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Comparison Between Myoinositol and Metformin on Biochemical Profile in Women with Polycystic Ovarian Syndrome

Zaib Un Nisa[1], Faiza Murtaza[2], Sidra Kiran[3], Sehrish Sabir[4], Sidra Anam[5], Irem Khurshid[6]

[1]Medical Frequency and Healthcare Clinic, DG Khan; [2]Department of Gynecology and Obstetrics, Ahmed Medical Complex, Rawalpindi; [3] Department of Gynecology and Obstetrics, Medicsi Hospital, Rawalpindi; [4] Department of Gynecology and Obstetrics, Benazir Bhutto Hospital, Rawalpindi; [5]Tehsil Headquarter Hospital, Hazro, District Attock; [6] Department of Gynecology and Obstetrics, Akhtar Saeed Medical College, Rawalpindi

ABSTRACT

Objectives: To compare the outcome of myoinositol and metformin on biochemical profile in women with polycystic ovarian disease.

Methodology: This comparative randomized controlled trial was carried out at the Gynecology and Obstetrics Department of Benazir Bhutto Hospital Rawalpindi, from October 2022 to April 2023. The study involved 100 female patients aged 18 to 35 diagnosed with polycystic ovarian syndrome. The participants randomly were assigned to two groups: Group-I received myoinositol (1 gram twice daily) for 24 weeks, and Group-II received metformin (500mg thrice daily) for the same duration. Hormonal parameters, including FSH, LH, LH/FSH ratio, and fasting blood glucose (measured after 8 hours of overnight fasting), were assessed at baseline and after 24 weeks.

Results: The patients mean age was 28.12±4.84 years. The metformin-treated group exhibited mean baseline values of 7.65±2.79, 5.19±1.79, 1.54±0.68, and 90.82±10.72 for LH, FSH, LH/FSH ratio, and fasting blood sugar, respectively. After 24 weeks of treatment, these values decreased to 6.16±2.57, 4.34±1.65, 1.50±0.68, and 85.96±5.72 ($p \leq 0.05$). In the myoinositol-treated group, the mean baseline values were 6.37±3.90, 4.66±1.37, 1.51±1.29, and 88.52±11.13 for LH, FSH, LH/FSH ratio, and fasting blood sugar, respectively. After 24 weeks of treatment, these values decreased to 4.54±2.56, 3.71±1.39, 1.37±1.05, and 88.10±4.43 ($p \leq 0.05$).

Conclusion: This study concluded that myoinositol demonstrates superior efficacy compared to metformin in enhancing the biochemical profile of individuals with polycystic ovarian syndrome.

Keywords: Biomarkers; Inositol; Metformin; Polycystic ovarian syndrome.

Authors' Contribution:
[1,2]Conception; Literature research; manuscript design and drafting; [2,3] Critical analysis and manuscript review; [5,6] Data analysis; Manuscript Editing.

Correspondence:
Zaib Un Nisa
Email: zaib966@gmail.com

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Introduction

The most common endocrine disorder in women during their reproductive years is polycystic ovary syndrome (PCOS).[1] The global prevalence of PCOS is estimated to range from 5-10%,[2] varies area to area especially as in south Asia in Pakistan its prevalence is as high as 52%.[3] This syndrome is characterized by heightened androgen secretion by the ovaries, irregular menstrual cycles (oligomenorrhea), anovulatory cycles, dyslipidemia, and insulin resistance.[1] PCOS prevalence increased in overweight and obese women when compared to their lean counterparts.[4] Its genetic etiology is unknown, but it has seen to have a multifactorial, heterogenous, clinical and biochemical phenotype.[5] Insulin resistance results from subsequent defects in receptor signaling, possibly due to enhanced

receptor and insulin receptor substrate-1 serine phosphorylation. It selectively affects metabolic pathways in normal insulin target tissues and the ovary.[6] Elevated insulin levels contribute to the abnormal functioning of the hypothalamic-pituitary-ovarian axis, ultimately leading to the development of PCOS. In individuals with PCOS, the frequency of hypothalamic GnRH impulses increases, resulting in an elevated LH/FSH ratio.[7] Metformin is one of the effective oral insulin sensitizing agent it is also considered first line agent in treatment of PCOS.[8] Metformin, as a hepato-selective insulin sensitizer, exhibits significant impacts on weight reduction, lipid lowering, and modulation of endothelial function.[1] Additionally, it proves to be an effective means of stimulating ovulation in non-obese women with PCOS.[9] Myoinositol is a new emerging agent in treatment of PCOS, evidences are showing myoinositol is the good addition for the treatment of PCOS.[7] Myoinositol, a naturally occurring substance within the human body and part of the vitamin B complex group, is found in fruits and beans.[1,10] Among the nine different types of inositol, both myoinositol (MI) and D-chiro-inositol exhibit insulin sensitizing capabilities.[1] These inositol bind to the cell membrane as phosphatidyl-MI and serves as a precursor to the second messenger of inositol triphosphate for various hormones, including insulin and follicle-stimulating hormone. Disruption of this pathway leads to impaired insulin signaling, leading to insulin resistance. This rationale supports the use of inositol in treating insulin resistance syndromes like PCOS.[10] The rationale of this study was to assess the efficacy of these two-treatment modality in our local population. Upon extreme research, it was revealed that there is limited local data on these two treatments modality. This study also helps clinicians to formulate guidelines for the management of PCOS which ultimately helps us to improve quality of life of our patients, being cost effective. Therefore, the aim of this study was to compare the outcome of myoinositol and metformin on biochemical profile in women with polycystic ovarian disease.

Methodology

This This comparative randomized controlled trial was carried out at the Gynecology and Obstetrics Department of Benazir Bhutto Hospital Rawalpindi, from October 2022 to April 2023. The study involved 100 female patients aged 18 to 35 diagnosed with polycystic ovarian syndrome. The WHO calculator was used for sample, whereas confidence level of 95%, alpha error of 5%, and test power of 80%. The LH/FSH ratio mean for the metformin group was 1.64±0.19, while for the myoinositol group, it was 1.75±0.29.[1] The sampling technique was non-probability consecutive sampling. Patients with androgen secreting tumors, hyperprolactinemia (defined as prolactin levels ≥ 500 mIU/L), hypothyroidism (meeting all the following criteria: TSH ≥ 5.2 mIU/L, FT3 ≤ 1.5 pg/ml, FT4 ≤ 0.8 pg/ml, T3 ≤ 70 ng/dl, T4 ≤ 5.2 µg/dl), and chronic renal failure (creatinine ≥ 1.1 mg/dl) were excluded. After approval from ethics committee of institute, an informed consent was taken from each patient. Each case biodata and demographics (age, BMI) were measured. Ultrasonography was performed by a consultant radiologist and PCOS was diagnosed according to anyone or both ovaries with 12 or more follicles, ranging in size from 2mm to 10mm and an ovarian volume of 10ml without any dominant follicle. Past medical record was assessed for diabetes mellitus (blood glucose levels record of last 2 years; random ≥ 200mg/dl, or fasting ≥ 126mg/dl). Patients randomly were assigned to two groups (n=50, each group) by computer generated random sequence numbers. The allocation was sealed in opaque envelops. Myoinositol group or Group-I took myoinositol 1gram twice daily for 24 weeks, while Metformin group or Group-II took metformin 500mg thrice daily for 24 weeks. Hormonal parameters/biochemicals profile (outcomes) like FSH, LH and LH/FSH ratio and fasting blood glucose (after 8 hours overnight fasting) were measured at baseline (zero week) and 16 weeks in main laboratory of the same setting hospital of the study.

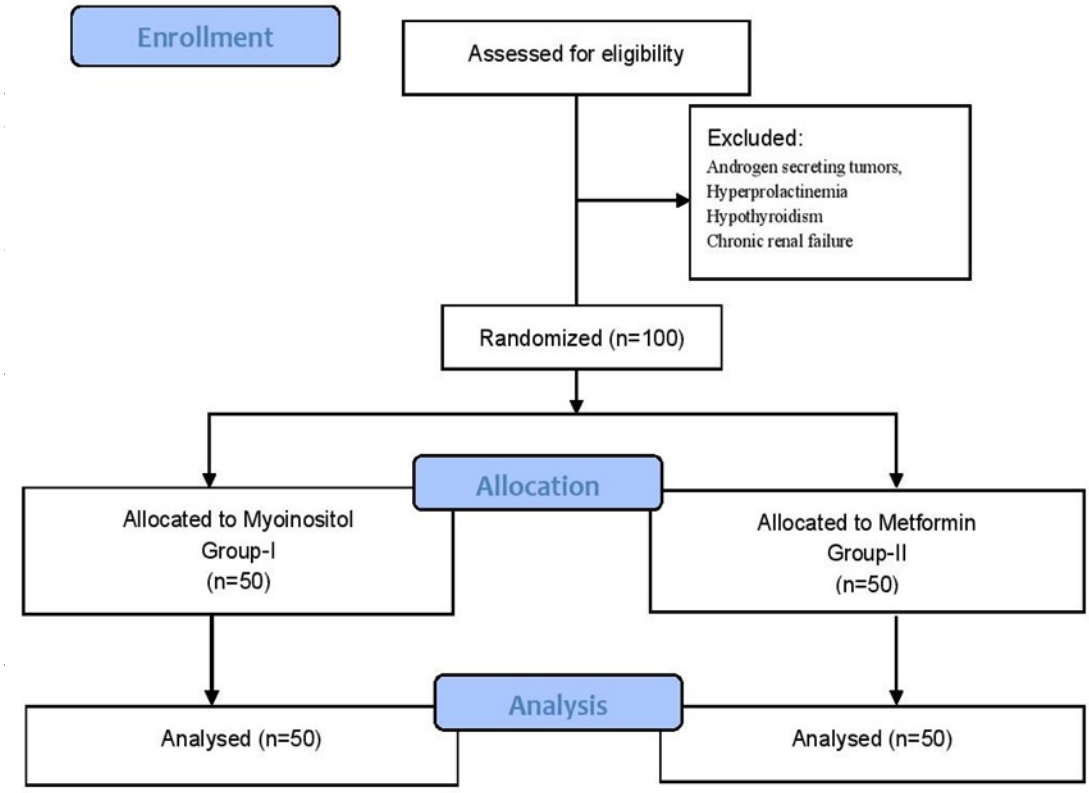

Fig. 1 Consort Diagram

The patient's follow-up and inquired the abovementioned treatments by a senior gynecologist.

All data was entered using SPSS v 23. Mean and standard deviation of age and weight were measured in each group once at baseline. Mean and standard deviation of FSH, LH, LH/FSH ratio and fasting blood glucose were calculated at baseline and after 24 weeks of treatment for both groups. A comparison of outcomes between the groups was conducted using the independent sample t test. Kolmogorov–Smirnov test was used for normality data between the groups. Effect modifier was adjusted by stratification. Post stratification involved the application of the independent sample t test, with a significance value of $p \leq 0.05$ for determining significance.

Discussion

One hundred (n=100) patients with PCOS were enrolled. Kolmogorov-Smirnov test was used for normality of the data and it was found throughout the assessment that the data was normative ($p \geq 0.05$). The patients mean age was 28.12±4.84 years, majority (64.0%) falling in 26 to 35 years of age. The mean BMI was 29.92±3.40 kg/m^2. Comparative analysis was performed on biochemical profiles, including FSH, LH, LH/FSH ratio, and fasting blood glucose (FBG) in Table 1. As indicated by independent sample t test, there was no distinction seen at baseline in all parameters. However, a significant difference was seen in FSH, LH and fasting blood sugar between two groups after treatment.

Table 1: Comparison of pre and post treatment for all parameters in both groups, n=100

Biochemical parameters	Myoinositol; Group-I	Metformin; Group-II	t*	p-value
	Mean±SD	Mean±SD		
FSH at baseline week 0	4.66±1.37	5.19±1.79	1.921	.099
FSH at 24 weeks	3.71±1.39	4.34±1.65	-9.324	.042
LH at baseline week 0	6.37±3.90	7.65±2.79	1.654	.062
LH at 24 weeks	4.54±2.56	6.16±2.57	-7.571	.002
FSH/LH at baseline week 0	1.51±1.29	1.54±0.68	5.547	.885
FSH/LH at 24 weeks	1.37±1.05	1.50±0.68	5.221	.181
Fasting blood sugar at week 0	88.52±11.13	90.82±10.72	2.234	.295
Fasting blood sugar at 24 weeks	88.10±4.43	85.96±5.72	-8.247	.039

Stratification of FSH, LH, FSH/LH ratio and FBG with respect to age and BMI is shown in Table 2. Myoinositol has significant effect in age group of 18-25 years (p = 0.042) as compare to metformin when stratified with FSH. Myoinositol has significant effect in age group of 18-25 years (p = 0.014), and BMI ≥ 27 kg/m^2 (p = 0.002) as compare to metformin when stratified with LH biomarker. Likewise, myoinositol has significant effect in age group of 26-35 years (p = 0.033), and BMI ≥ 27 kg/m^2 (p = 0.019) as compare to metformin when stratified with fasting blood sugar.

Discussion

We compare the outcome of myoinositol and metformin on biochemical profile in women with polycystic ovarian disease. In this study, myoinositol showed significant effects on biochemical of LH, FSH

Table 2: The biochemical parameters were stratified based on age and BMI, n=100

Variables		Myoinositol; Group-I	Metformin; Group-II	p-value
		FSH	FSH	
		Mean±SD	Mean±SD	
Ages (years)	18-25	3.43±1.45	4.21±1.09	.042
	26-35	3.95±1.32	4.45±2.08	.299
BMI (kg/m^2)	≤ 27	3.77±1.44	4.35±1.87	.092
	≥ 27	3.57±1.32	4.31±1.21	.115
LH				
Ages (years)	18-25	4.26±3.08	6.38±2.60	.014
	26-35	4.77±2.04	5.95±2.57	.069
BMI (kg/m^2)	≤ 27	4.63±2.81	5.97±2.91	.056
	≥ 27	4.32±1.92	6.51±1.75	.002
FSH/LH ratio				
Ages (years)	18-25	1.50±1.32	1.55±0.61	.867
	26-35	1.27±0.76	1.45±0.75	.389
BMI (kg/m^2)	≤ 27	1.38±1.05	1.46±0.76	.720
	≥ 27	1.37±1.08	1.57±0.52	.504
Fasting blood sugar (FBS)				
Ages (years)	18-25	87.13±4.50	86.21±5.27	.524
	26-35	88.93±4.27	85.73±6.20	.033
BMI (kg/m^2)	≤ 27	87.74±4.07	86.97±5.53	.509
	≥ 27	88.93±5.23	84.0±5.73	.019

LH/FSH ratio and fasting blood sugar (p ≤ 0.05) when compare with metformin at 24 weeks after treatment. In a study by Nehra et al, myoinositol treated group has significant effect after 24 weeks of treatment when compare with metformin treated group.[1] These results are comparable with our study.

Awalekar et al study participants were divided into three treatment groups: one receiving metformin (500 mg three times a day), another receiving myoinositol (2 g twice a day) along with folic acid (5 mg once a day), and a third undergoing lifestyle modification. This treatment regimen spanned a period of 12 weeks. The myoinositol group has significant effect on biochemicals in PCOS.[11] Genazzani et al study patients were assigned to receive either myoinositol 2g plus folic acid 200µg daily or folic acid 200µg daily over a 12-week period. The study noted changes in biochemical parameters. Patients receiving myoinositol experienced a decrease in BMI by 0.70, while those receiving folic acid showed an increase of 0.10.[12]

Angik et al study, the effects of metformin and myoinositol on fasting blood glucose levels (FBS) were compared. The myoinositol group received 1g twice daily, while the metformin group received 500mg twice daily over a period of 6 months. At the end of 24 weeks, the myoinositol group showed a reduction of 0.46 mg/dl in fasting blood glucose levels, whereas the metformin group exhibited a reduction of 0.10 mg/dl.[13] Ali et al study patients were subjected to different treatments, including metformin (850 mg twice daily), choline & inositol (500/500 twice daily) along with metformin, and lifestyle modification with diet control for a duration of 6 months. The metformin group demonstrated a reduction of 2.98 in insulin resistance (HOMA-IR), while the choline & inositol plus metformin group showed a reduction of 2.78. The lifestyle modification group exhibited a reduction of 1.98 in HOMA-IR at the end of 24 weeks.[14] In a study, the mean LH/FSH ratio on day 1 was 2.56±0.49 and 2.23±0.53, respectively, and decreased to 2.06±0.47 and 1.83±0.37 at the final follow-up at 9 months in myoinositol and metformin groups, respectively. There was no significant decrease in the LH/FSH ratio between groups ($p \geq 0.05$).[15] Similar findings were reported in Artini et al study, which also demonstrated a decrease in LH/FSH ratio with myoinositol. The mean random blood glucose at baseline and after the final follow-up at 9 months between the groups did not show statistically significant differences ($p \geq 0.05$).[16]

In a study, significant relative changes were observed in all studied parameters after 3 months of treatment when compared with baseline levels in both study groups (myoinositol versus metformin) with a significance level of $p \leq 0.05$.[11] Clinical data from Bevilacqua et al supports the positive effects of inositol, demonstrating a reduction in glycaemia levels and hyperinsulinemia. In addition, it buffers the adverse effects of prolonged insulin stimulation on adipose tissue and the endocrine system. Due to these diverse effects, myoinositol has emerged as a dependable treatment option for insulin-resistant PCOS patients, offering an alternative to hormonal stimulation.[17]

Conclusion

This study concluded that myoinositol demonstrates superior efficacy compared to metformin in enhancing the biochemical profile of individuals with PCOS. So, we recommend that myoinositol should be add as a first line therapy in women with PCOS which ultimately improve the biochemical profile in PCOS and thus reduce the morbidity of these patients.

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