综合征合并不孕 72 例. 中国中医药现代远程教育 Chinese Medicine Modern Distance Education of China, 12(19), 134.
- Guo, M., Yang, Y., Sun, C., & Zhang, Y. (2017). 中药联合针刺治疗痰湿瘀滞型多囊卵巢综合 征不孕症的临床观察. 云南中医中药杂志, 38(8), 44.
- Lee, J. W., Hyun, M. K., Kim, H. J., & Kim, D. I. (2021). Acupuncture and herbal medicine for female infertility: An overview of systematic reviews. Integrative Medicine Research, 10(3), 100694. https://doi.org/10.1016/j.imr.2020.100694

Li, Y. (2019). 中药联合针灸治疗多囊卵巢综合征不孕的临床疗效观察. 家庭医药, 67.

- Lim, C. E. D., Ng, R. W. C., Cheng, N. C. L., Zhang, G. S., & Chen, H. (2019). Acupuncture for polycystic ovarian syndrome. Cochrane Database of Systematic Reviews. https://doi.org/10.1002/14651858.cd007689.pub4
- Liu, Z.-W., Shu, J., Tu, J.-Y., Zhang, C.-H., & Hong, J. (2017). Liver in the Chinese and Western Medicine Keywords Brain · Emotion · High blood pressure · Liver · Digestive system · Circulatory system · Reproductive system · Traditional Chinese medicine. *Integr Med Int*, 4, 39–45. https://doi.org/10.1159/000466694
- Moini Jazani, A., Nasimi Doost Azgomi, H., Nasimi Doost Azgomi, A., & Nasimi Doost Azgomi, R. (2019). A comprehensive review of clinical studies with herbal medicine on

polycystic ovary syndrome (PCOS). DARU Journal of Pharmaceutical Sciences, 27(2), 863–877. https://doi.org/10.1007/s40199-019-00312-0

- Saadia, Z. (2020). Follicle Stimulating Hormone (LH: FSH) Ratio in Polycystic Ovary Syndrome (PCOS) - Obese vs. Non- Obese Women. Medical Archives, 74(4), 289. https://doi.org/10.5455/medarh.2020.74.289-293
- Shi, P. (2019). 中药联合针刺治疗多囊卵巢综合征不孕不育效果分析. 健康大视野 中医 Shuai, Y. (2013). 针灸联合中药与来曲唑治疗 多囊卵巢综合征不孕症(肾虚痰湿型) 的疗效观察. 实用妇科内分泌杂志 Journal of Practical Gynecology

Endocrinology, 44(2), 6.

- Wang, Y. (2013). 针刺配合中药治疗肥胖型多囊卵巢综合征不孕症 56 例. 福建中医药, 44(2), 6.
- Wu, J., Chen, D., & Liu, N. (2020). Effectiveness of acupuncture in polycystic ovary syndrome. Medicine, 99(22), e20441. https://doi.org/10.1097/md.00000000020441
- Xiao, H., & Lai, S. (2014). 中药联合针刺治疗多囊卵巢综合征不孕不育 42 例. 实用中医药杂志 Journal of Practical Traditional Chinese Medicine, 12(19).
- Xu, J. (2019). 中药联合针灸疗法治疗多囊卵巢综合症合并不孕对患者体内相关激素水平影响观察. 临床医药文献电子杂志 Electronic Journal of Clinical Medical Literature, 6(57), 61.
- Xu, J., & Zuo, Y. (2018). *Zhongguo zhen jiu* = *Chinese acupuncture & moxibustion*, *38*(4), 358–361. https://doi.org/10.13703/j.0255-2930.2018.04.004
- Xue, H. (2017). 中药结合针刺治疗多囊卵巢综合征所致不孕临床观察. 实用中医药杂志 Journal of Practical Traditional Chinese Medicine, 33(12), 1360.
- Yang, G. (2017). 中药汤剂联合针刺治疗多囊卵巢综合征合并不孕的效果探析. 当代医药论丛 ContemporaryMedicalSymposium, 15(13), 142.
- Yin, Y., Zhang, Y., Zhang, H., Jiang, D., & Guo, G. (2018). *Zhongguo zhen jiu = Chinese acupuncture & moxibustion*, 38(1), 27–32. https://doi.org/10.13703/j.0255-2930.2018.01.006

- Yu, Z. (2018). 中药+针刺治疗多囊卵巢综合征不孕不育的效果分析. 实用妇科内分泌杂志 Journal Of Practical Gynecologic Endocrinology, 5(32), 90.
- Yu, L., Cao, L., Xie, J., & Shi, Y. (2018). *Zhongguo zhen jiu = Chinese acupuncture & moxibustion*, 38(3), 263–268. https://doi.org/10.13703/j.0255-2930.2018.03.009
- Zhang, C. (2019). 中药联合针灸疗法治疗多囊卵巢综合征合并不孕的临床疗效观察. 饮食保健, 6(49), 7.
- Zhang, J., Xia, H., & Wang, P. (n.d.). 中药联合针刺治疗多囊卵巢综合征不孕不育效果观察. 诊断技术, 12(19).
- Zhong, C., & Liang, B. (2016). 中药联合针灸疗法治疗多囊卵巢综合征合并不孕的临床效果. 海峡医学, 28(7).
- Zhou, L., Ren, X., Mu, W., Wang, Y., Gao, S., & Cheng, X. (2016). 中药针灸结合治疗多囊卵 巢综合征并不孕 128 例分析. 饮食保健 中医中药 中西医结合, 3(10), 72.
- Zhu, C. (2019). 中药联合雷火灸、针刺治疗多囊卵巢综合征不孕临床研究. 临床医药文献电子杂志 Electronic Journal of Clinical Medical Literature, 6(33), 71.

药, 5(419).