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Hydroxychloroquine enhances insulin sensitivity and ameliorates abnormal lipid metabolism in obese women with polycystic ovary syndrome

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Abstract

Background Hydroxychloroquine (HCQ) is frequently utilized in rheumatic immune disorders and has been discovered to exert hypoglycemic effects in some obese women with polycystic ovary syndrome(PCOS), however, the precise efficacy and mechanism of action remain ambiguous.

Objective To examine the impact of HCQ on glucose and lipid metabolism as well as sex hormone levels in obese women with PCOS.

Method Fifty obese women with PCOS were randomly allocated into two groups: HCQ group ($n=25$) and metformin (MET) group ($n=25$). The HCQ group received a daily dose of 200 mg hydroxychloroquine, while the MET group received a daily dose of 1000 mg metformin. Body fat parameters, glucose and lipid metabolism levels, as well as hormone levels were evaluated. Additionally, the incidence of pregnancy within six months following treatment was also assessed. Network pharmacology was also employed to analyze the potential molecular mechanism.

Result Patients in the HCQ group ($n=20$) and MET group ($n=23$) were ultimately included for analysis. Following treatment, both groups exhibited significant improvements in body fat distribution and glucose metabolism status, with the HCQ group demonstrating a notable advantage over the MET group in increasing insulin sensitivity index (ISI)(HCQ:1.87 ± 0.21,MET:1.75 ± 0.29). Serum lipid levels [Serum total cholesterol(TC, mmol/L) (HCQ:4.51 ± 0.87,MET:5.05 ± 0.65), triglyceride(TG, mmol/L)(HCQ:1.36 ± 0.51,MET:1.67 ± 0.72), low-density lipoprotein (LDL, mmol/L)(HCQ:2.66 ± 0.98,MET:0.47 ± 1.42),decreased in both groups post-treatment, with the HCQ group displaying clear advantages compared to the MET group. The improvement of sex hormone levels was not pronounced in either group, although there was an overall downward trend.

Conclusion The potential benefits of HCQ in the management of in obese women with PCOS include significant improvements in body fat distribution, glucose and lipid metabolism levels, as well as correction of hormonal disorders.

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Keywords Hydroxychloroquine, Polycystic ovary syndrome, Insulin resistance, Lipid metabolism

Introduction

Polycystic ovary syndrome (PCOS) is the most prevalent endocrine disorder in women of reproductive age, with an incidence of approximately 10% [1]. The syndrome is marked by hypoovulation or anovulation, polycystic ovary morphology, and clinical or biochemical manifestations of hyperandrogenemia [1–3]. The most frequent symptoms encompass irregular menstruation, infertility, and hirsutism [4]. PCOS is also associated with a long-term heightened risk of obesity and insulin resistance (IR), along with type 2 diabetes (T2D) and metabolic syndrome [5, 6].It has been reported that over 60% of PCOS patients are obese or overweight [7], obesity can give rise to severe anxiety and a decreased quality of life [8]. Furthermore, Obesity-induced lipotoxicity not only results in chronic inflammation and hyperinsulinemia, but also is closely associated with hyperandrogenism [9, 10], which significantly impacts the menstrual function and fertility of women of reproductive age.

Lifestyle interventions (including any combination of exercise, diet, and behavior modification interventions) are the recommended first-line treatment for women with PCOS [11]. A number of studies have demonstrated that a minor weight loss of up to 5% can restore menstrual cycles and ovulation, and can also enhance metabolic variables [11–13]. However, numerous patients are unable to lose weight through lifestyle modifications or regain weight rapidly after initial weight loss, which poses a significant clinical issue [14, 15].And now, PCOS women with fertility requirements are often treated with oral contraceptives, anti-androgen drugs, insulin sensitizers, and ovulation inducers [16]. However, correcting the metabolic disorder in PCOS patients with obesity or abnormal lipid metabolism is challenging. Additionally, they exhibit poor responsiveness to ovulation-promoting drugs, resulting in a low clinical pregnancy rate and live birth rate which exacerbates the occurrence and development of pregnancy complications.

Hydroxychloroquine (HCQ), a traditional anti-rheumatic medication, is considered the primary treatment for various autoimmune diseases. In recent years, it has been discovered to have hypoglycemic effects [17–20] and is recommended as a third-line option for treating type 2 diabetes mellitus [21]. We have observed improvement in abnormal glucose and lipid metabolism as well as sex hormone levels in obese PCOS patients with rheumatoid immune disease following HCQ treatment. The study recruited obese women with PCOS and abnormal glucose and lipid metabolism to investigate the potential of HCQ in improving their metabolic abnormalities, sex hormone status, and fertility.

Materials and methods

Research object selection and grouping

The study included 50 obese women with PCOS who visited the Outpatient Department of Reproduction and Genetics at the Affiliated Hospital of Shandong University of Traditional Chinese Medicine from November 1, 2022 to 2023. (Our actual recruitment date was postponed by one year due to the epidemic.). According to the simple randomization principle, the patients were randomly allocated into two groups: The HCQ group received a daily dose of 200 mg hydroxychloroquine, while the MET group received a daily dose of 1000 mg metformin. The study was approved by the Ethics Committee of the Center for Reproduction and Genetics of the Affiliated Hospital of Shandong University of Traditional Chinese Medicine. Figure 1 illustrates the main research line of this paper.

Inclusion criteria: women diagnosed with PCOS according to the Rotterdam criteria 2003 [22], with at least two of the following symptoms; infrequent ovulation or anovulation; hyperandrogenism or clinical manifestations of high blood androgen; ultrasound findings of polycystic ovaries in one or two ovaries, or ≥12 follicles measuring 2–9 mm in diameter, and/or ovarian volume≥10 mL; aged between 20 and 36 years; According to the literature, a body mass index (BMI) value greater than or equal to 24 kg/m^2 [23, 24] and the value of homeostasis model insulin resistance index (HOMA-IR) value greater than or equal to 2.69 [25]; low titer positive anti-nuclear antibody (1:100-1:320) present without clinical manifestations of rheumatic immune disease, and negative anti-nuclear antibody spectrum.

Exclusion criteria: individuals were excluded from the study if they had other endocrine disorders, such as androgen-secreting tumors, suspected Cushing's syndrome, non-classic congenital adrenal hyperplasia (17-hydroxyprogesterone <3 nmol/L), thyroid dysfunction (thyroid stimulating hormone≥4.78 mIU/ml), hyperprolactinemia (fasting prolactin<26 ng/ml), type I diabetes or poorly controlled type II diabetes, stage 2 hypertension (resting blood pressure≥160/100 mmHg), psychiatric diagnoses, or were using psychiatric medications including antidepressants. Additionally, participants who had received any pharmacological treatment within the past 12 weeks (such as cortisone, antidepressants, antidiabetic medications including insulin and

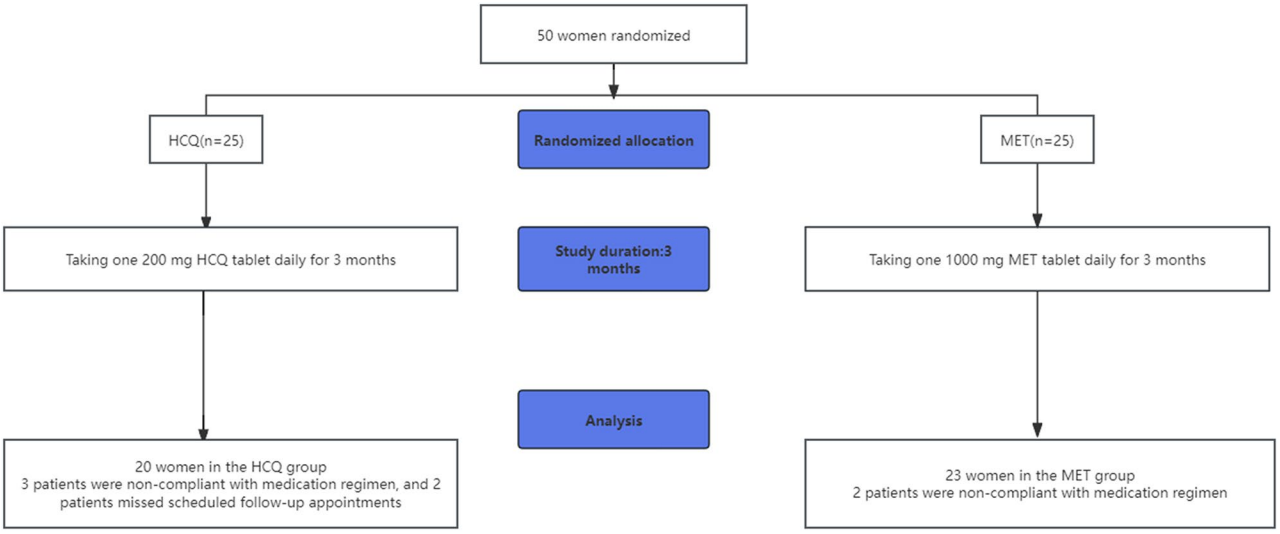

Fig. 1 Flow chart

acarbose, hormonal contraceptives, hormonal ovulation induction, or other drugs deemed at the discretion of the investigator) were also excluded from the study.

Shedding criteria: Patients who voluntarily withdrew from the trial or failed to return to the clinic on time due to personal reasons, resulting in a lack of major clinical data.

Treatment methods

The HCQ group received a daily dose of 200 mg hydroxychloroquine (Fenle, Shanghai Shangyao Sino-Western Pharmaceutical Co., LTD.); The MET group received a daily dose of 1000 mg metformin. (Gewatazi, Merck Jiangsu Co., LTD.). All patients had a daily dietary intake of 1500–1700 kcal and maintain moderate exercise three to five days a week. A course of treatment lasted for three months.

Measurement of observation indicators

Body fat parameters

Body composition analysis was carried out on an empty stomach in the morning during the non-menstruating period(Only in one's shirt).Weight(kg), body mass index (BMI, kg/m2), Waist(cm), Waist-to-hip ratio(WHR), Body fat percentage(FAT, kg), body fat percentage(BFP,%),Visceral fat index and area(VFI and VFA, cm^2), and Basal metabolic rate(BMR, kcal) were measured with a body composition analyzer (Jawon Medical Co., Ltd., Korea), with a precision of 0.1 kg and 1 cm, respectively. All the study participants were required to fast for 12 h.

Biochemical analysis

Peripheral blood samples were obtained from all study participants after overnight fasting using a standard venipuncture technique for hormonal and metabolic assessments. On the second day of the follicular phase, blood samples were taken to measure the levels of testosterone (T, nmol/L), luteinizing hormone (LH, mIU/ mL), follicle-stimulating hormone (FSH, mIU/mL), LH/FSH is the ratio of the two. Concurrently, Venous blood samples were drawn to measure fasting blood glucose (FBG, mmol/L) using the hexokinase method and fasting insulin (FINS,μU/mL) levels using the chemiluminescence technique. IR was assessed using the following formula: FBG × FINS/22.5 = HOMA-IR, ISI was calculated using the formula 1/FBG×FINS [26]. Sex hormone binding globulin (SHBG, nmol/L) and free testosterone (FT, pg/mL) were measured by liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS). Blood lipids, including total cholesterol (TC, mmol/L), triglyceride (TG, mmol/L), high-density lipoprotein cholesterol (HDL-C, mmol/L), and low-density lipoprotein cholesterol (LDL-C, mmol/L), apolipoproteinA1 (APOA1,g/L) and apolipoprotein B(APOB, g/L) were analyzed using the enzymatic analysis technique.

Tests were done using standard commercial kits (Randox Laboratories, Antrim, U.K.) and measured by Siemens Immulite 2000 immunoassay system (Siemens Healthcare Diagnostics, Siemens, Germany).

Pregnancy follow-up

Pregnancy follow-up was carried out through outpatient visits, telephone calls or WeChat to document their pregnancy condition.

Network pharmacological analysis

The 2D and 3D structures of HCQ were retrieved from Pubchem, followed by target identification using Pharmmapper and SwissTargetPrediction databases.

Relevant targets for PCOS were obtained from GeneCards, OMIM, DisgeNet, and PharmGKB databases. The protein interaction network was constructed using String database, and visualization analysis was performed with cytoscape3.9.1 to identify the top 10 core genes based on degree value. GO and KEGG enrichment analysis of intersection genes was carried out using DAVID database to determine the top 10 pathways. Finally, we performed molecular docking on the primary target to verify its binding activity.

Statistical methods

Statistical analysis was conducted using SPSS 26.0 software. For measurement data conforming to normal distribution, the mean±standard deviation (SD) was used for representation. Paired sample t-tests were employed for intra-group comparison when variance was homogeneous, and two independent samples t-tests were used for inter-group comparison. Non-parametric tests were utilized when variance was uneven. Measurements that did not conform to the normal distribution were represented by the median (interquartile distance) [M (IQR)], and comparison between groups was performed using the Wilcoxon rank sum test. The statistical data were expressed as frequency and percentage (n,%), with group comparisons conducted using $\chi 2$ test. Bilateral testing was applied in all cases, with $P<0.05$ considered statistically significant. Origin 2022 software was used for statistical mapping.

Results

Comparison of baseline characteristics

In the HCQ group, 3 patients were non-compliant with medication regimen, and 2 patients missed scheduled follow-up appointments. In the MET group, 2 patients were non-compliant with medication regimen. None of the included patients in either the HCQ group ($n=20$) or MET group ($n=23$) experienced serious adverse reactions during treatment. The mean age of patients in the HCQ group was 27.11±3.05 years, ranging from 22 to 33 years. The mean age of patients in the MET group was 28.33±3.77 years, ranging from 20 to 36 years. There were no significant differences in baseline characteristics between the two groups, indicating comparability ($P>0$ 0.05). Additionally, there were no significant differences in body fat distribution, glucose and lipid metabolism, as well as sex hormones between the two groups before treatment ($P>0$ 0.05).

Comparison of body fat parameters

After treatment, the body fat distribution index parameters in both groups were significantly lower compared to before treatment ($P<0.05$). However, there was no significant difference between the two groups after treatment. Please refer to Table 1; Fig. 2 for detailed information.

Comparison of glucose metabolism

Following treatment, the FBG levels in both groups decreased compared to pre-treatment levels. The HCQ group did not show statistical significance ($P>0.05$), while the MET group demonstrated statistical significance ($P<0.05$). Additionally, FINS and HOMA-IR levels in both groups were lower post-treatment, with statistically significant differences ($P<0.05$). The ISI for both groups was higher post-treatment, although the difference was not statistically significant ($P>0.05$). However, it is evident that the HCQ group had a greater advantage in increasing ISI. There were no significant differences in glucose metabolism indexes between the groups before and after treatment ($P>0.05$). Please refer to Table 2; Fig. 3 for further details.

Comparison of lipid metabolism

The levels of TC, TG, LDL-C and APOB in both groups were significantly lower after treatment compared to before treatment. Specifically, the HCQ group showed a statistically significant decrease ($P<0.01$), while the MET group did not show a significant difference ($P>0.05$). HDL-C and APOA1 levels increased significantly in the HCQ group after treatment ($P<0.05$), whereas there

Table 1 Body fat distribution in the two groups before and after treatment

Index	HCQ			MET		
	Before	After	*P*	Before	After	*P*
Weight (kg)	84.72±13.68	80.99±12.45	0.003	82.14±11.09	78.88±10.69	0.004**
BMI(kg/m^2)	32.16±4.96	30.59±4.23	0.006	30.98±4.03	29.72±4.19	0.003**
Waist(cm)	94.42±9.35	91.67±8.99	0.003	91.85±7.32	89.35±6.96	0.005**
WHR	0.86±0.05	0.85±0.05	0.034	0.85±0.04	0.84±0.03	0.045*
Fat(kg)	32.74±7.93	30.39±7.63	0.003	30.55±6.22	28.43±5.92	0.005**
BFP(%)	38.12±3.40	37.07±3.95	0.020	36.86±3.26	35.73±3.04	0.023*
VFI	12.88±2.23	12.24±2.66	0.029	12.21±2.39	11.42±2.24	0.035*
VFA(cm^2)	109.13±28.69	99.119±31.881	0.004	99.47±25.43	90.74±23.06	0.018*
BMR(kcal)	1338.24±66.54	1320.41±59.49	0.009	1331.05±51.97	1317.00±50.09	0.008**

Note $P<0.05$**, $P<0.01$**

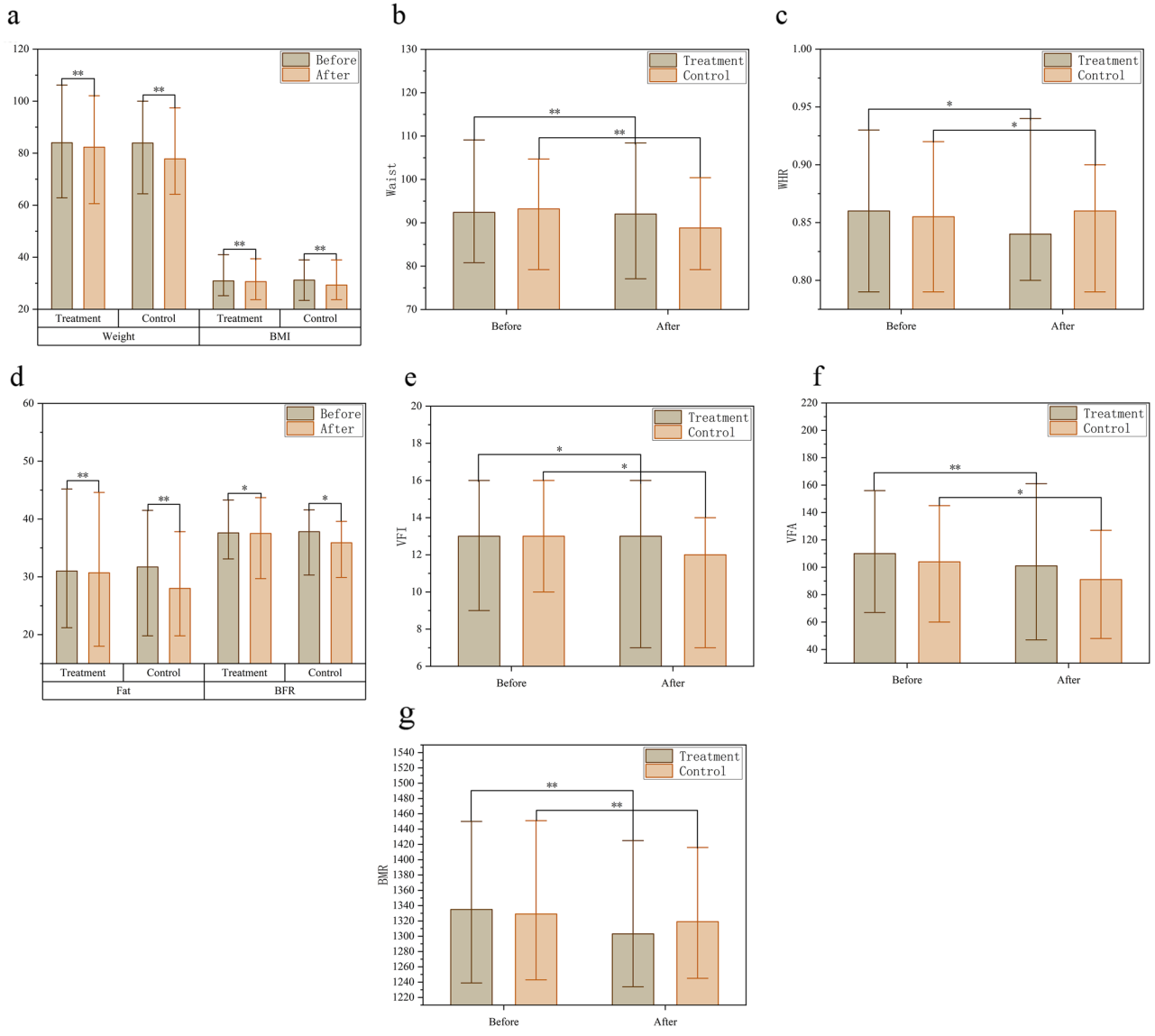

Fig. 2 The weight (**a**), BMI (**a**), waist (**b**), WHR (**c**), fat (**d**), BFR (**d**), VFI (**e**), VFA (**f**) and BMR (**g**) were compared between the two groups before and after treatment

Table 2 Glucose metabolism distribution in the two groups before and after treatment

Index	HCQ			MET		
	Before	After	*P*	Before	After	*P*
FBG(mmol/L)	5.63 ± 0.58	5.45 ± 0.51	0.153	5.94 ± 0.69	5.63 ± 0.29	0.040*
FINS(μU/mL)	27.59 ± 15.67	17.14 ± 8.90	0.015	26.01 ± 14.54	16.48 ± 8.04	0.001**
HOMA-IR	6.86 ± 3.73	4.27 ± 2.61	0.012	7.35 ± 3.77	4.83 ± 2.88	0.007**
ISI	1.79 ± 0.25	1.87 ± 0.21	0.095	1.74 ± 0.35	1.75 ± 0.29	0.825

Note *P*<0.05**, *P*<0.01**

was no significant change in the MET group ($P>0.05$). There were no significant differences in TC, TG, APOA1 and APOB between groups before and after treatment ($P>0.05$), but there were significant differences in HDL-C and LDL-C between groups before and after treatment ($P<0.01$). Please refer to Table 3; Fig. 4 for more details.

Comparison of sex hormone levels

The levels of FSH, T and FT in both groups were lower after treatment compared to before treatment, but the difference was not statistically significant ($P>0.05$). The LH/FSH ratio in both groups showed an increase compared to before treatment, with no statistical significance

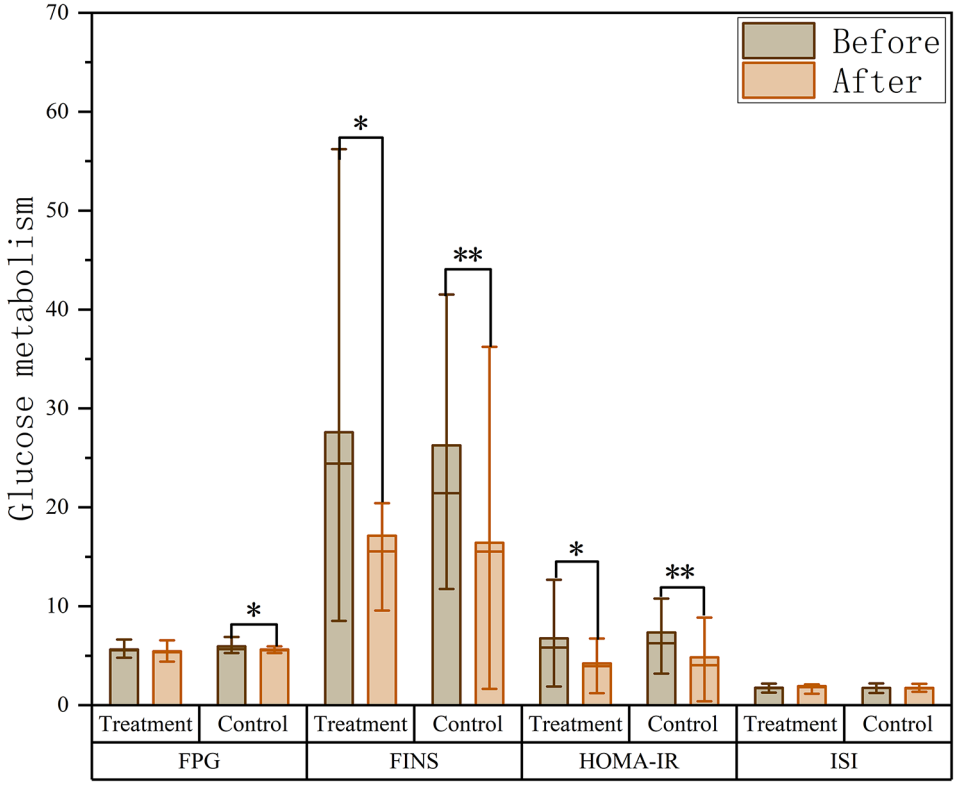

Fig. 3 Glucose metabolism indexes were compared between the two groups before and after treatment

Table 3 Comparison of lipid metabolism indexes between the two groups

Index	HCQ			MET		
	Before	After	*P*	Before	After	*P*
TC(mmol/L)	5.06 ± 0.77	4.51 ± 0.87	0.004	5.15 ± 0.82	5.05 ± 0.65	0.593
TG(mmol/L)	1.65 ± 0.66	1.36 ± 0.51	0.013	1.73 ± 0.68	1.67 ± 0.72	0.655
HDL-C(mmol/L)	1.01 ± 0.18	1.09 ± 0.24	0.046	1.08 ± 0.18	1.07 ± 0.12	0.845
LDL-C(mmol/L)	3.18 ± 0.77	2.66 ± 0.98	0.001	3.14 ± 0.54	3.06 ± 0.47	0.647
APOA1(g/L)	1.39 ± 0.20	1.32 ± 0.23	0.013	1.33 ± 0.17	1.42 ± 0.24	0.193
APOB(g/L)	0.99 ± 0.21	0.87 ± 0.26	0.044	1.06 ± 0.34	0.97 ± 0.14	0.388

Note *P*<0.05**, *P*<0.01**

($P>0.05$). In the HCQ group, SHBG levels were higher after treatment, while in the MET group they were lower after treatment, with no statistical significance ($P>0.05$). LH levels decreased in the HCQ group and increased in the MET group after treatment, with no statistical significance ($P>0.05$). Please refer to Table 4; Fig. 5 for more details.

Pregnancy outcome within six months after treatment

In the HCQ group, among the 20 patients, 1 had no fertility requirement(Patient unmarried), and the remaining patients underwent a pregnancy test after an average of 3.39±1.24 months. In the MET group, there were 23 patients with a pregnancy test time of 2.74±1.28 months, and there was no statistically significant difference between the two groups ($P>0.05$). The periodic pregnancy rate also showed no significant difference between the two groups ($P>0.05$). Please refer to Table 5 for more details.

Results of network pharmacological analysis

Through screening, 256 action targets of hydroxychloroquine were identified, with 133 overlapping genes found among PCOS disease targets. The construction and analysis of the PPI network revealed the top 10 targets based on degree value: HSP90AA1, EGFR, MAPK1, PIK3R1, PIK3CA, IGF1, ESR1, CASP3, JAK2 and ALB. GO analysis indicated involvement in biological processes such as apoptosis and proliferation; molecular functions including steroid binding and polymerase II transcription factor activity; and cell components such as receptor complexes, class IA phosphatidylinositol 3-kinase

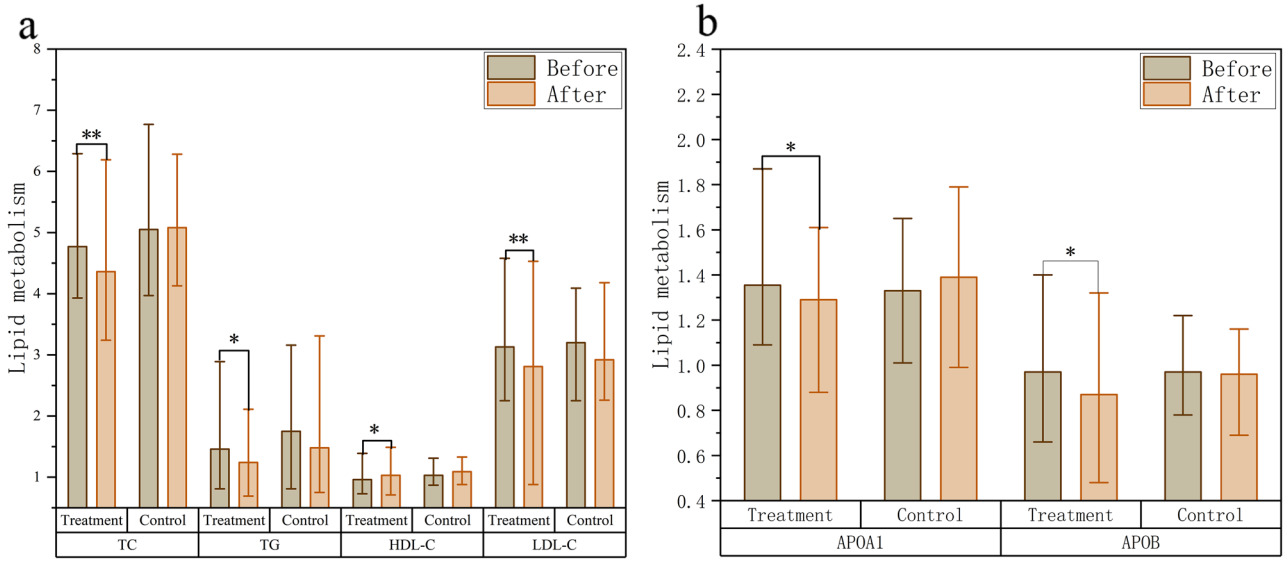

Fig. 4 Lipid metabolism indexes were compared between the two groups before and after treatment

Table 4 Comparison of sex hormone levels before and after treatment between the two groups

Index	HCQ			MET		
	Before	After	*P*	Before	After	*P*
FSH (mIU/mL)	6.17 ± 1.33	5.42 ± 1.27	0.545	5.82 ± 1.79	5.78 ± 1.08	0.353
LH(mIU/mL)	7.42 ± 4.38	6.42 ± 2.65	0.393	7.84 ± 3.59	8.47 ± 4.27	0.375
LH/FSH	1.11 ± 0.72	1.17 ± 0.52	0.811	1.43 ± 0.66	1.43 ± 0.71	0.973
T (nmol/L)	0.59 ± 0.21	0.54 ± 0.19	0.244	0.49 ± 0.16	0.44 ± 0.14	0.068
FT (pg/mL)	6.17 ± 1.33	5.42 ± 1.27	0.545	5.82 ± 1.79	5.78 ± 1.08	0.353
SHBG(nmol/mL)	15.03 ± 3.99	23.07 ± 11.34	0.100	20.12 ± 11.34	20.96 ± 12.05	0.709

Note *P*<0.05**, *P*<0.01**

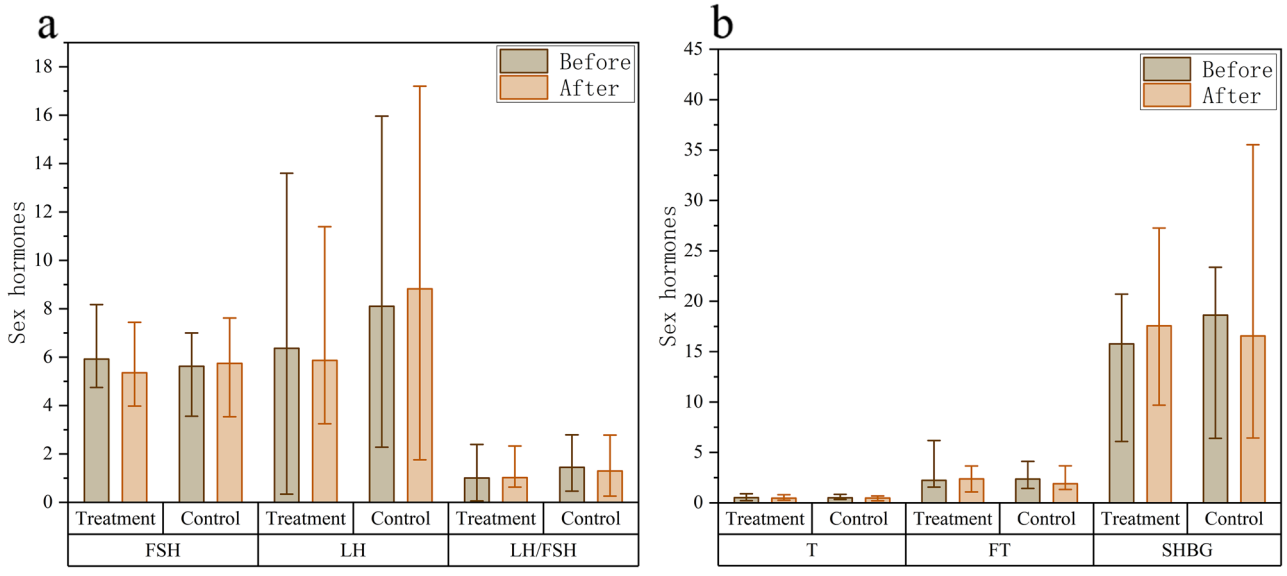

Fig. 5 The sex hormone indexes of the two groups were compared before and after treatment

Table 5 Pregnancy status of the two groups after six months

Group	Pregnancy test cycle	Gestation cycle	Cycle pregnancy rate (%)	χ2	*p*
HCQ	61	12	19.67	1.974	0.259
MET	52	9	17.31		

Note *P*<0.05**, *P*<0.01**

Table 6 Pregnancy status of the two groups after six months

EGFR-HCQ	-8.0
HSP90AA1-HCQ	-7.7
PIK3R1-HCQ	-7.2
MAPK1-HCQ	-7.1
PIK3CA-HCQ	-6.8

complexes, fine matter and cytosol. KEGG pathway analysis primarily focused on cancer signaling pathways like PI3K-Akt and Endocrine resistance as well as EGFR tyrosine kinase inhibitor resistance (Fig. 6). Molecular docking demonstrated strong binding activity between HCQ and HSP90AA1, EGFR, MAPK1 ,PIK3R1 and PIK3CA (Table 6; Fig. 7).

Discussion

The pathophysiological mechanisms of PCOS involve multiple abnormalities, including dysregulation of reproductive endocrine function and disturbances in energy metabolism. Therefore, interventions or medications that can simultaneously improve glucose and lipid metabolism abnormalities as well as sex hormone disturbances are anticipated to lead to breakthroughs in the treatment of obese PCOS.The study demonstrated that HCQ, in comparison with metformin, can significantly reduce body fat distribution and effectively control weight in patients. Additionally, HCQ also presents clear advantages in promoting lipid metabolism. Elevated levels of FFAs in obese patients contribute to lipid toxicity, disrupting the balance between glucose consumption and production [27], worsening insulin resistance and diabetes [28]. In vivo studies have shown that improving lipid toxicity can reduce the hyperreactivity of PCOS androgens to LH [29]and ACTH, while reducing the hyperreactivity to insulin [30]. This study confirmed that HCQ can effectively lower levels of TG, TC, LDL, etc., and improve abnormal lipid metabolism in patients. Its lipid-lowering effect may be achieved through interference with lipoprotein secretion, increased density of LDL receptors, and stimulation of β-hydroxy-β-methylglutaryl (HMG)-CoA reductase activity [31, 32].

Simultaneously, this study has demonstrated that HCQ is capable of reducing blood glucose levels and enhancing insulin sensitivity. Relevant literature [33–35] suggests that HCQ not only lowers fasting plasma glucose (FBG) and glycated hemoglobin (HbA1C) in diabetic patients, but also significantly decreases the risk of prediabetes. Mercer et al. [36]have postulated that HCQ may enhance insulin function in obese patients with metabolic disorders. Furthermore, animal experiments have shown that both chloroquine and HCQ can protect β cells and reduce insulin clearance in vitro [37, 38]. Our clinical data validates these findings.

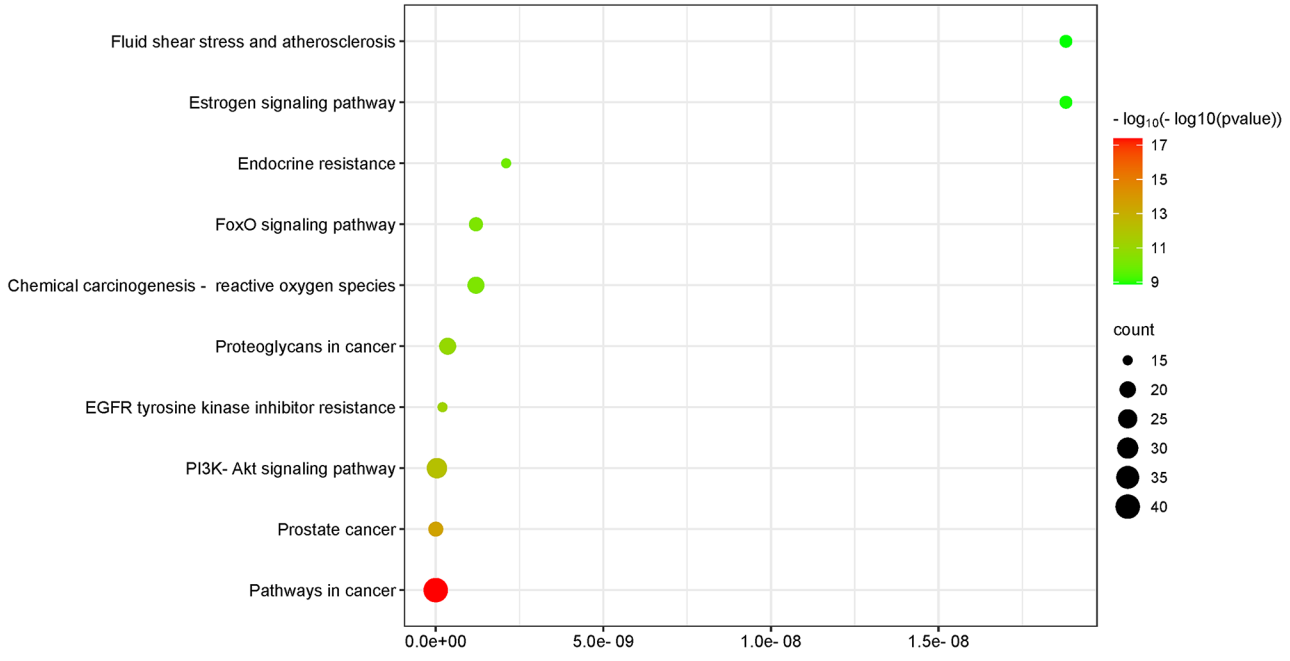

Fig. 6 KEGG analysis of HCQ in the treatment of PCOS

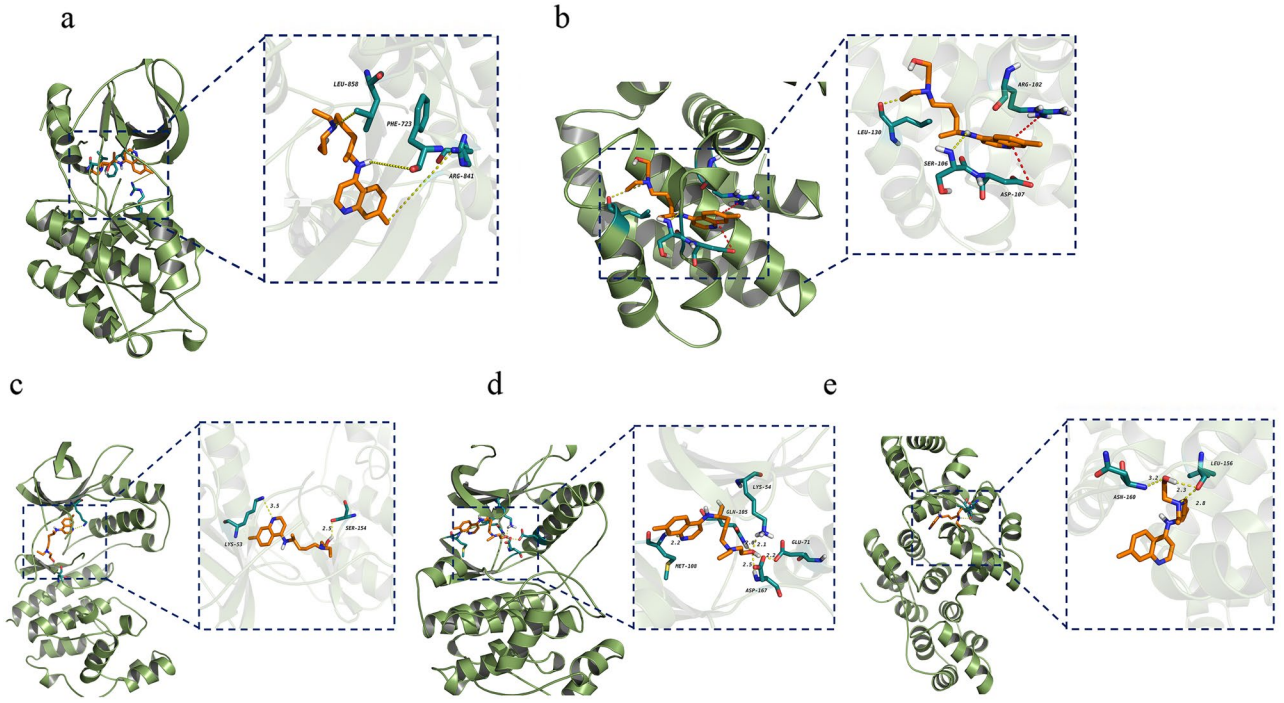

Fig. 7 Molecular docking diagram of HCQ and key targets, EGFR-HCQ (**a**), HSP90AA1-HCQ (**b**), PIK3R1-HCQ (**c**), MAPK1-HCQ (**d**), PIK3CA-HCQ (**e**)

The characteristics of PCOS include HPO axis dysfunction and abnormal gonadal hormone secretion [39], leading to ovulation disorders and infertility in patients of childbearing age. Research has indicated that obesity can exacerbate hormone imbalance in PCOS patients [40], by promoting androgen synthesis in the ovaries, inhibiting SHBG production in the liver, and increasing the biological activity of androgens [41].Simultaneously, elevated androgen levels will decrease the sensitivity of hypothalamic gonadotrophin cells to estradiol and progesterone, leading to a significant increase in the secretion of gonadotrophin releasing hormone and LH, as well as relatively insufficient secretion of FSH, resulting in abnormal follicle growth and development. Elevated levels of LH inhibit the production of SHBG in the liver, thereby increasing FT level [42].The previous studies [43, 44]suggested that metformin may enhance ovulation and pregnancy in PCOS patients by reducing blood sugar levels and improving insulin sensitivity. The findings of this study indicated that in the treatment of obese PCOS, HCQ did not show significant differences in sex hormone levels except for weight, lipid and glucose reduction. However, compared to the MET group, the HCQ group exhibited a decreasing trend in LH, T and FT levels while showing an increasing trend in SHBG levels. It is uncertain whether the relatively small sample size and short observation period decreased the likelihood of obtaining significant changes.

Furthermore, research has demonstrated that HCQ can modulate the development of adipose tissue inflammation and suppress cytokine release [45]. Nevertheless, studies have indicated that inflammatory cycle markers are relatively insensitive in detecting tissue-level inflammation [46]. In this study, we also did not analyze indicators related to inflammation; therefore, further exploration is needed to determine whether the therapeutic mechanism of HCQ for the disease involves inhibiting inflammation.

In order to gain a more comprehensive understanding of the mechanism of HCQ, we conducted a network pharmacology study. KEGG enrichment analysis indicated that the key targets of HCQ in treating PCOS include HSP90AA1, EGFR, MAPK1, PIK3R1, PIK3CA, etc. The primary signaling pathway involved is the PI3K-Akt pathway. HSP90 serves as the principal target of HCQ in PCOS treatment by targeting low density lipoprotein receptor-associated protein 1 (LRP1) on the cell membrane, activating downstream AKT signaling pathways and exerting protective effects against oxidative stress [47]. Additionally, binding between HSP90 and Akt can prevent degradation of Akt proteome and contribute to functional stability within the PI3K/Akt signaling cascade and cell survival [48].

To the best of our knowledge, there have been no studies assessing the efficacy of HCQ in treating obese PCOS. Our clinical data analysis has demonstrated that, in comparison to metformin, the conventional drug for PCOS treatment, HCQ can significantly reduce body fat content in obese patients, improve glucose and lipid metabolism, and correct hormone level disorders. However, its

impact on pregnancy rates is not statistically significant. This study has some limitations: a small sample size and relatively limited detection indicators which may affect the assessment of drug effects; The conservative dosage used may also influence the significance of improvement in certain indicators. Future research should focus on expanding sample sizes and optimizing experimental content to obtain more comprehensive data.

Conclusion: The potential benefits of HCQ in the management of obese women with PCOS include significant improvements in body fat distribution, glucose and lipid metabolism levels, as well as correction of hormonal disorders.

Abbreviations

HCQ	Hydroxychloroquine
PCOS	Polycystic ovary syndrome
MET	Metformin
ISI	Insulin sensitivity index
TC	Serum total cholesterol
TG	Triglyceride
LDL	Low-density lipoprotein
APOB	Apolipoprotein B
IR	Insulin resistance
CVD	Cardiovascular disease
T2D	Type 2 diabetes
BMI	Body mass index
HOMA-IR	Homeostasis model insulin resistance index
WHR	Waist-to-hip ratio
FAT	Body fat percentage
BFP	Body fat percentage
VFI	Visceral fat index
VFA	Visceral fat area
BMR	Basal metabolic rate
FSH	Follicle-stimulating hormone
LH	Luteinizing hormone
T	Testosterone
FT	Free testosterone
SHBG	Sex hormone binding globulin
FINS	Fasting insulin
FBG	Fasting blood glucose
HDL-C	High density lipoprotein
APOA1	Apolipoproteina1

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12902-024-01827-7.

Supplementary Material 1

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Jiajia Lang, Shanqin Qi, Qi Wang, Conghui Pang and Ruihan Wang. The first draft of the manuscript was written by Ruihan Wang and Kehua Wang and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability

All data generated from this study are available from the corresponding author upon reasonable request.

Declarations

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. The research protocol has been approved by the Ethics Committee of the Reproductive and Genetic Center of Shandong University of Traditional Chinese Medicine (2021 Clinical Research Application No. 17). Informed consent was obtained from all individual participants included in the study.

Consent for publication

Informed consent was obtained from all individual participants included in the study. Identifying images or personal or clinical details of other participants presented in this article are anonymous, so this statement does not applicable.

Statements& declaration

The main findings in the paper were independently conducted by the author or the research team. It is important to avoid plagiarism and properly cite the work of other authors. Additionally, there were no instances of submitting the same work to multiple publications or presenting it at different conferences.

CONSORT guidelines

This manuscript is in line with the CONSORT clinical trial reporting guidelines, and we have uploaded the CONSORT guidelines as attachments.

Competing interests

The authors declare no competing interests.

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