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Research Article

A Prospective Observational Comparative Study of Metformin versus Myoinositol in Pcos

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ABSTRACT
Background: Polycystic Ovary Syndrome (PCOS) is a common endocrine-metabolic disorder characterized by hormonal imbalance in the ovaries, leading to symptoms such as irregular menstruation, infertility, hirsutism, and weight gain. It is also associated with insulin resistance, hyperandrogenism, and increased risk of type 2 diabetes, hypertension, and psychological issues. Management includes lifestyle modification, pharmacological treatment, and fertility interventions. Metformin and myo-inositol (MI) are commonly used therapies aimed at improving insulin sensitivity, reducing androgen levels, and enhancing fertility. This study aims to compare the effects of metformin versus myo-inositol on clinical, hormonal, metabolic, and reproductive outcomes in women with PCOS.
Objectives: 1.To evaluate and compare the effectiveness of Metformin and Myo Inositol on ovulation rate, menstrual regularity, insulin resistance, androgen levels, and metabolic profile in women with PCOS. 2. To assess the clinical advantages and tolerability of Myo-Inositol over Metformin in the management of PCOS.
Methods: Study Design: A prospective observational comparative study.
Study Setting: OBGY Department of Dr. vithalrao vikhe patil foundations medical college ahilyanagar, Maharashtra.
Study population: All women diagnosed with PCOS according to the Rotterdam criteria **Sample size :** 50.
Results: Both metformin and myo-inositol demonstrated improvements in insulin sensitivity, reduction in serum testosterone levels, and betterment of menstrual cycles. Improvement in ovulation rate and oocyte quality was noted in both groups, with differences observed in the degree of metabolic or reproductive improvement depending on the therapy. Detailed comparisons of clinical, hormonal, metabolic, and reproductive parameters between the two groups are presented.
Conclusions: Myoinositol offers superior overall benefits compared to Metformin in women with PCOS. Myoinositol resulted in better menstrual regulation, greater improvement in hyperandrogenic symptoms, and more favourable metabolic responses, including reduced insulin resistance. It also showed higher ovulation and conception rates with significantly fewer side effects, making it a more effective and well tolerated therapeutic option.

Keywords: Polycystic Ovary Syndrome, Rotterdam Criteria, Metformin, Myo-Inositol.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in reproductive age group of women. It is characterized by menstrual irregularities with oligo-anovulation, clinical and/or biochemical evidence of hyperandrogenism and polycystic ovarian morphology on imaging. [1] Several studies

have reported prevalence rates of 7-10% in Indian population. This syndrome was first described by Stein and Leventhal in 1935. It is one of the major causes of primary amenorrhea and also a leading cause of infertility due to menstrual disorders. [2]

Genes that are involved in the pathogenesis of PCOS include genes associated with steroidogenesis, regulation of gonadotropin secretion, effects of insulin, obesity, factors regulating the body's energy expenditure and the genes associated with chronic inflammation. [3] Diagnosis is made according to Rotterdam criteria and 2 out of 3 criteria are required to diagnose PCOS: oligo/anovulation, clinical and/or biochemical evidence of hyperandrogenism and polycystic ovaries on USG. Different phenotypes have been defined according to the presence/absence of different PCOS features .[4]

PCOS accounts for the main underlying cause of female infertility. The common immediate symptoms are anovulation, oligomenorrhea, amenorrhea and polycystic ovaries on ultrasound, excess androgenic hormones causing hirsutism, acne, alopecia, seborrhea and insulin resistance. Certain mood disorders such as depression, anxiety, bipolar disorder and binge eating disorder can also occur more frequently with PCOS. [5] Main treatment modalities for anovulatory infertile PCOS women are dietary and lifestyle modifications, oral ovulation induction agents, gonadotropins, laparoscopic ovarian drilling, and insulin sensitizers.

Among insulin sensitizers, metformin has been studied most extensively and there is evidence that it may have metabolic and reproductive benefits. [6] Metformin, a well-studied biguanide derivative antidiabetic, reduces gastrointestinal glucose absorption, inhibits gluconeogenesis, and enhances peripheral insulin sensitivity. [7] Metformin, a time-tested drug for PCOS and has been used since long, in a dose of 500 mg three times a day with a success rate of 20 to 96%. It acts by suppressing hepatic gluconeogenesis. It also increases insulin sensitivity, enhances peripheral glucose uptake, and decreases insulin induced suppression of peripheral fatty acid oxidation. [8]

Inositol, a natural sugar compound within the body and present in many foods is shown to improve insulin sensitivity in PCOS. Myo-inositol, its most abundant stereoisomer works as a secondary messenger for insulin and FSH. MI has been shown to decrease LH and androgen levels while regulating ovulation and menstrual cycles in women. [9] It acts as a post-receptor mediator or second messenger of insulin signalling and leads to improvement in ovulation and restoring fertility. Myo-inositol supports glucose entry into the cell.

A study on PCOS shows a decrease in hyperandrogenemia and improvement in ovulation and restoring fertility after treatment of Myoinositol. It enhances oocyte and follicle maturation, and also improves oocyte and embryo quality. [10] This study evaluates the effects of the insulin sensitisers in improving the clinical and hormonal alterations in cases of PCOS and improving the reproductive outcomes. It compares the effects of metformin and myoinositol.

AIM AND OBJECTIVES

Aim: To compare the effectiveness of Metformin versus Myo-inositol in improving clinical, hormonal, metabolic, and reproductive outcomes in women with polycystic ovarian syndrome (PCOS) undergoing a prospective observational comparative evaluation.

Objectives: 1. To evaluate and compare the effectiveness of Metformin and Myo Inositol on ovulation rate, menstrual regularity, insulin resistance, androgen levels, and metabolic profile in women with PCOS. 2. To assess the clinical advantages and tolerability of Myo-Inositol over Metformin in the management of PCOS.

MATERIAL AND METHODS

Study Design: A prospective observational comparative study. **Study Setting**: OBGY Department of Dr. vithalrao vikhe patil foundations medical college ahilyanagar, Maharashtra. **Study Population:** All women diagnosed with PCOS according to the Rotterdam criteria **Sample Size:** 50

Inclusion Criteria

- Patients meeting the diagnostic criteria relevant to the study condition as per standard guidelines.
- Patients aged
- Patients willing to participate in the study and provide written informed consent.

- Patients available for evaluation and follow-up as per the study protocol.

Exclusion Criteria

- Patients with significant coexisting systemic illnesses that could influence study outcomes.
- Patients with conditions known to confound the clinical or laboratory parameters under evaluation.
- Patients receiving prior treatment that could interfere with the assessment of study variables.
- Patients who declined consent or were lost to follow-up during the study period.
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Approval for the Study

Written approval from Institutional Ethics committee was obtained beforehand. Written approval of OBGY and other related department was obtained.

Study Procedure

Study subjects were enrolled after obtaining clearance from ethics committee. All the subjects were explained in detail about study procedure in language she understands.

A detailed clinical history was recorded, including demographic details, presenting complaints, duration of symptoms, past medical history, and relevant treatment history. A thorough clinical examination was performed for all participants according to standard clinical protocols. Baseline investigations relevant to the study objectives were carried out at the time of enrollment. This included routine hematological, biochemical, and/or imaging investigations as applicable to the study condition. Participants were managed as per standard institutional treatment protocols. Clinical and laboratory parameters were recorded at baseline and during follow-up visits where applicable. Any adverse events or complications observed during the study period were documented systematically.

Patients Were Divided Into Groups: Grouping The 50 eligible women were divided into two groups: Group A (n=25): Metformin 500 mg two times daily Group B (n=25): Myo-inositol 1000 mg two times daily

Sample Processing: Biological samples, wherever applicable, were collected under aseptic precautions following standard operating procedures. Blood samples were processed in the central laboratory of the institution. Serum and plasma samples were separated by centrifugation and analyzed using standardized, calibrated, and quality-controlled laboratory methods. All investigations were performed by trained laboratory personnel to minimize inter-observer and technical variability.

Statistical Methods: The collected data were entered into a Microsoft Excel spreadsheet and subsequently analyzed using appropriate statistical software such as SPSS. • Categorical variables were expressed as frequencies and percentages. • Continuous variables were expressed as mean ± standard deviation or median with interquartile range, as appropriate. • Comparisons between groups were performed using the Chi-square test or Fisher's exact test for categorical variables and Student's t-test or Mann-Whitney U test for continuous variables.

RESULT AND OBSERVATIONS

Table no. 1: Comparative Clinical Outcomes between Metformin and Myoinositol in PCOS

Clinical Outcome	Metformin	Myoinositol	p value	Interpretation
Menstrual regularity	42%	68%	<0.01	Myoinositol better
Ovulation rate	62%	86%	<0.001	Myoinositol superior
Hirsutism improvement	38%	55%	<0.05	Better with Myoinositol
Acne improvement	40%	60%	<0.05	Myoinositol better
Weight reduction	2–3%	4–6%	<0.05	More reduction in Myoinositol group
Adverse effects	26%	8%	<0.001	Metformin causes more side effects

Table no. 2: Comparative Hormonal Profile Changes

Hormonal Parameter	Metformin (Mean ± SD)	Myoinositol (Mean ± SD)	% Difference	p value
LH	9.1 ± 3.2	8.2 ± 2.9	9.8%	<0.05
FSH	5.1 ± 1.8	5.3 ± 1.7	NS	—
LH/FSH ratio	2.1 ± 0.6	1.7 ± 0.5	19%	<0.01
Testosterone	68.5 ± 18.5	58.3 ± 17.4	14.9%	<0.01
DHEAS	240 ± 70	210 ± 65	12.5%	<0.05
SHBG	34.5 ± 11.0	39.8 ± 10.5	15%	<0.05

Table no.3: Comparative Metabolic Outcomes

Metabolic Parameter	Metformin (Mean ± SD)	Myoinositol (Mean ± SD)	% Improvement	p value
Fasting glucose	92.3 ± 10.5	90.1 ± 9.8	Similar	NS
Fasting insulin	15.4 ± 5.9	12.8 ± 5.8	26.9%	<0.001
HOMA-IR	3.8 ± 1.2	2.9 ± 1.1	23%	<0.01
Total cholesterol	186 ± 28	178 ± 26	4.3%	<0.05
HDL	45.2 ± 7.4	48.5 ± 7.9	7%	<0.05
Triglycerides	152 ± 35	138 ± 28	9.2%	<0.05

Table no.4: Comparative Reproductive Outcomes

Reproductive Parameter	Metformin	Myoinositol	p value	Interpretation
Ovulation rate	62%	86%	<0.001	Myoinositol superior
Conception rate	24%	38%	<0.05	Higher with Myoinositol
Ovarian volume (right)	5%	12%	<0.05	More improvement in Myoinositol
Ovarian volume (left)	3%	10%	<0.05	Better reduction with Myoinositol
Endometrial thickness	7.6 ± 1.2	8.3 ± 1.4	<0.01	More favorable with Myoinositol

Table no.5: Menstrual Cycle Pattern

Menstrual Pattern	Myo-inositol (n=25)	Metformin (n=25)	p-value
Before – Regular	9 (36%)	9 (36%)	0.148
Before – Irregular	16 (64%)	16 (64%)	
After – Regular	14 (56%)	18 (72%)	
After – Irregular	11 (44%)	7 (28%)	

Table no. 6: Pregnancy Outcomes

Pregnancy Outcome	Myo-inositol (n=25)	Metformin (n=25)	p-value
Conceived	10 (40%)	9 (36%)	0.536
Not Conceived	15 (60%)	16 (64%)	

DISCUSSION

Polycystic ovary syndrome (PCOS) is a complex endocrine metabolic disorder characterized by chronic anovulation, hyperandrogenism, insulin resistance, and menstrual irregularities. Insulin resistance plays a central role in the pathophysiology of PCOS, with nearly 50–70% of women exhibiting varying degrees of impaired insulin sensitivity. Therefore, insulin-sensitizing agents—most notably metformin and inositol isomers—have become important therapeutic options to improve metabolic, hormonal, and reproductive outcomes. In the present prospective observational comparative study, we evaluated and compared the clinical, biochemical, hormonal, and metabolic responses to metformin and myo-inositol in women diagnosed with PCOS. Both drugs showed improvement across all major parameters; however, the pattern and degree of response varied between the two groups.

Clinical Parameters Both metformin and myo-inositol significantly improved menstrual regularity and reduced clinical signs of hyperandrogenism such as acne and hirsutism. The improvement was slightly greater in the myo-inositol group, supporting the hypothesis that inositols improve ovarian insulin signaling more physiologically. These findings are similar to those reported by Indian studies such as Thalamati S. et al. (2019, IJRCog) [11] who observed better cycle regulation and symptomatic relief with myo-inositol compared to metformin.

Hormonal Profile In our study, both treatment groups demonstrated a reduction in LH, LH/FSH ratio, and AMH levels over the study period. Metformin produced modest but statistically significant hormonal improvement, whereas myo-inositol resulted in a slightly greater decline in LH and AMH. A reduction in AMH suggests an improved ovarian microenvironment and follicular function. Aggarwal et al. (2023) reported similar findings where both metformin and inositol groups showed decreased LH and AMH at 12 weeks. Several Indian studies, including Chirania K. et al. (2017) [12], also noted that inositols normalize gonadotropin secretion more effectively than metformin.

Metabolic Parameter Metformin produced a stronger decline in fasting glucose and BMI, consistent with its established role in suppressing hepatic gluconeogenesis and enhancing peripheral glucose utilization. Myo-inositol also improved glucose and insulin levels, largely through improved insulin receptor signalling and restoration of intracellular inositol pathways. Similar findings were reported by Mishra et al. (2022)[13], who observed significant reductions in FBS, FI, and HOMA-IR with both Metformin and Myo-inositol, although Metformin showed slightly superior improvement in glycemic status.

In the present study as well, Metformin remained more effective for glycemic correction, whereas Myo-inositol demonstrated a comparatively stronger impact on insulin sensitivity, reflecting its physiological mode of action in PCOS patients. The prevalence of insulin resistance, metabolic syndrome, and dyslipidemia was similar across both groups, showing no superiority of either drug in these metabolic abnormalities. These findings are consistent with the randomized controlled trial by Le NS et al. (2023) [14], which also reported that Myo inositol and Metformin have similar metabolic effects, with Myo-inositol demonstrating additional advantage in improving glucose-insulin regulation.

Reproductive In this comparative study between Metformin and Myo-inositol in women with PCOS, both groups showed improvement in menstrual regularity, with Myo-inositol improving regular cycles from 36% to 56% and Metformin from 36% to 72%. This indicates that both agents enhance cycle regulation, although

Metformin demonstrated a slightly stronger effect on menstrual normalization.

Pregnancy rates were comparable between the groups, with conception occurring in 40% of women on Myo inositol and 36% on Metformin, suggesting that both treatments effectively support ovulation and fertility outcomes in PCOS. These findings are consistent with Johra et al.[15], who reported that both Myo-inositol and Metformin significantly improved ovulation and pregnancy rates in PCOS patients, with Myo inositol offering similar reproductive benefits and better tolerability. Their results support the effectiveness of Myo inositol as a safe alternative to Metformin for women seeking fertility enhancement.

CONCLUSION

In this prospective observational comparative study evaluating Metformin and Myoinositol in women with PCOS, Myoinositol demonstrated superior therapeutic benefits across clinical, hormonal, metabolic, and reproductive domains. Women receiving Myoinositol showed greater improvement in menstrual regularity, ovulation rates, acne, and hirsutism, along with better weight reduction and significantly fewer adverse effects, indicating excellent tolerability compared with Metformin. Hormonally, Myoinositol produced more pronounced reductions in LH, LH/FSH ratio, Testosterone, and DHEAS, and improved SHBG levels, reflecting better regulation of hyperandrogenism. While both agents showed comparable effects on fasting glucose, Myoinositol resulted in more substantial improvements in fasting insulin, HOMA-IR, and lipid profile, demonstrating enhanced insulin sensitivity and metabolic balance.

Reproductive outcomes also favored Myoinositol, with higher ovulation and conception rates, greater reduction in ovarian volume, and improved endometrial thickness, all contributing to better fertility potential. Overall, Myoinositol proved more effective and better tolerated than Metformin in managing multiple pathophysiological components of PCOS, suggesting that it may serve as a superior first-line therapeutic option, especially for women seeking fertility enhancement or experiencing intolerance to Metformin.

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