META-ANALYSIS

Treatment of Polycystic Ovary Syndrome-Related Infertility Using a Combination of Compound Xuanju Capsules and Hormones: A Meta-Analysis

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ABSTRACT

Objective • Our aim was to perform a meta-analysis to compare the therapeutic effects of compound Xuanju capsules combined with hormone therapy vs hormone therapy alone in polycystic ovary syndrome (PCOS)-related infertility.

Methods • Electronic databases including PubMed, The Cochrane Library, Web of Science, Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Wanfang Data and VIP database were manually searched. The quality of included studies was evaluated based on Cochrane Systematic Review standards, and the valid data were extracted for meta-analysis using RevMan 5.3 software (Cochrane Review).

Results • A total of 14 randomized controlled trials (RCTs) including 1249 patients were included in the study. Meta-analysis showed that patients in the compound Xuanju capsule + hormone therapy group had higher estradiol (E_2) levels and overall rates of effective treatment than patients in the hormone therapy alone group. Moreover, they exhibited lower levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), as well as lower Kupperman scores, than the hormone therapy alone group.

Conclusions • The combination of compound Xuanju capsules and hormone therapy is more effective than hormone therapy alone in the treatment of PCOS-related infertility. However, the quality of current studies is low, and high-quality clinical trials are warranted. (*Altern Ther Health Med.* 2023;29(2):271-281)

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INTRODUCTION

In today's modern society, work-related stress has substantially increased, resulting in rising rates of female reproductive disorders such as polycystic ovary syndrome (PCOS), infertility, premature ovarian failure and irregular menstruation. PCOS is a common condition associated with multimorbidity in women of reproductive age and often accompanied by insulin resistance and obesity.[1-5] It is characterized by ovulatory disorders, hyperandrogenism and polycystic ovarian changes, and its primary clinical manifestations are menstrual abnormalities, infertility and acne. Infertility refers to a condition in which women fail to achieve pregnancy after 1 year or more of regular unprotected sexual intercourse. In PCOS, ovulatory disorder is an important inducer of infertility. Currently, western allopathy-based treatments for PCOS-related infertility use anti-androgens, aiming to regulate the menstrual cycle and induce ovulation. Hormone therapy with agents such as clomiphene, letrozole, tamoxifen, tripurelin and progesterone is often the preferred modality for PCOS treatment.[6-10]

Although hormone therapy can improve hormone levels and ovulation rate to a certain extent, it can cause several adverse

effects and is less effective in improving clinical symptoms. Over the past few decades, the advantages of Traditional Chinese Medicine (TCM)—which is gradually being applied for the treatment of PCOS-related infertility—are being highlighted. Some researchers have suggested that hormone therapy combined with TCM can improve therapeutic effects and pregnancy rates while exerting low toxicity and exhibiting a good safety profile.[11] Studies have suggested that compound Xuanju capsules are effective in warming the kidneys and uterus.

Therefore, in our study, we aimed to conduct a meta-analysis of the current clinical findings related to the effectiveness of compound Xuanju capsules combined with hormone therapy for the treatment of PCOS-related infertility in order to elucidate whether this combination provides more advantages than hormone therapy alone.

MATERIALS AND METHODS

Inclusion and Exclusion Criteria

Inclusion criteria. All randomized controlled trials (RCTs) examining the effect of compound Xuanju capsules combined with hormone therapy for treating PCOS-related infertility were retrieved.

Exclusion criteria. Duplicate publications and studies containing erroneous, incomplete or unavailable data were excluded. In addition, studies in which compound Xuanju capsules + hormone therapy was not adopted in the treatment arm and those in which hormone therapy alone was not adopted in the control arm were excluded from the analysis.

Intervention and Outcome Measures

The treatment arm included compound Xuanju capsules + hormone therapy, while the control arm included hormone therapy alone. The outcome measures were the overall rate of effective treatment, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels, the LH/FSH ratio, estradiol (E_2) levels, testosterone (T) levels, overall rate of effective TCM-based treatment, ovarian volume, ovulation rate, pregnancy rate, basal body temperature (BBT), antral follicle count, endometrial thickness, maximum follicle diameter, follicle count and hepatocyte growth factor (HGF) and vascular endothelial growth factor (VEGF) levels.

Search Strategy

Electronic databases including PubMed, The Cochrane Library, Web of Science, Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Wanfang Data and the VIP database were manually searched. The keywords used were: "compound Xuanju capsule," "Xuanju," "compound Xuanju," "hormone," "western medicine," "E_2," "progesterone," "clomiphene," "letrozole," "tamoxifen," "tripurelin," "PCOS," "sterility," and "infertility," etc. There were no publication date or journal restrictions applied.

Data Extraction and Quality Evaluation

A total of 2 evaluators read the title and abstract of each study independently. After excluding studies that clearly did not meet the inclusion criteria, they reviewed the full text to determine whether the studies should be included. Any disagreements were resolved via discussion. Based on the quality evaluation standards described in the *Cochrane Handbook for Systematic Reviews of Interventions*, the following aspects were evaluated:[12] (1) What random sequence generation was adopted?; (2) Was allocation concealment adopted?; (3) Was blinding adopted?; (4) Was there any incomplete outcome data bias?; (5) Was there selection bias?; and (6) Was there any other bias?

Statistical Analyses

All statistical analyses were performed using ReviewManager (RevMan) version 5.3 provided by the Cochrane Collaboration Network. Chi-square (χ^2) analysis was performed to evaluate heterogeneity. At I^2 <50%, studies were considered to have homogeneity, and the fixed effects model was used for analysis. At $I^2 > 50\%$, studies were considered to have high heterogeneity, and the random effects model was used. Sensitivity analysis was performed to identify the source of heterogeneity. The efficacy indices were estimated based on intervals. Enumeration data were expressed as odds ratios (ORs) with 95% CIs, and measurement data were expressed as weighted mean difference (MDs) and 95% CIs. The *Z(u)* test was used to combine statistics, and the probability *(P)* was obtained according to the *Z(u)* value. At $P \leq .05$, the combined results of multiple studies were considered statistically significant.

RESULTS

Literature Search Results

A total of 572 articles was obtained after searching the databases. Of these, 262 were retrieved from CNKI, 56 from Wanfang Data, 253 from VIP and 1 from Medline. No articles were obtained from the Cochrane Library or Web of Science databases. Of the 572 articles, 550 (including inter-database duplications and irrelevant studies) were excluded, and 22 full texts were obtained. A total of 8 articles that did not meet the inclusion criteria were excluded after full-text review, and 14 random controlled trials (RCTs) were finally included (see Figure 1).

Methodological Quality Assessment of Included Studies

A total of 14 RCTs performed in China, with a total of 1249 patients with comparable baseline characteristics, were included in this study. The characteristics of the included population are shown in Table 1. As for outcome measures, 6 studies reported the ovulation rate, 11 the pregnancy rate, 12 follicle-stimulating hormone (FSH) levels; 7 estradiol (E_2) levels; 12 luteinizing hormone (LH) levels; 2 the LH/FSH ratio; 9 testosterone (T) levels; 5 endometrial thickness; 6 the overall rate of effective treatment; 2 the overall rate of effective TCM-based treatment; 2 luteinizing hormone (LH), basal body temperature (BBT), 2 ovarian volume; 2 maximum follicle diameter; 2 follicle count; 2 hepatocyte growth factor (HGF) levels; 2 vascular endothelial growth factor (VEGF)

Figure 1. Data screening process

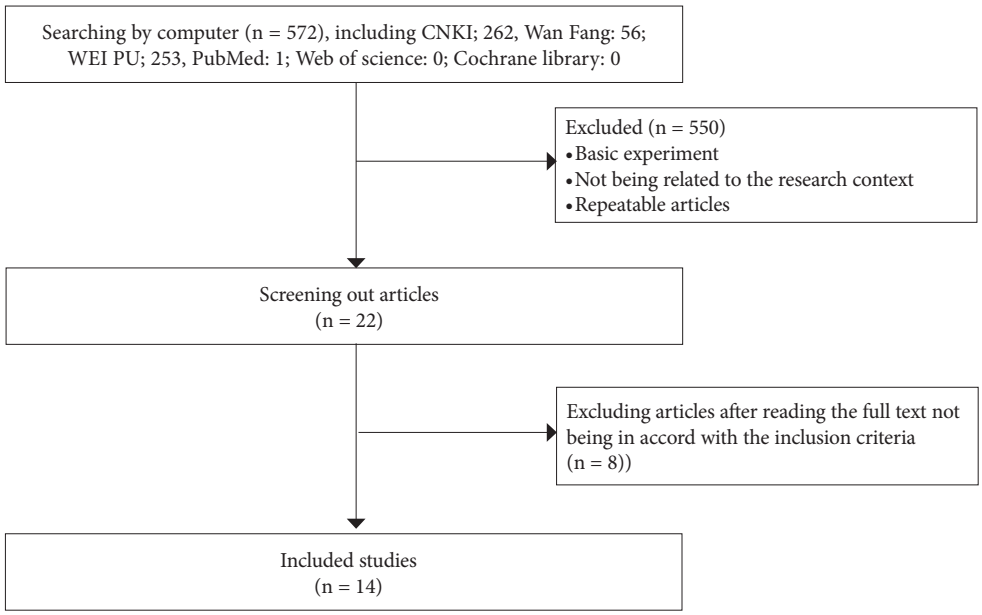


Table 1. Basic Information of Included Studies

Study	N	Treatment Group	Control Group	Main Results	Treatment Course
Sun JL 2009[13]	90	Letrozole + HCG + progesterone + compound Xuanju capsules n = 30	Letrozole + HCG + progesterone n = 25	Better effect in the treatment group	3 menstrual cycles or to pregnancy
Huang XH 2012[14]	60	Clomiphene + compound Xuanju capsules n = 30	Clomiphene n = 30	Better effect in the treatment group	3 months or to pregnancy
Wang HY 2016[15]	42	Clomiphene + HCG + compound Xuanju capsules n = 21	Clomiphene+HCG n=21	Better effect in the treatment group	1 menstrual cycle
Zhang JJ 2017[16]	78	Clomiphene + HCG + progesterone + compound Xuanju capsules n = 39	Clomiphene + HCG + progesterone n = 39	Better effect in the treatment group	3 months or to pregnancy
Hu YF 2017[17]	93	Clomiphene + estradiol valerate + HCG + progesterone + compound Xuanju capsules n = 46	Clomiphene + estradiol valerate + HCG + progesterone n = 47	Better effect in the treatment group	1 menstrual cycle
Hao LN 2018[18]	150	Letrozole+compound Xuanju capsules n = 75	Letrozole n = 75	Better effect in the treatment group	1 menstrual cycle
Chen ZF 2019[19]	86	Clomiphene + HCG + progesterone + compound Xuanju capsules n = 43	Clomiphene + HCG + progesterone n = 43	Better effect in the treatment group	3 months or to pregnancy
Yan L 2019[20]	98	Tamoxifen+compound Xuanju capsules n = 49	Tamoxifen n = 49	Better effect in the treatment group	3 menstrual cycles or to pregnancy
Cai DD 2019[21]	104	Clomiphene + HCG + progesterone + compound Xuanju capsules n = 52	Clomiphene + HCG + progesterone n = 52	Better effect in the treatment group	1 menstrual cycle
Li G 2020[22]	88	Triptorelin+compound Xuanju capsules n = 44	Triptorelin n = 44	Better effect in the treatment group	4 months
Zhou QM 2020[23]	96	Tamoxifen+compound Xuanju capsules n = 48	Tamoxifen n = 48	Better effect in the treatment group	3 menstrual cycles or to pregnancy
Ge BB 2021[24]	108	Clomiphene + progesterone + compound Xuanju capsules n = 54	Clomiphene + progesterone n = 54	Better effect in the treatment group	1 menstrual cycle
Li YY 2021[25]	70	Ethinylestradiol-cyproterone acetate+compound Xuanju capsules n = 35	Ethinylestradiol-cyproterone acetate n = 35	Better effect in the treatment group	16 weeks or to pregnancy
Yu XR 2021[26]	86	Clomiphene + progesterone + compound Xuanju capsules n = 43	Clomiphene + progesterone n = 39	Better effect in the treatment group	3 months or to pregnancy

Figure 2. Comparison of ovulation rate.

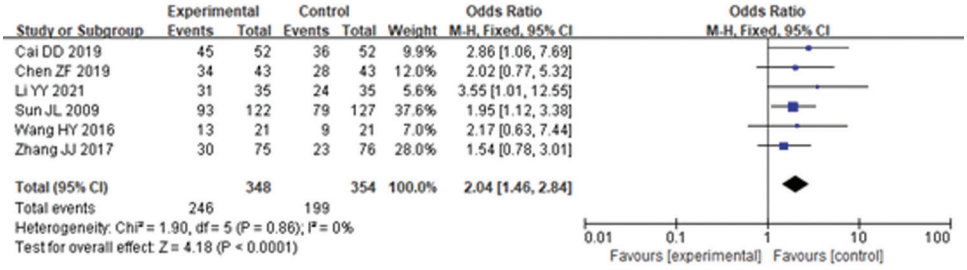


Figure 3. Comparison of pregnancy rate.

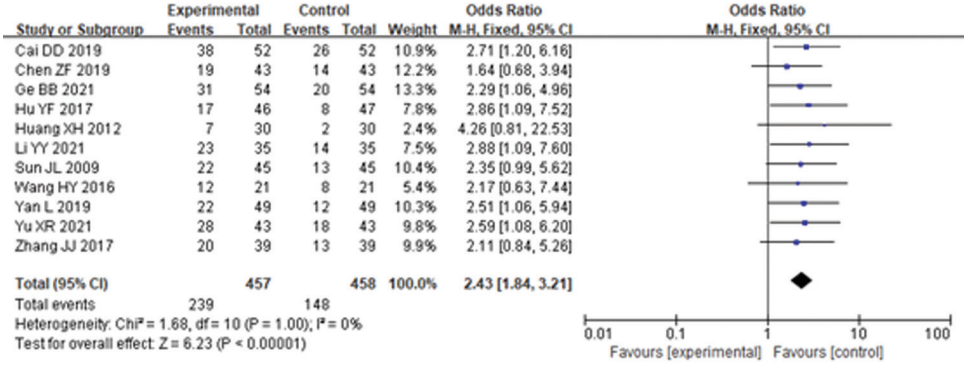
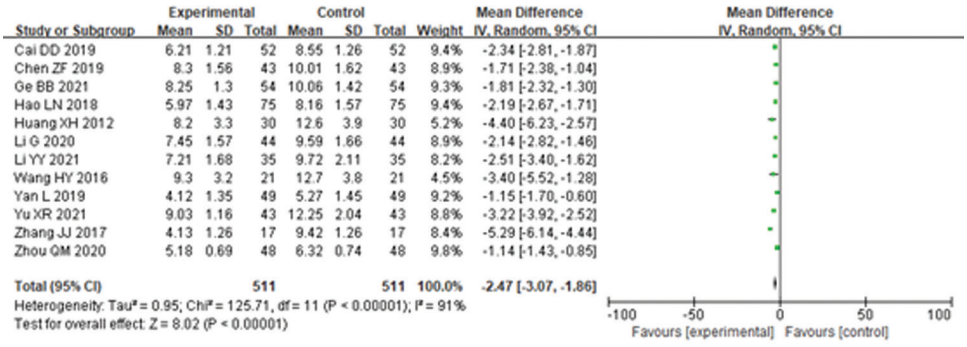


Figure 4. Comparison of LH level.



levels; and 2 reported adverse effects. The general characteristics of all included studies are summarized in Table 1.

Ovulation Rate

No heterogeneity was observed among the 6 studies reporting the ovulation rate ($P = .86$; $I^2 = 0\%$). Meta-analysis with the fixed effects model showed the following: MD = 2.04; 95% CI, 1.46-2.84; $Z = 4.18$; $P < .0001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a higher ovulation rate than the hormone therapy alone group (see Figure 2).

Pregnancy Rate. No heterogeneity was observed among the 11 studies that reported the pregnancy rate ($P = 1.00$; $I^2 = 0\%$). Meta-analysis with the fixed effects model showed the following: MD = 2.43; 95% CI, 1.84-3.21; $Z = 6.23$; $P < .0001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a higher pregnancy rate than the hormone therapy alone group (see Figure 3).

Luteinizing Hormone Level

Heterogeneity was observed among the 12 studies reporting LH levels ($P < .00001$; $I^2 = 91\%$). Meta-analysis with the random effects model showed the following: MD = -2.47; 95% CI, -3.07 to -1.86; $Z = 8.02$; $P < .00001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a lower LH level than the hormone therapy alone group (see Figure 4).

Sensitivity analysis. The heterogeneity decreased significantly after excluding the study by Juanjuan Zhang, suggesting that this study may have been the main source of heterogeneity.

Figure 5. Comparison of follicle stimulating hormone level.

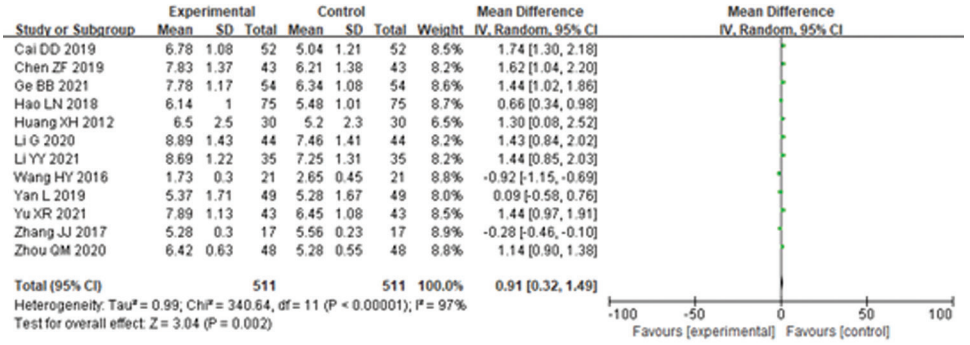


Figure 6. Comparison of estradiol level.

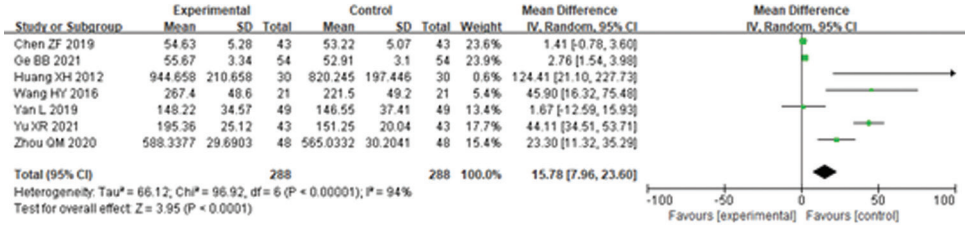
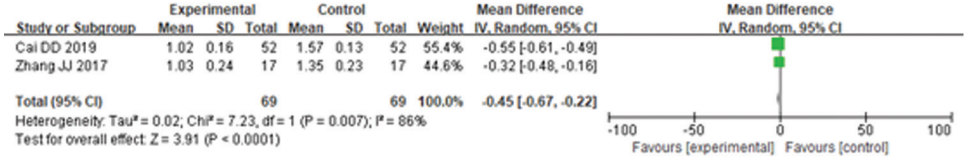


Figure 7. Comparison of luteinizing hormone/follicle stimulating hormone ratio.



Follicle-Stimulating Hormone Level

Heterogeneity was observed among the 12 studies reporting FSH levels. Meta-analysis via the random effects model showed the following: MD = 0.91; 95% CI, 0.32-1.49; $Z = 3.04$; $P = .002$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a higher FSH level than the hormone therapy alone group (see Figure 5).

Sensitivity analysis. The heterogeneity decreased significantly after excluding the studies by Haiyan Wang and Juanjuan Zhang, suggesting these papers may have been the main source of heterogeneity.

Estradiol Level

Heterogeneity was observed among the 7 studies that reported E_2 levels. Meta-analysis via the random effects model showed the following: MD = 15.78; 95% CI, 7.96-23.60; $Z = 3.95$; $P < .0001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a higher E_2 level than the hormone therapy alone group (see Figure 6).

Sensitivity analysis. The heterogeneity decreased significantly after excluding the paper by Xianrong Yu, suggesting that this study may have been the main source of heterogeneity.

Luteinizing Hormone/Follicle Stimulating Hormone Ratio

Heterogeneity was observed in the 2 studies that reported the LH/FSH ratio. Meta-analysis with the random effects model showed the following: MD = -0.45; 95% CI, -0.67 to -0.22; $Z = 3.91$; $P < .0001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a lower LH/FSH ratio than the hormone therapy alone group (see Figure 7).

Testosterone Level

Heterogeneity was observed among the 9 studies that reported testosterone (T) levels. Meta-analysis with the random effects model showed the following: MD = -0.36; 95% CI, -0.52 to -0.20; $Z = 4.31$; $P < .0001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a lower T level than the hormone therapy alone group (see Figure 8).

Sensitivity analysis. Heterogeneity decreased significantly after excluding the article by Juanjuan Zhang, suggesting that this study may have been the main source of heterogeneity.

Endometrial Thickness

Heterogeneity was observed among the 5 studies that reported endometrial thickness. Meta-analysis with the

Figure 8. Comparison of testosterone level.

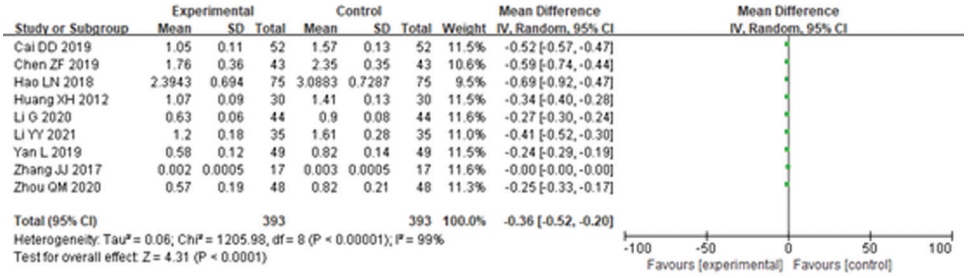


Figure 9. Comparison of endometrial thickness.

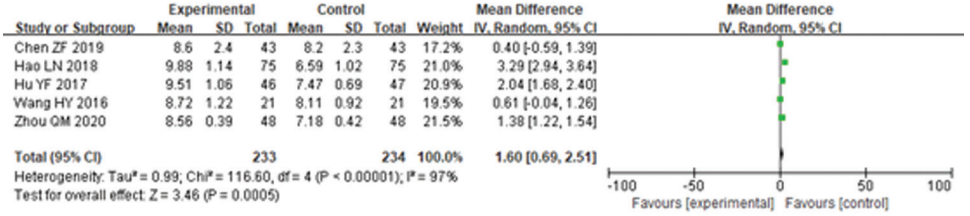


Figure 10. Comparison of overall rate of effective treatment.

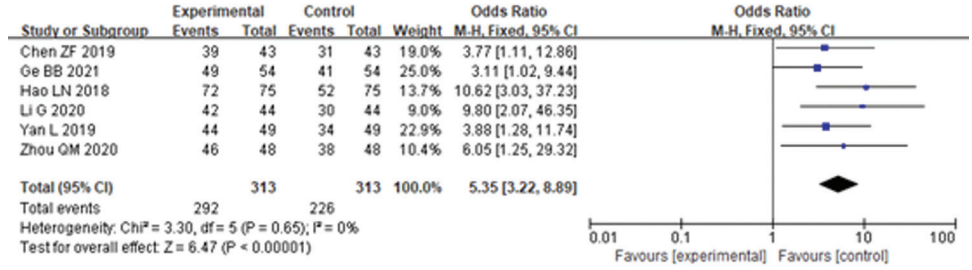
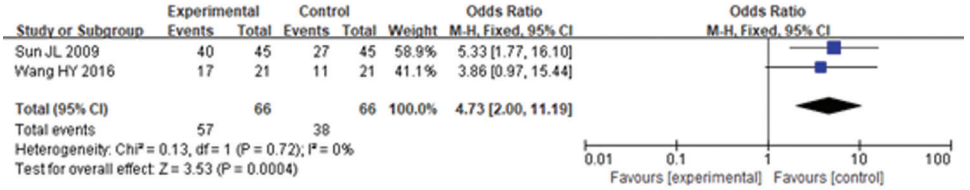


Figure 11. Comparison of overall rate of effective Traditional Chinese Medicine-based treatment.



random effects model showed the following: MD = -0.36; 95% CI, -0.52 to -0.20; $Z = 4.31$; $P < .0001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a lower T level than the hormone therapy alone group (see Figure 9).

Sensitivity analysis. Heterogeneity decreased significantly after excluding the article by Lina Hao, suggesting that this study may have been the main source of heterogeneity.

Overall Rate of Effective Treatment

There were 6 studies that reported the overall rate of effective treatment. Meta-analysis via the fixed effects model showed the following: Odds ratio (OR) = 5.35; 95% CI, 3.22-8.89; $Z = 6.47$; $P < .0001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a higher overall rate of effective treatment than the hormone therapy alone group (see Figure 10).

Overall rate of Effective Traditional Chinese Medicine-based Treatment

There were 2 studies that reported the overall rate of effective TCM-based treatment. Meta-analysis with the fixed effects model showed the following: OR = 4.73; 95% CI, 2.00-11.19; $Z = 3.53$; $P = .0004$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a higher overall rate of effective TCM-based treatment than the hormone therapy alone group (see Figure 11).

Figure 12. Comparison of basal body temperature.

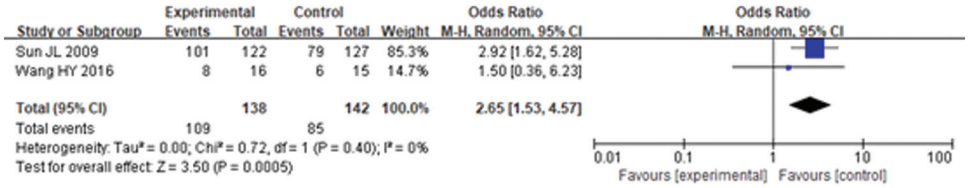


Figure 13. Comparison of left antral follicle count.

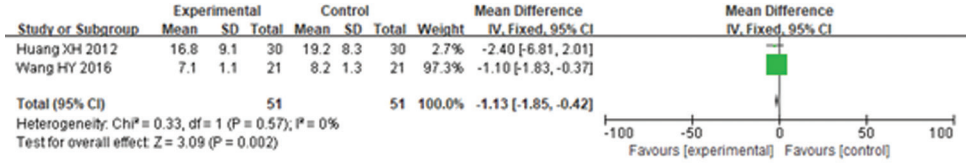


Figure 14. Comparison of right antral follicle count.

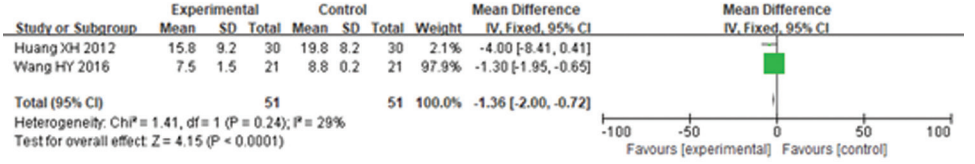


Figure 15. Comparison of left ovarian volume.

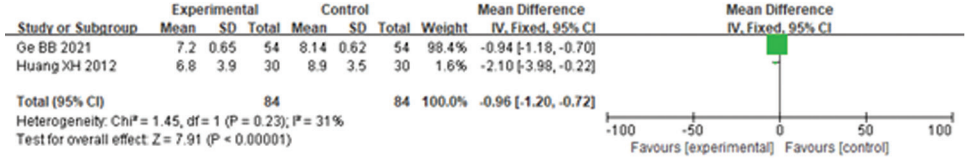
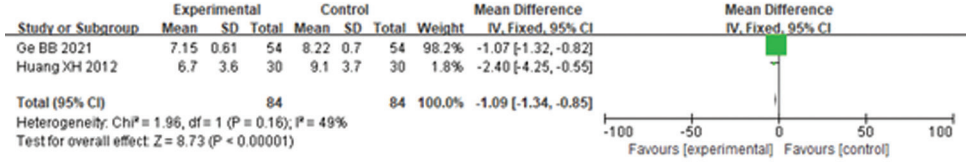


Figure 16. Comparison of right ovarian volume.



Basal Body Temperature

There were 2 studies reporting BBT. Meta-analysis with the fixed effects model showed the following: OR = 2.65; 95% CI, 1.53-4.57; $Z = 3.50$; $P = .0005$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a higher biphasic BBT than the hormone therapy alone group (see Figure 12).

Antral Follicle Count

There were 2 studies that reported left antral follicle count. Meta-analysis with the fixed effects model showed the following: MD = -1.13; 95% CI, -1.85 to -0.42; $Z = 3.09$; $P = .002$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a lower left antral follicle count than the hormone therapy alone group (see Figure 13).

Moreover, there were 2 other studies that reported right antral follicle count. Meta-analysis with the fixed effects model showed the following: MD = -1.36; 95% CI, -2.00 to -0.72; $Z = 4.15$; $P < .0001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a lower right antral follicle count than the hormone therapy alone group (see Figure 14).

Ovarian Volume

There were 2 studies that reported left ovarian volume. Meta-analysis with the fixed effects model showed the following: MD = -0.96; 95% CI, -1.20 to -0.72;, Z = 7.91; $P < .00001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a lower left ovarian volume than the hormone therapy alone group (see Figure 15).

There were 2 studies reporting right ovarian volume. Meta-analysis with the fixed effects model showed the following: MD = -1.09; 95% CI, -1.34 to -0.85; $Z = 8.73$;

Figure 17. Comparison of follicle count.

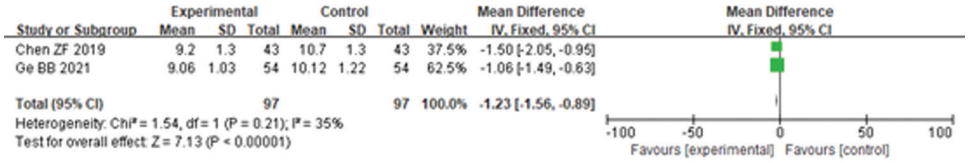


Figure 18. Comparison of maximum follicle diameter.

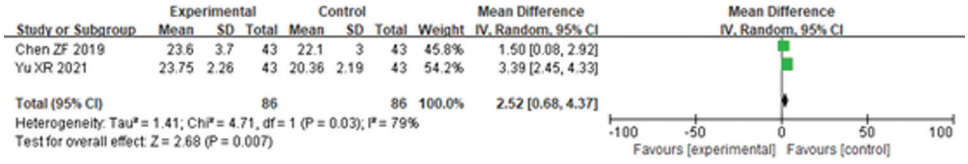


Figure 19. Comparison of hepatocyte growth factor.

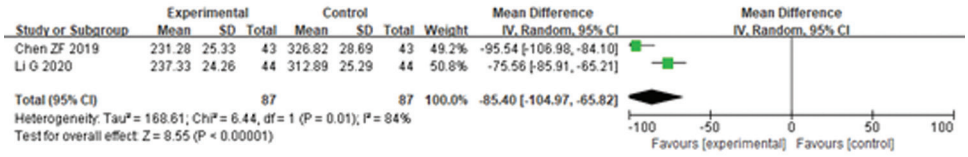
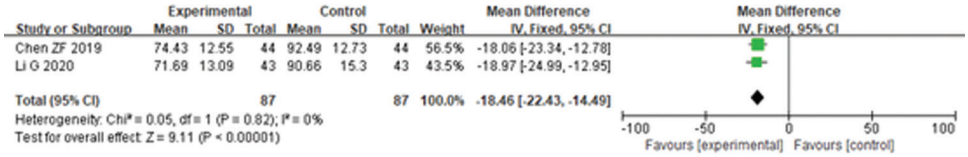


Figure 20. Comparison of vascular endothelial growth factor.



$P < .00001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a lower right ovarian volume than the hormone therapy alone group (see Figure 16).

Follicle Count

There were 2 studies that reported follicle count. Meta-analysis with the fixed effects model showed the following: MD = -1.23; 95% CI, -1.56 to -0.89; $Z = 7.13$; $P < .00001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a lower follicle count than the hormone therapy alone group (see Figure 17).

Maximum Follicle Diameter

Heterogeneity was observed in the 2 studies that reported maximum follicle diameter. Meta-analysis with the random effects model showed the following: MD = 2.52; 95% CI, 0.68-4.73; $Z = 2.68$; $P = .007$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a larger maximum follicle diameter than the hormone therapy alone group (see Figure 18).

Hepatocyte Growth Factor Level

Heterogeneity was observed in the 2 studies that reported HGF levels. Meta-analysis with the random effects model showed the following: MD = -85.40; 95% CI, -104.97 to -65.82; $Z = 8.55$; $P < .00001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a lower HGF level than the hormone therapy alone group (see Figure 19).

Vascular Endothelial Growth Factor Level

There were 2 studies that reported VEGF levels. Meta-analysis with the fixed effects model showed the following: MD = -18.46; 95% CI, -22.43 to -14.49; $Z = 9.11$; $P < .00001$. The statistically significant difference between the 2 groups suggested that the compound Xuanju capsule + hormone therapy group had a lower VEGF level than the hormone therapy alone group (see Figure 20).

Safety and Publication Bias

Adverse effects were reported in only 2 studies, and the details were not provided; hence, we were unable to perform a safety evaluation. We performed an inverted funnel plot analysis of the reciprocal of the OR standard errors for ovulation and pregnancy rates, LH, FSH, T, E_2 levels, endometrial thickness and overall rate of effective treatment because there were more than 5 metrics. We could analyze the publication bias by these metrics, and we found asymmetric distributions, suggesting that the studies had a small sample size and possible publication bias. The plots are displayed in Figures 21 through 28.

Figure 21. Funnel plot of ovulation rate.

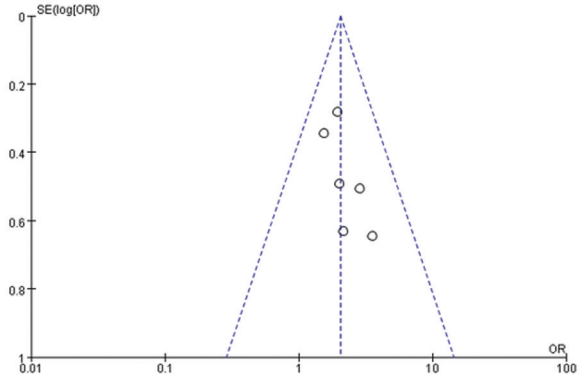


Figure 22. Funnel plot of pregnancy rate.

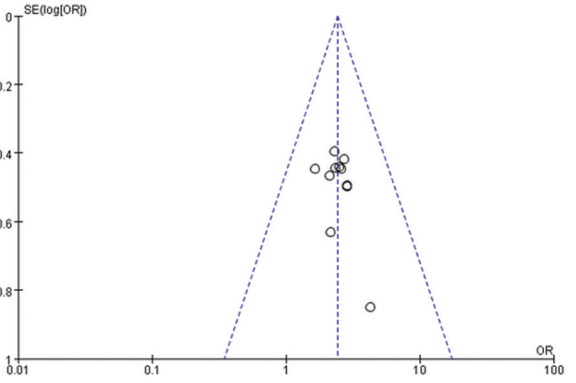


Figure 23. Funnel plot of luteinizing hormone level.

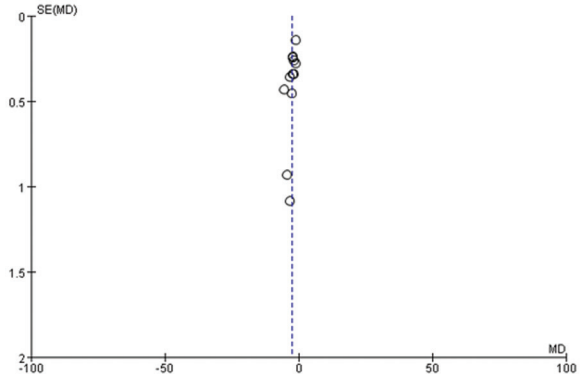


Figure 24. Funnel plot of follicle-stimulating hormone level.

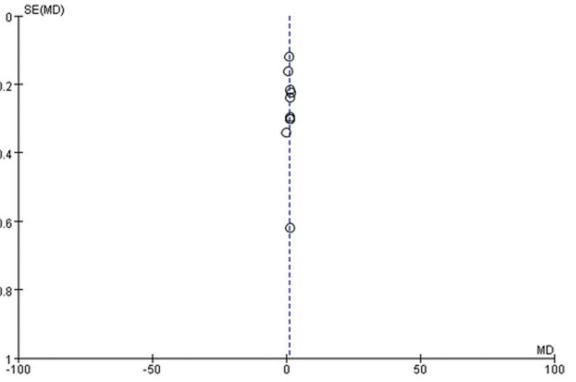


Figure 25. Funnel plot of estradiol level.

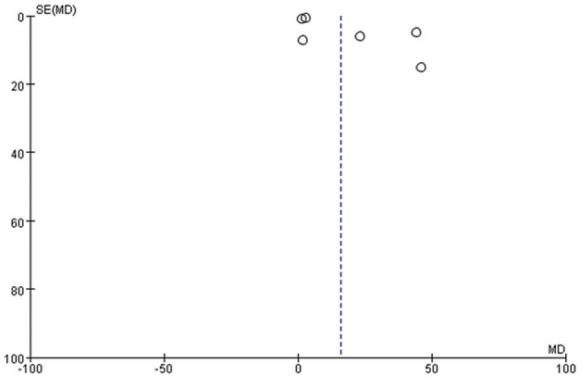


Figure 26. Funnel plot of testosterone level.

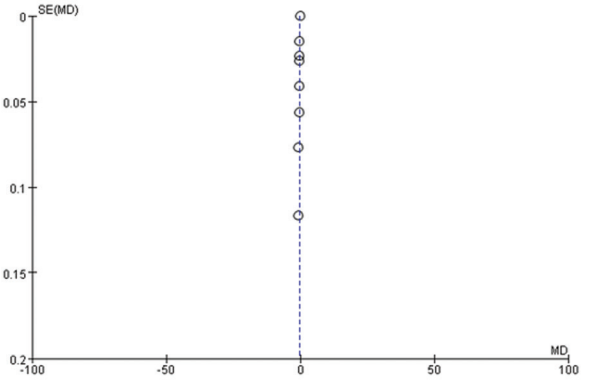


Figure 27. Funnel plot of endometrial thickness.

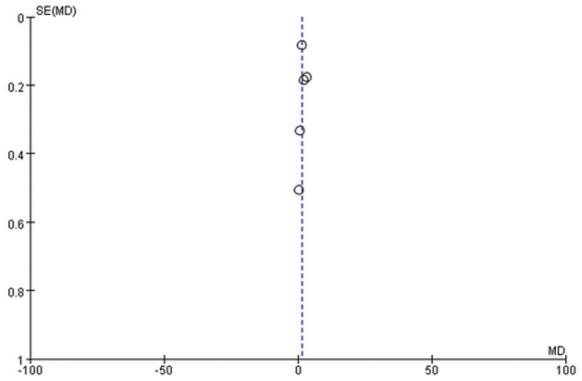
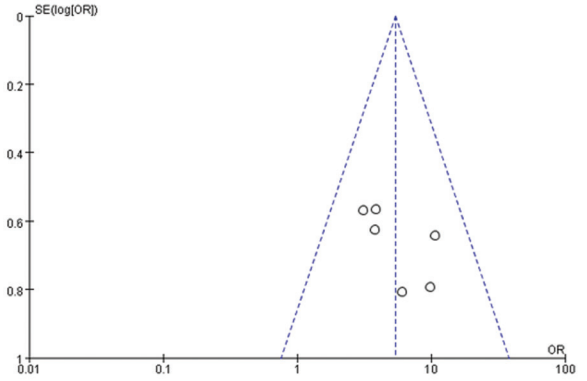


Figure 28. Funnel plot of overall rate of effective treatment.



DISCUSSION

The results of our study showed that the combination of compound Xuanju capsules and hormone therapy was more effective than hormone therapy alone in improving LH, FSH and E_2 levels; the overall rate of effective treatment; Kupperman score; ovulation rate; pregnancy rate; LH/FSH ratio; T level; endometrial thickness; overall rate of effective TCM-based treatment; BBT; ovarian volume; maximum follicle diameter; follicle count; and HGF and VEGF levels in patients with PCOS-related infertility.

PCOS is the main cause of ovulatory disorder-related infertility in women of reproductive age. PCOS causes hyperandrogenism, polycystic changes in the ovaries, obesity and hirsutism and eventually results in infertility, leading to a high physiological and psychological burden and affecting quality of life. Western allopathy-based hormone therapy—which relies on E_2, progesterone, clomiphene, letrozole, tamoxifen and tripurelin—is the most common method for treating PCOS-related infertility. Such treatment can improve sex hormone levels, promote ovulation and regularize the menstrual cycle. However, hormone therapy also has several adverse effects, such as cervical mucosal thickening, luteal insufficiency, luteinized unruptured follicle syndrome and endometrial thinning. Moreover, it also has shown low efficacy in improving clinical symptoms.

Some researchers have suggested that hormonal therapy combined with TCM can improve clinical effects in the treatment of gynecological diseases such as PCOS. Recent studies have suggested that compound Xuanju capsules are effective in the treatment of PCOS-related infertility. Compound Xuanju capsules are mainly composed of *Formica fusca* L., *Epimedium brevicornu*, *Fructus cnidii* and *Fructus lycii*. Monarch *Formica fusca L*. ants are sour, salty and warm and can promote healthy energy, nourish the blood and induce Yang Qi, thereby promoting ovulation. *Epimedium brevicornu* and *Fructus cnidii* can warm the kidney and invigorate Yang energy, as well as dispel wind and dampness. Among these, *Epimedium brevicornu* exhibits a hormone-like effect and can increase the weight of reproductive organs in animals. *Fructus lycii* can have good effects on the kidneys and negate emptiness, draw Yang from Yin and prevent the aforementioned disadvantages. Studies have suggested that compound Xuanju capsules are effective in warming the kidneys and uterus. Therefore, the use of compound Xuanju capsules along with hormone therapy provides combinatorial benefits and creates a more harmonious environment in the female reproductive system.

In our study, methodological quality assessment showed that most included studies were of low quality, with methodological issues related to randomization, blinding and follow-up. Such issues can lead to bias and affect the accuracy and reliability of the studies. A total of 14 studies were included in this meta-analysis, and although all articles mentioned the use of randomization, only 8 described the specific method (eg, randomization using a random number table). Concealment was not mentioned in most studies, and details of blinding, loss to follow-up and withdrawal were not specifically provided, affecting the strength of the evidence provided by the studies.

In most studies, the measures of efficacy were the ovulation and pregnancy rates; LH, FSH, T and E_2 levels; endometrial thickness; and overall rate of effective treatment. In contrast, few studies focused on the overall rate of effective TCM-based treatment, BBT, ovarian volume, maximum follicle diameter, follicle count or HGF and VEGF levels. Future RCTs should not only be designed in a more systematic and robust manner but should also include large sample sizes, strict randomization protocols and a double-blind approach.

SUMMARY

In summary, our meta-analysis showed that the combination of compound Xuanju capsules and hormone therapy is more effective than hormone therapy alone in treating PCOS-related infertility. However, these findings require validation via more rigorous double-blind RCTs with a large sample size. Such validation could increase the credibility of the results and provide more reliable evidence supporting the use of compound Xuanju capsules in combination with hormone therapy in treating PCOS-related infertility.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All experimental protocols involving animals were approved by the Ethics Committee of Zhenjiang Hospital of Traditional Chinese Medicine, Zhenjiang, China.

CONFLICT OF INTEREST

None.

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