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Original Research Article

Efficacy of pretreatment D-chiro-inositol and cyproterone acetate-ethinyl estradiol combination therapy compared to cyproterone acetate-ethinyl estradiol alone for ovarian response in polycystic ovary syndrome with high AMH

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a leading cause of anovulatory infertility, often associated with elevated AMH levels. This study evaluates whether adding D-chiro-inositol to cyproterone acetate–ethinyl estradiol improves ovarian response in PCOS women with high AMH. To assess the effects of pre-treatment with D-chiro-inositol and Cyproterone acetate-ethinyl estradiol compared to Cyproterone acetate-ethinyl estradiol alone for ovarian response in high AMH patient of PCOS.
Methods: This open-label randomized controlled trial was conducted at the Department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka, from July 2023 to June 2024. Sixty sub-fertile women with PCOS were randomized into two groups (n=30). Data were analyzed using SPSS version 25.0 and comparisons between groups were made using the Chi-square test, t-test or Mann-Whitney U test as appropriate. A p-value of <0.05 was considered statistically significant.
Results: Serum AMH and LH levels significantly decreased in both groups, with no significant difference between them. Although the experimental group showed a slightly higher ovarian response (74.07% compared to 69.23% in cycle 1; 76.92% compared to 72.73% in cycle 2), this was not statistically significant. Similarly, cumulative ovulation and pregnancy rates did not differ significantly between groups.
Conclusions: Pre-treatment with D-chiro-Inositol and cyproterone acetate–ethinyl estradiol combination therapy compared to cyproterone acetate–ethinyl estradiol alone, provides similar efficacy in terms of hormonal profile changes, ovarian response, cumulative ovulation rate and cumulative pregnancy rate in PCOS with high AMH.

Keywords: Cyproterone acetate ethinyl estradiol, D chiro-inositol, Polycystic ovary syndrome

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a multifactorial disorder identified when at least two of the following criteria are present: infrequent menstruation, signs or laboratory evidence of excess androgens and the presence of polycystic ovaries on ultrasound.[1] It is the most common female endocrinopathy among the reproductive age group and a primary cause of anovulatory infertility, affecting 5-10% of the female population.[2] The condition

is multifactorial and its management often involves addressing ovarian dysfunction, which can be linked to elevated anti-müllerian hormone (AMH) levels.[3] AMH, a member of the transforming growth factor beta (TGF-β) superfamily, plays a significant role in chronic anovulation by inhibiting continued follicular growth and development necessary for follicular maturation.[3] AMH levels are typically 2-4 times higher in women with PCOS than in healthy women, reflecting an increased production of AMH per follicle rather than an increased follicular pool.[4] Elevated AMH is associated with suppressed ovarian aromatase expression and FSH receptor expression, leading to follicular arrest and impaired dominant follicle selection.[4] This contributes to diminished ovarian response and the need for higher doses of ovulation-inducing drugs, such as clomiphene, letrozole or gonadotropins.[5-7]

The oral contraceptive pill (OCP) containing cyproterone acetate plus ethinyl estradiol (CPA/EE) combines the anti-androgenic properties of synthetic progestin (Cyproterone Acetate) with synthetic estrogen (Ethinyl Estradiol). CPA/EE has been shown to lower AMH levels in women with PCOS by reducing androgen production from the ovaries and adrenal glands, as well as improving clinical signs of hyperandrogenism, such as hirsutism.[8] Additionally, insulin-lowering medications like D-chiro-inositol are often used in PCOS treatment to improve metabolic function, lower AMH and regulate hyperandrogenism.[9] Research has demonstrated that OCP (CPA/EE) can reduce AMH levels by suppressing luteinizing hormone (LH) secretion, which is often elevated in anovulatory PCOS patients.[10,11] This reduction in LH may subsequently decrease AMH production by downregulating the overexpression of AMH-specific type 2 receptors on granulosa cells, which are typically enhanced by LH in PCOS.[12,13] By lowering testosterone and suppressing LH, CPA/EE significantly reduces AMH levels in the bloodstream.[14]

D-chiro-inositol, a second messenger of insulin, plays a critical role in ovarian physiology. It is converted from myoinositol by an insulin-dependent enzyme of the epimerase class and in PCOS, the ratio between D-chiro-inositol and myoinositol is altered due to insulin resistance.[9] D-chiro-inositol improves insulin signalling and has antioxidant, anti-aging and anti-inflammatory properties.[15] It also downregulates the expression of the steroidogenic enzyme aromatase, thereby increasing FSH release and promoting ovulation.[16] Additionally, D-chiro-inositol decreases circulating insulin and androgens, leading to a reduction in AMH levels.[17,18] Given these effects, D-chiro-inositol pre-treatment, along with CPA/EE, may offer a promising strategy for improving ovarian response in PCOS patients, particularly those with high AMH levels. The combination therapy of D-chiro-inositol and CPA/EE could provide a novel approach to improve ovarian response outcomes, especially in cases where conventional treatments such as letrozole fail.[19-21]

In conclusion, the present study aims to evaluate the impact of D-chiro-inositol combined with CPA/EE therapy compared to CPA/EE alone on AMH levels and ovarian response in PCOS women, addressing a significant gap in the management of PCOS with high AMH levels. This approach holds potential for optimizing fertility treatments and improving outcomes in anovulatory women with PCOS.

In conclusion, the present study aims to evaluate the impact of D-chiro-inositol combined with CPA/EE therapy compared to CPA/EE alone on AMH levels and ovarian response in PCOS women, addressing a significant gap in the management of PCOS with high AMH levels. This approach holds potential for optimizing fertility treatments and improving outcomes in anovulatory women with PCOS.

Objective

To assess the effects of pre-treatment with D-chiro-inositol and cyproterone acetate-ethinyl estradiol compared to cyproterone acetate-ethinyl estradiol alone for ovarian response in high AMH patient of PCOS.

METHODS

This open-label, parallel-design, randomized controlled trial was conducted at the Department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka, Bangladesh, from July 2023 to June 2024. A total of 60 patients diagnosed with polycystic ovary syndrome (PCOS), presenting with subfertility and elevated serum Anti-Müllerian Hormone (AMH) levels, were included, selected based on specific inclusion and exclusion criteria using purposive sampling. They were randomly allocated into two groups, with 30 patients in each group.

Inclusion criteria

Women diagnosed with polycystic ovary syndrome (PCOS) according to the rotterdam criteria. Age between 18 and 35 years. Body mass index (BMI) between 18.5 and 29.9 kg/m². Serum anti-müllerian hormone (AMH) level >5 ng/ml. History of primary or secondary subfertility

Exclusion criteria

Diagnosed case of endometriosis, bilateral tubal block, abnormal semen parameters of the husband, serum AMH level >15 ng/ml, contraindications to cyproterone acetate/ethinyl estradiol (CPA/EE), such as obesity, thromboembolism or breast carcinoma, known pulmonary, cardiac, hepatic or renal disease, use of hormonal therapy or metformin within the past 3 months, presence of uncontrolled endocrine disorders (e.g., diabetes mellitus, hypothyroidism) After obtaining approval from the Institutional Review Board (IRB), this Randomized Controlled Trial (RCT) was conducted at the Department

of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Patients diagnosed with polycystic ovary syndrome (PCOS) and subfertility, with serum Anti-Müllerian Hormone (AMH) levels≥5 ng/ml, attending the outpatient department (OPD) of Reproductive Endocrinology and Infertility at BSMMU, were considered for inclusion. On days 2–5 of a menstrual cycle, participants underwent a baseline transvaginal ultrasound to assess ovarian volume and antral follicle count (AFC), ensuring the absence of ovarian cysts before initiating treatment. Blood samples were collected during the follicular phase (Day 2–3) for measurement of serum FSH, LH and AMH levels. Participants were randomized in a 1:1 ratio using computer-generated random numbers into two groups. Group A (experimental group) received pre-treatment with D-chiro-inositol 500 mg once daily along with 2 mg cyproterone acetate (CPA) – 35 mcg ethinyl estradiol (EE) cyclically for 21 days over 3 months. Group B (control group) received only CPA–EE on the same dosage and schedule.

After completion of the 3-month pre-treatment, serum LH and AMH were reassessed and both groups underwent ovulation induction with letrozole 7.5 mg daily starting from Day 2 of menstruation for 5 days, repeated for 3 cycles. Follow-up visits included folliculometry via transvaginal ultrasound on Day 12 of each cycle to assess ovarian response, with further scans conducted until at least one preovulatory follicle of ≥18 mm diameter was observed.

A 5000 IU intramuscular hCG injection was administered when the follicle reached the appropriate size, followed by timed intercourse. Ovulation was confirmed by measuring serum progesterone on Day 21 and pregnancy was confirmed by serum β-HCG testing. If pregnancy was not achieved, the process was repeated for up to three cycles. Data were analyzed using SPSS version 25.0, with Chi-square, t-test or Mann-Whitney U test used as appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS

Table 1 shows the baseline demographic and clinical characteristics of participants in both Group A (D-Chiro-inositol and Cyproterone Acetate Ethinyl-estradiol) and Group B (Cyproterone Acetate Ethinyl-estradiol alone). The mean age was 24.9±3.9 years in Group A and 25.1±3.8 years in Group B, with most participants aged 22–25 years. Primary infertility was more prevalent in both groups. The mean BMI was comparable (25.7±2.6 kg/m² in Group A and 25.9±2.5 kg/m² in Group B) and mean waist circumference was 85.5±2.6 cm in Group A and 85.8±3.5 cm in Group B. No statistically significant differences were observed between groups (p>0.05).

Table 2 demonstrates that in Group A (D-Chiro-inositol and Cyproterone Acetate Ethinyl-estradiol combination group), the mean serum LH level significantly decreased from 9.8±5.8 mIU/mL before pre-treatment to 4.8±2.5 mIU/mL after pre-treatment, with a mean difference of 5.49 (95% CI: 3.99 to 6.98). Similarly, the mean serum AMH level reduced from 9.3±3.8 ng/mL to 4.9±2.1 ng/mL, with a mean difference of 4.43 (95% CI: 3.42 to 5.44). These reductions were statistically significant (p<0.001), indicating large effect of the pre-treatment. Table 3 shows that in Group B (Cyproterone acetate–ethinyl estradiol alone group), mean serum LH and AMH levels decreased significantly from their pre-treatment values, with a mean difference of 5.08 for LH and 3.48 for AMH. Table 4 shows that, after pre-treatment, the mean serum LH and AMH levels decreased in both groups but were not statistically significantly different between them. Table 5 shows that the ovarian response, in terms of the presence of a mature follicle, was comparable between the two groups across the 1st, 2nd and 3rd cycles. In the 1st cycle, 74.07% in Group A and 69.23% in Group B had mature follicles (RR=1.07; p=0.700). In the 2nd cycle, the rates were 76.92% in Group A compared to 72.73% in Group B (RR=1.05; p=0.738) and in the 3rd cycle, 71.43% in Group A and 76.47% in Group B (RR=0.93; p=0.510). These differences were not statistically significant.

Table 1: Baseline characteristics of the study participants (n=60).

Variable		Group A (Experimental group) (n=30)	Group B (Control group) (n=30)	P value
Age (in years)	18–21	6 (20.0%)	6 (20.0%)	a0.842^{ns}
	22–25	16 (53.3%)	10 (33.3%)	
	26–29	3 (10.0%)	10 (33.3%)	
	30–35	5 (16.7%)	4 (13.3%)	
	Mean±SD	24.9±3.9	25.1±3.8	
	Range (min–max)	19.0–35.0	19.0–35.0	
Type of infertility	Primary	19 (63.3%)	22 (73.3%)	b0.405^{ns}
	Secondary	11 (36.7%)	8 (26.7%)	
BMI (kg/m²)	18.5–24.9	13 (43.3%)	8 (26.7%)	a0.783^{ns}
	25.0–29.9	17 (56.7%)	22 (73.3%)	
	Mean±SD	25.7±2.6	25.9±2.5	
	Range (min–max)	21.2–29.9	19.7–29.8	
Waist circumference (cm)		85.5±2.6	85.8±3.5	a0.774^{ns}
Range (min–max)		79.0–92.0	77.0–93.0	

Note: ns: not significant, a- P value derived from unpaired t-test; b- P value derived from Chi-square test.

Table 2: Comparison of biochemical parameters before and after pre-treatment in group A (D-chiro-inositol and cyproterone acetate ethinyl-estradiol combination group).

Variables	Before pre-treatment (n=30) Mean±SD	After pre-treatment (n=27)* Mean±SD	Mean difference (95% CI)	Effect Size	P value
Serum LH (mIU/ml)	9.8±5.8	4.8±2.5	5.49 (3.99 to 6.98)	1.452	0.001[s]
Serum AMH (ng/ml)	9.3±3.8	4.9±2.1	4.43 (3.42 to 5.44)	1.741	0.001[s]

s: *3 cases dropped out at 3rd month; s = significant; P value derived from paired t-test

Table 3: Comparison of biochemical parameters before and after pre-treatment in group B (cyproterone acetate ethinyl-estradiol alone group).

Variables	Before Pre-treatment (n=30)	After pre-treatment (n=26)*	Mean Difference (95% CI)	Effect Size	P value
	Mean±SD	Mean±SD			
Serum LH (mIU/ml)	10.1±6.4	5.4±3.3	5.08 (3.56 to 6.59)	1.357	0.001[s]
Serum AMH (ng/ml)	9.1±2.5	5.5±2.3	3.48 (2.54 to 4.41)	1.502	0.001[s]

s: *4 cases dropped out at 3rd month; s = significant; P value derived from paired t-test

Table 4: Comparison of biochemical parameters between the two groups after pre-treatment (n=53).

Variables	Group A (Experimental group) (n=27) Mean±SD	Group B (Control group) (n=26) Mean±SD	Mean Difference (95% CI)	Effect Size	P value
Serum LH (mIU/ml)	4.8±2.5	5.4±3.3	-0.64 (−2.24 to 0.96)	0.204	0.428[ns]
Serum AMH (ng/ml)	4.9±2.1	5.5±2.3	-0.61 (−1.82 to 0.58)	0.272	0.305[ns]

ns = not significant; P value derived from unpaired t-test

Table 5: Comparison of ovarian response in terms of presence of mature follicle between two groups.

Mature follicle	Group A (Experimental group)		Group B (Control group)		RR (95%CI)	P value
	N	%	N	%		
1st cycle	**(n=27)**		**(n=26)**			
Yes	20	74.07	18	69.23	1.07 (0.76 to 1.50)	0.700[ns]
No	7	25.93	8	30.77		
2nd cycle	**(n=26)**		**(n=22)**			
Yes	20	76.92	16	72.73	1.05 (0.75 to 1.47)	0.738[ns]
No	6	23.08	6	27.27		
3rd cycle	**(n=21)**		**(n=17)**			
Yes	15	71.43	13	76.47	0.93 (0.64 to 1.36)	0.510[ns]
No	6	28.57	4	23.53		

ns = not significant; P value derived from unpaired t-test

Table 6: Comparison of ovulation rate between the two groups.

Ovulation rate	Group A (Experimental group)		Group B (Control group)		RR (95%CI)	P value
	N	%	N	%		
1st cycle	**(n=27)**		**(n=26)**			
Yes	20	74.07	20	76.92	0.96 (0.70 to 1.30)	0.810[ns]
No	7	25.93	6	23.08		
2nd cycle	**(n=26)**		**(n=22)**			
Yes	20	76.92	16	72.73	1.05 (0.75 to 1.47)	0.738[ns]
No	6	23.08	6	27.27		
3rd cycle	**(n=21)**		**(n=17)**			
Yes	15	71.43	12	70.59	1.01 (0.67 to 1.52)	0.617[ns]

Continued.

Ovulation rate	Group A (Experimental group)		Group B (Control group)		RR (95%CI)	P value
	N	%	N	%		
No	6	28.57	5	29.41		
Cumulative ovulation rate	**(n=27)**		**(n=26)**			
Yes	21	77.78	20	76.92	1.01(0.75 to 1.35)	0.941[ns]
No	6	22.22	6	23.08		

ns = not significant; P value derived from unpaired t-test

Table 7: Comparison of pregnancy rate between the two groups.

Pregnancy rate	Group A (Experimental group)		Group B (Control group)		RR (95% CI)	P value
	N	%	N	%		
1st cycle	**(n=27)**		**(n=26)**			
Yes	1	3.7	4	15.38	0.24 (0.02 to 2.01)	0.164[ns]
No	26	96.3	22	84.62		
2nd cycle	**(n=26)**		**(n=22)**			
Yes	5	19.23	4	18.18	1.05 (0.32 to 3.46)	0.611[ns]
No	21	80.77	18	81.82		
3rd cycle	**(n=21)**		**(n=17)**			
Yes	3	14.29	2	11.76	1.21 (0.22 to 6.45)	0.604[ns]
No	18	85.71	15	88.24		
Cumulative pregnancy rate	**(n=27)**		**(n=26)**			
Yes	9	33.33	10	38.46	0.86 (0.42 to 1.78)	0.697[ns]
No	18	66.67	16	61.54		

ns = not significant; P value derived from unpaired t-test

Table 6 shows that the cumulative ovulation rate was 77.78% in the experimental group and 76.92% in the control group, but the difference was not statistically significant when compared between the two groups. Table 7 shows that the cumulative pregnancy rate was 33.33% in the experimental group and 38.46% in the control group, but the difference was not statistically significant when compared between the two groups.

DISCUSSION

In this randomized clinical trial, we evaluated the effectiveness of pre-treatment with D-chiro-inositol combined with cyproterone acetate–ethinyl estradiol (CPA/EE) compared to CPA/EE alone prior to ovulation induction in patients with polycystic ovary syndrome (PCOS). PCOS presents with various phenotypes, including: hyperandrogenism with ovulatory dysfunction; hyperandrogenism with polycystic ovarian morphology; ovulatory dysfunction with polycystic ovarian morphology; and oligo-ovulation with both polycystic ovarian morphology and hyperandrogenism. Due to considerable individual variation among these phenotypes, the clinical response to treatment remains inconsistent.[22] D-chiro-inositol (DCI), a naturally occurring molecule, has drawn interest for its role in PCOS management due to its insulin-sensitizing properties, which help in enhancing insulin signalling and reducing insulin resistance.[23] The combined oral contraceptive CPA/EE, which contains cyproterone acetate (an antiandrogen) and ethinyl estradiol (a synthetic estrogen), has been shown to effectively regulate menstrual cycles, improve symptoms such as hirsutism and acne and lower serum anti-Müllerian hormone (AMH) levels.

In the study, the mean age was 24.9±3.9 years in Group A (DCI + CPA/EE) and 25.1±3.8 years in Group B (CPA/EE alone). A randomized controlled trial by Banu et al, reported a comparable mean age of 26.8±3.6 years in the group receiving CPA/EE for six months.[2] Similarly, Akhter et al, found the mean age to be 26.3±4.3 years in the DCI-treated group.[24] These findings are similar with the present study. Most patients in both groups in our study had primary subfertility, accounting for 63.33% in Group A and 73.33% in Group B, with no statistically significant difference between them ($p>0.05$). Akhter et al, similarly reported primary infertility in 76.7% of DCI group patients and 73.3% in the placebo group.[24] Chowdhury et al, found that 86% of patients in the EE/CPA+letrozole group had primary infertility.[8] These findings are consistent with our study. The mean BMI in our study was 25.7±2.6 kg/m² in Group A and 25.9±2.5 kg/m² in Group B, with mean waist circumference of 85.5±3.6 cm and 85.8±3.5 cm, respectively. The differences between groups were not statistically significant ($p>0.05$). Akhter et al, also reported non-significant differences in BMI and waist circumference between the DCI and placebo groups. Chowdhury et al, observed a mean BMI of 25.3±3.0 kg/m² in the EE/CPA+letrozole group, while Banu et al, reported

a mean BMI of 26.3±4.9 kg/m² in the CPA/EE group.[2,8,24] These values are comparable to our findings. After three months of pre-treatment in Group A, there was a significant reduction in mean serum LH levels, declining from 9.8±5.8 to 4.8±2.5 mIU/mL (mean difference: 5.49). Similarly, the mean serum AMH levels decreased notably from 9.3±3.8 to 4.9±2.1 ng/mL (mean difference: 4.43). Genazzani et al, found a significant LH reduction (mean difference: 2.6) after 12 weeks of DCI (500 mg/day).[25] Pizzo et al reported a mean LH reduction of 4.6 with DCI therapy (1 g/day for 6 months).[26] La Marca et al observed a significant decrease in AMH (mean difference: 1.4) after 12 months of DCI (1000 mg/day).[27] The higher LH and AMH reductions observed in our study may be due to the additive effect of CPA/EE combined with DCI.

In Group B, the mean serum LH decreased significantly from 10.1±6.4 to 5.4±3.3 mIU/ml (mean difference: 5.08) and AMH dropped from 9.1±2.5 to 5.5±2.3 ng/ml (mean difference: 3.48). According to Chowdhury et al, LH decreased with a mean difference of 5.37 and AMH decreased with a mean difference of 3.7 after three months of pre-treatment with 35 µg ethinyl estradiol and 2 mg cyproterone acetate in a randomized controlled trial.[8] Banu et al found even greater reductions (LH: 10.6, AMH: 5.2), likely due to their longer treatment duration of six months.[2] This explains the slightly lower reductions observed in our study. Although both groups showed significant reductions in LH and AMH after 3 months of pre-treatment, the difference in mean reduction between the groups was not statistically significant. Akhter et al, reported a significant LH reduction in the DCI group (mean difference: -2.43±1.88) compared to placebo (-0.08±0.22).[24] Banu et al, also observed significantly greater reductions in LH and AMH with CPA/EE compared to metformin (mean difference: 2.62).[2] The lack of significant difference in our study may be attributed to the small sample size, shorter duration and single-center design. Regarding follicular response, in the first and second cycles, more patients developed mature follicles in Group A compared to Group B, while in the third cycle, Group B had a higher number of mature follicles. Mean endometrial thickness was also higher in Group A. However, none of these differences reached statistical significance ($p>0.05$). To date, no human studies have specifically assessed the effects of DCI+CPA/EE or CPA/EE alone on follicular maturation and endometrial thickness.

Ovulation, assessed via day 21 serum progesterone, was slightly more frequent in Group A than Group B, though the difference was not statistically significant. The overall ovulation rate observed was 77.78% in Group A and 76.92% in Group B, indicating comparable efficacy between the two treatment groups. Galazis et al, in a systematic review of eight studies (n=479), found increased ovulation rates with DCI in PCOS patients.[28] Iurono et al, showed 60% ovulation in the DCI group (600 mg/day) compared to 20% in placebo.[29] Chowdhury et al, reported a significantly higher cumulative ovulation rate (82.4%) in the letrozole+CPA/EE group compared to the letrozole-only group (43%).[8] Similarly, Chen et al, found ovulation rates of 82.44% with CPA/EE pre-treatment followed by letrozole compared to 81.1% in the letrozole-only group.[30] These findings are in line with our study. In the study, the cumulative pregnancy rate was 33.33% in Group A (D-chiro-inositol plus CPA-EE) and 38.46% in Group B (CPA-EE alone), with no significant difference between groups. Unfer et al, reported a lower pregnancy rate (24%) with DCI during ICSI cycles, possibly due to different protocols.[31] Our slightly higher rate may result from three months of combined pre-treatment reducing AMH and improving folliculogenesis. Chowdhury et al, found pregnancy rates 2.68 times higher with CPA+EE pre-treatment before letrozole versus letrozole alone.[8] Chen et al, reported similar cumulative pregnancy rates between CPA+EE plus letrozole and letrozole-only groups, consistent with our findings.[30]

This study had some limitations like the study was conducted with a relatively small sample size and over a short duration, primarily due to a restricted timeframe. Neither participants nor investigators were blinded to the treatment allocation following randomization, which may have introduced performance bias. All participants were recruited from a single department of one tertiary-level hospital, limiting the generalizability of the findings and challenging the external validity. Detection bias may have occurred due to the lack of blinding during outcome assessment. Attrition bias could not be ruled out, as participant dropouts may have influenced the results.

CONCLUSION

Pre-treatment with D-chiro-Inositol and cyproterone acetate–ethinyl estradiol combination therapy, compared to cyproterone acetate–ethinyl estradiol alone, provides similar efficacy in terms of hormonal profile changes, ovarian response, cumulative ovulation rate and cumulative pregnancy rate in PCOS with high AMH.

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