

A Comparative Study of Myo Inositol Versus Metformin in Improving Symptoms of Menstrual Irregularities in Polycystic Ovarian Syndrome Women

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorder affecting 5 to 10% women of reproductive age leading to anovulation, menstrual cycle irregularities and other metabolic disorders.

Objective: To compare the efficacy and safety of myo-inositol versus metformin in improving symptoms of menstrual irregularities in patients with PCOS.

Material and Methods: It was a randomized controlled trial carried out in the department of Obstetrics and Gynaecology, Arif Memorial Teaching Hospital, Lahore over a period of six months from December 2022 to May 2023. In this study 100 patients (50 patients in Group A and 50 patients in Group B) were included. Group A patients were given myoinositol while group B patients were given metformin. Efficacy was assessed by observing improvement in menstrual cycle irregularity. Safety assessment of both drugs was also done at the end of treatment.

Results: A total of 100 cases were enrolled. Mean \pm SD of age in group A was 24.20 ± 4.02 years and in group B was 24.86 ± 4.91 years. Mean \pm SD of BMI, Parity and Duration of disease of patients from group A was 26.40 ± 2.35 , 1.38 ± 0.99 and 5.86 ± 1.32 respectively; whereas from group B it has been observed as 26.10 ± 2.16 , 1.16 ± 0.86 , and 6.10 ± 1.27 respectively. There were almost 40% improvement in menstrual cycle regularity in group A whereas group B has shown improvement in 84% of patients. There was statistically significant association of efficacy among both groups as p-value 0.000. In terms of safety profile, myoinositol proved to have better side effect profile.

Conclusion: Both Myoinositol and metformin were found to be safe and efficacious, however, Metformin significantly increased achievement of regular menstrual cycle in patients suffering from PCOS. But myoinositol has better safety profile with less side effects.

Keywords: PCOS, Myo-inositol, Metformin, Regular Menstrual Cycle

Introduction:

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age having hormonal and metabolic impairments which lead to ovarian dysfunction and menstrual irregularities in >50% of affected women.^{1,2} The diagnosis of PCOS is made through the Rotterdam criteria with the presence of two out of three clinical features of oligo-anovulation, hyperandrogenism, and/or polycystic ovaries on ultrasound.³

Menstrual cycle irregularities are common in PCOS ranging from amenorrhea in 30%–40%, oligomenorrhea in 85%–90% and normal menses in 30% of women and these are thought to be due to insulin resistance.⁴ Insulin resistance and compensatory hyperinsulinemia are found in around 70%–80% of obese women with PCOS and 15%–30% of lean women with PCOS. This hyperinsulinemia increases ovarian androgen synthesis via amplified luteinizing hormone (LH) secretion and main pathophysiological contributor of PCOS and associated symptoms.^{5,6}

This hyperinsulinemia in PCOS is found to be due to deficiency of inositol causing decreased level of phosphatidylinositol 3-kinase (PI3K) which acts as second messenger for insulin action. In a normal cell insulin binds with its receptor forming insulin receptor substrate complex to release second messenger PI3K which then activates glucose transporter type 4 (GLUT4) which in turn lead to uptake of glucose to be used either as energy or stored as glycogen. So, deficiency of inositol leads to decreased level of PI3 kinase leading to decreased glucose uptake thereby causing hyperglycemia and hyperinsulinemia and thus insulin resistance.⁷ This hyperinsulinemia causes deficiency of sex hormone-binding globulin leading to high levels of circulating free androgens which together with persistently elevated luteinizing hormone (LH) levels arrest ovulation, hence menstrual irregularities.⁸ Also hyperinsulinemia together with beta-cell dysfunction considerably increases the risk of developing other metabolic abnormalities such as type 2 diabetes (T2D), hypertension, dyslipidemia, and cardiovascular diseases.⁹ Myo-inositol helps in both production and activation of PI3 kinase.⁷

Due to the role of insulin resistance in the pathophysiology of PCOS, several insulin sensitizers drugs have been used to improve signs and symptoms present in PCOS. Metformin though reduces weight, lessen insulin resistance, lower testosterone levels, and restore normal menstrual cycle and ovulation but its usage is constrained by gastrointestinal side effects.¹⁰ Although metformin has represented the landmark of PCOS therapy, myo-inositol is an insulin sensitizer drug that addresses hyperinsulinemia and improves hormonal balance, ovarian function, oocyte quality, and menstrual cycle regularity.¹¹ Aside from insulin resistance, myo-inositol leads to a decrease in LH and androgen levels with the re-establishment of ovulatory menstrual cycles.¹² Also myo-inositol plays a critical role in oocyte development specifically, in meiotic resumption by acting as a second messenger in calcium signaling.¹³

Different studies show different results such as in a study conducted by Ranwa M et al 74.65% cases achieved regular menstrual cycle during the course of myo-inositol therapy.¹⁴ Menstrual cycle regularity was seen in 66% of women using myo inositol in one study¹⁵ while 97% of women using metformin shows regularity in menstrual cycle in other studies.¹⁶

The rationale of this study is to compare the effects of myo-inositol versus metformin on improvement of menstrual irregularities in women with PCOS. Pakistan has higher prevalence of around 52% of PCOS as compared to western countries where it is up to 25%. Despite this high prevalence it is yet considered a debatable disease in terms of treatment.¹⁷ Also there is

dearth of literature in our local studies regarding comparison of efficacy of these two drugs. So, the present study was planned to evaluate the effects of Myoinositol vs Metformin in treatment of menstrual irregularities in patients with PCOS.

Objective

To compare the efficacy and safety of myo-inositol versus metformin in improving symptoms of menstrual irregularities in patients with PCOS.

Material And Methods:

This randomized controlled trial was conducted in the Department of Obstetrics & Gynaecology, Arif Memorial Teaching Hospital/Rashid Latif Medical college, Lahore over a period of six months from December 2022 to May 2023 after approval from Hospital Ethical Committee. Non- probability, consecutive sampling technique was used and sample size of 100 cases was calculated with 95% confidence interval, 80% power of the test and expected percentage of efficacy in terms of improvement in menstrual cycle as 50%¹⁸ in myo inositol group and in metformin group as 97%.¹⁹ All females of age 20-40 years presenting with features of PCOS and irregular menstrual cycle were included in the study. Females with diabetes, hyperprolactinemia, Cushing's disease, hypothyroidism/ hyperthyroidism, pregnancy and those unable to come for regular follow-ups were excluded from the study.

Patients were randomized through lottery method and divided into two groups 50 patients in each group. Written Informed consent was obtained from patients after explaining pros and cons of trial drugs. Group A was given Tab Myo-inositol 1g two times daily and Group B was given Tab Metformin 500mg three times daily for 6 months. Efficacy was assessed by observing improvement in regularity of menstrual cycle and safety profile was assessed by observing side effects. The data was then entered and analyzed using SPSS 21. The numeric data like age, parity and BMI was presented in the form of mean±S.D. Qualitative data like Efficacy (regular menstrual cycle) and side effects were presented in the form of frequency and percentage. Both groups were compared for efficacy using chi-square test taking P-value of ≤0.05 as significant. Data was stratified for age, BMI, duration of disease and parity. Post stratification chi-square test was applied taking p-value ≤0.05 as significant.

Results

Mean age of patients in group A was 24.95±6.21years and in group B it was 24.21±5.87 years. Mean BMI, Parity and Duration of disease of patients from group A was 26.40±2.35, 1.38±0.99 and 13.43±0.68 respectively; whereas from group B it has been observed as 26.10±2.16, 1.16±0.86, and 12.59±9.47 respectively. There was no significant difference in age between two groups (p value: 0.87) thus ensuring age matching. On comparison of duration of disease at the initiation of treatment between two groups, no significant difference in duration of disease in both groups, ensuring adequate matching with respect to duration (p value: 0.539). Also, groups were matched for BMI and parity (Table no. 1).

Table No. 1: Demographics and Baseline Characteristics Of Patients In Both Groups

Characteristics	Group-A (Mean \pm SD)	Group-B (Mean \pm SD)	P value
Age (years)	24.95 \pm 6.21	24.21 \pm 5.87	0.87
Parity	1.38 \pm 0.99	1.16 \pm 0.86	0.510
BMI (kg/m ²)	26.40 \pm 2.35	26.10 \pm 2.16	0.57
Duration of disease (months)	13.43 \pm 0.68	12.59 \pm 9.47	0.539

The efficacy measured in terms of relief from menstrual complaints and after six months of treatment, 62 out of 100 patients achieved regular menstrual cycles. Out of 50 patients in group A 20(40.0%) achieved regular menstrual cycle while 42(84.0%) patients from group B (Table no. 2).

Table No. 2: Comparison of Efficacy

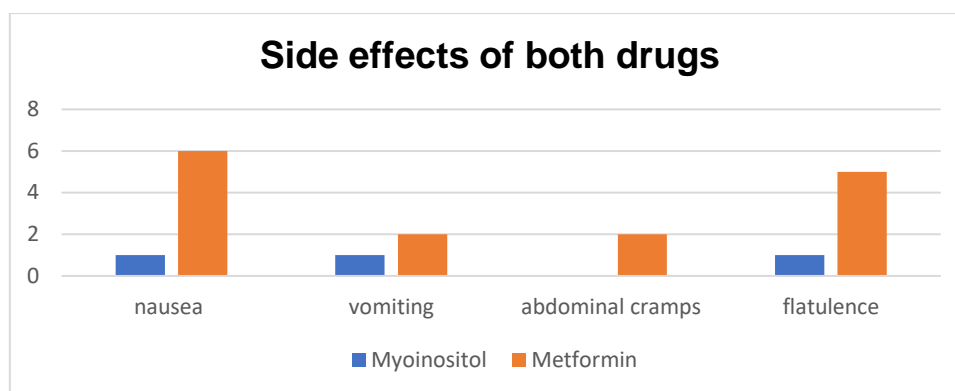
Efficacy (menstrual cycle)	Group-A F(%)	Group-B F(%)	Total F(%)	P value
Regular	20(40)	42(84.0)	62(62.0)	0.000
Irregular	30(60)	8(16.0)	38(38.0)	
Total	50(100)	50(100)	100(100)	

Statistically significant association has been observed with respect to BMI more than 25 in achieving efficacy while in BMI less than 25, p-value was calculated as 0.057 (Table 3).

Table No. 3: Stratification for Efficacy with Respect To BMI

BMI	OUTCOME	Group-A		Group-B		Total n(%)	P value
		No. of cases	Percentage	No. of cases	Percentage		
<25	Yes	7	25.9	11	40.7	18(66.7)	0.057
	No	7	25.9	2	7.4	9(33.3)	
	Total	14	51.9	13	48.1	27(100)	
\geq 25	Yes	13	17.8	31	42.5	44(60.3)	0.000
	No	23	31.5	6	8.2	29(39.7)	
	Total	36	49.3	37	50.7	73(100)	

Regarding side effects, only 3 patients in myoinositol group experienced some side effects while 47 patients had no side effects.



Discussion:

In our study the regular use of myoinositol helped in the resumption of spontaneous menstrual cycles in 40% of women with PCOS with menstrual complaints, and in patients who took metformin regular cycle was seen in 84% of patients.

Different studies showed different results in terms of achievement of regular menstrual cycle. A study conducted by J. Nehra on Myoinositol (MI) and Metformin for improvement in menstrual cycle showed that in MI group, 50% of PCOS patients showed improvement while in metformin group, improvement was seen in 60% of patients.¹⁸ In another study done by Angik et al, in which metformin and MI were compared to observe their effects on regularity of menstrual cycle, 100 patients were randomly allocated to treatment with either MI or metformin. After six months of treatment, 37.73% achieved regular cycles, 28.57% with MI and 48% after metformin treatment. However, difference between the two groups was not statistically significant.²⁰ But in our study the two groups differ significantly regarding improvement of regular menstrual cycle.

In another study conducted by Johat TH et al, there was improvement seen in menstrual cycle regularity in both MI and metformin groups in PCOS after treatment but regarding side effects of both drugs, in the myoinositol group, the majority of the study subjects (82%) had no adverse effect after treatment and from remaining patients 12% had menorrhagia, 4% had nausea and 2% had a weakness. On the other hand, in the metformin group, only 34% had no adverse effect while 30% had a weakness, 26% had nausea, 8% had abdominal pain and 2% had vomiting.²¹ Our study also showed better side effect profile of myoinositol as compared to metformin.

The regular use of myoinositol helped in the resumption of spontaneous menstrual cycles in 66.66% of women with PCOS with menstrual complaints while only 15.78% patents taking metformin showed improvement in menstrual cycle, as observed in a study conducted by Chirania K et al.²²

In another study conducted by Fruzzetti F et al 50 PCOS women were randomized to treatment with metformin or myo-inositol and after six months of treatment a normal menstrual cycle was present in 53% of the women in the metformin group and in the 44% of women in the inositol group showing that both drugs are similiarly efficacious in patients with PCOS.²³

Limitations of the Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

Conclusion: Polycystic ovarian syndrome (PCOS) is a common endocrine disorder in women of reproductive age associated with insulin resistance leading to hyperandrogenism, anovulation, infertility and weight gain. Both drugs, myoinositol and metformin are safe and efficacious in patients suffering from polycystic ovarian syndrome. Metformin is more effective in achieving regular menstrual cycle but with side effects. Hence, myoinositol can be a new addition in the armamentarium for the treatment of PCOS with comparable efficacy and better side effect profile.

Recommendations: After our study we recommend the use of Myoinositol for treatment of PCOS because it is well tolerated so will result in better compliance.

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Conflict Of Interest Statement: None

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