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EFFECT OF MYO-INOSITOL AND METFORMIN ON ANTHROPOMETRIC PARAMETERS OF WOMEN IN POLYCYSTIC OVARIAN DISEASE

TAYYBA A[1], HUMA ZE[1], AKHTAR S[2], RANA GE[3], BASHIR A[4], AZHAR S[5] AND RIZWAN B[6]

1: Obst. & Gynae. Amna Annayut Medical College, Lahore-Pakistan

2: Obst. & Gynae. Peshawar Medical College-Pakistan

3: Obst. & Gynae. Services Hospital Lahore-Pakistan

4: Obst. & Gynae. Sir Ganga Ram Hospital, Lahore-Pakistan

5: Obst. & Gynae. Bahria International Hospital, Lahore-Pakistan

6: Institute of Molecular Biology and Biotechnology (IMBB), The University of Lahore

*Corresponding Author: Zill e Huma: E Mail: drluckymao@gmail.com; Contact #: +92 333 4054927

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ABSTRACT

OBJECTIVE: The study was conducted to evaluate and compare the effect of insulin sensitizers i.e. metformin and myoinositol on anthropometric parameters in patients of the Polycystic ovarian syndrome (PCOS). **STUDY DESIGN:** Comparative study **METHODS:** Comparative, clinical study was conducted on 120 patients at kishwar fazal teaching hospital sheikhupura, from April 2018 to June 2019. The patients were randomly divided into two groups having 60 females in each group, two treatments (Tab Myoinositol and Tab Metformin) were given: group A: Tablet myoinositol 1000 twice daily. group B: Tablet metformin 500 mg three times a day for 24 weeks. Anthropometric parameters were assessed by measuring body weight, Body mass index (BMI), waist-hip ratio (WHR) at the start of study i,e baseline and subsequently at the end of 12 week and 24 weeks. **RESULTS:** In both groups, the improvement was seen over a period of 24 week. In group A, the values for weight at baseline, 12 week and 24 week expressed

in mean±SEM are 65.86±.80, 64.30±.78 and 63.10±.55 while in group B the values were 65.98±.99, 64.33±1.74 and 63.20±1.45. In group A, BMI at baseline, 12 week and 24 week was 26.45±.41, 25.78±.42 and 25.31±.40 while in group B the values were 27.56±.41, 26.58±.32 and 26.43±.70 respectively. In group A, WHR was 0.77±.007, 0.76±.005 and 0.76±.007 while in group B 0.78±.008, 0.77±0.88, 0.77±.011 at baseline, 12 w and 24 w respectively. However, no statistically significant difference was observed in all the parameters. **CONCLUSION:** The definitive improvement seen in anthropometric parameters with both metformin and myoinositol but on comparing these drugs, no significant difference was observed. Thus, myoinositol can also be used as an alternative to metformin for the treatment of PCOS.

Keywords: PCOS, BMI, WHR, Myo-inositol, Metformin, Anthropometric

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder among women of reproductive age. More than 30% of women with PCOS are obese (body mass index–BMI>30 kg/m2), reflecting primarily visceral adiposity **[1]**. Obesity is a prominent feature of PCOS, occurring in 40-50% of PCOS patients **[2, 3]**. Prevalence of PCOS is increased in overweight and obese women . The prevalence of PCOS in underweight, normal-weight, overweight, and obese women are 8.2%, 8.8%, 9.0% and 9.9% respectively. Increased fat deposition, particularly visceral fat that is reflected by an elevated waist circumference (>88 cm) or waist-to-hip ratio (WHR), it is associated with hyperandrogenemia, insulin resistance, glucose intolerance, and dyslipidemia **[4, 5]**. Genes responsible for the pathogenesis of PCOS are those associated with steroidogenesis, regulation of gonadotropin secretion, effects of insulin, obesity, factors regulating the body's energy consumption and the genes associated with chronic inflammation **[6]**. PCOS women tend to have an increased BMI and WHR i.e. abdominal (visceral) obesity **[7, 8]**. Anthropometric parameters suggesting insulin resistance are increased BMI and WHR>0.85. Numerous studies have demonstrated a pathogenetic association of PCOS with insulin resistance and hyperinsulinaemia **[9-11]**. Metformin and myoinositol being insulin sensitizers improve the metabolic, reproductive and anthropometric parameters i.e. weight, BMI and WHR in women suffering from PCOS **[12, 13]**. Efficacy and safety of myoinositol

and metformin is already established in various studies. Some studies have shown the comparable efficacy of these drugs regarding the improvement of clinical features, hormonal and biochemical parameters. The safety profile is shown to be better with myoinositol than metformin **[14]**. It is well known that metformin an insulin sensitizer causes weight loss. This study was planned to determine the beneficial effect and comparison of myoinositol and metformin on anthropometric parameters in women with PCOS.

MATERIALS AND METHODS

This was a comparative study conducted on 120 women in the department of Obstetrics and Gynaecology, at Kishwar fazal teaching Hospital, SHEIKHUPURA, on 120 women. The females of reproductive age group (15-40 yr), diagnosed with PCOS according to Androgen Excess Society (AES)/2006 criteria: presence of hyperandrogenism (clinical and/ or biochemical), oligomenorrhea, anovulation, polycystic ovarian morphology (PCOM) at least one ovary with 12 or more follicles (2-9 mm in diameter) or ovarian volume>10 ml and those willing to give a written informed consent were included in the study. The exclusion criteria was women suffering from hyperprolactinemia, Cushing's disease, hypothyroidism, hyperthyroidism, pregnancy and nursing mothers, active liver disease, renal impairment, established type 1 or type 2 diabetes mellitus, any history of drug intake of antidiabetic or estrogen and progesterone and patients who were unable to come for regular visits.The eligible patients were randomly divided into two study groups each to receive either of the following two treatments: group A: Tablet Myoinositol 1000 mg twice daily and group B: Tablet Metformin 500 mg three times a day for 6 months. During the study, patients were not permitted to take any other drug. Anthropometric parameters were assessed by measuring body weight, BMI, waist circumference, hip circumference, WHR at baseline and subsequently at the end of 12 weeks and 24 weeks. BMI is calculated as body weight in kilogrammes divided by square of height in meters. Waist circumference is measured with a tape midway between the lowest rib margin and the iliac crest in standing position. The hip circumference is measured over the widest part of gluteal region. Data was expressed as mean±SEM. Intergroup statistical analysis was done. Intergroup

analysis was done using unpaired 't' test for parametric data. A p-value<0.05 was considered as statistically significant.

RESULTS

Total of 120 patients with symptoms of PCOS included in the study , were randomly divided into two treatment groups. Patients in group A took myoinositol 1000 mg twice a day, while group B was given metformin 500 mg thrice a day for 24 week. The parameters of the patients assessed are shown in table I. Weight (kg) 65.86±0.80 64.30±.78 0.856 BMI (kg/m^2) 26.45±0.41 26.09±0.76 0.679 Waist hip ratio. There was a statistically significant improvement in anthropometric parameters as assessed by changes in body weight, BMI and WHR with both the drugs over a period of 24 weeks. Anthropometric parameters were slightly better improved with myoinositol than metformin. **Fig. 1** shows changes in body weight (kg) with both the drugs over a period of 24 w eek. There was reduction in weight at the end of 12 and 24 w compared to baseline values in both the groups, however, difference is not statistically significant. In group A and B mean decrease in weight was 1.56 and 1.63 respectively at the end of 12 weeks. With myoinositol mean reduction in weight was from 65.86 (baseline) to 63.10 (24 weeks), showed a decrease of 2.76. In metformin group mean reduction in weight was from 65.98 (baseline) to 63.20 (24 w), showed a decrease of 2.78. **Fig. 1** : Comparison of changes in weight in both the groups. Intergroup analysis Comparison of values between Group A and B is not statistically significant (P>0.05). **Fig. 1** shows changes in BMI (kg/m2) with both the drugs over a period of 24 w. In myoinositol group, the BMI decreased by 1.13, while in metformin group the BMI decreased by 1.14 at the end of 24 was as compared to baseline values. There was slightly more improvement in BMI with myoinositol than metformin (1.13 vs 1.14) at the end of 24 w, but the the difference was not statistically significant. Values are expressed as mean±SEM, Group A (n=60): Myo-inositol 1000 mg bd, Group B (n=60): Metformin 500 mg tds . Intergroup analysis Comparison of values between Group A and B is not statistically significant (P>0.05). **Table 1** shows changes in waist circumference and hip circumference followed by WHR over a period of 24 w. WHR decreased by 0.01 with myoinositol at the end of 12 week which was maintained over a period of 24 week whereas in metformin group no reduction in WHR was observed at the end of 24 w as

compared to baseline values. Intergroup analysis Comparison of values between Group A and B is not statistically significant (P>0.05). **Table 1**: Comparison of changes in weight, body mass index and waist-hip ratio (WHR) in both groups.parameters areBaseline 77.56±1.58 78.08±1.80 0.830 -5.32 4.29 12 w 76.13±1.54 76.46±1.77 0.888 -5.04 4.37 24 w 74.86±1.44 74.90±1.72 0.988 -4.53 4.46 Hip circumference (cm) Baseline 97.13±1.41 97.41±1.72 0.899 -4.74 4.17 12 w 96.23±1.37 95.93±1.69 0.891 -4.06 4.66 24 w 94.93±1.32 94.73±1.66 0.926 -4.06 4.66 Waist hip ratio (WHR) Baseline 0.79±0.007 0.79±.010 0.847 -0.028 0.023 12 w 0.78±0.007 0.79±.0108 0.610 -0.033 0.019 24 w 0.78±0.007 0.79±0.011 0.836 -0.029 0.023. All values are expressed as mean±SEM, Group A: Myo-inositol 1000 mg bd, Group B: Metformin 500 mg tds.

Table 1: Comparison of Different Parameters Between Two Groups (GPA and GP B)

Parameters		Myoinositol Group A (n=60)	Metformin Group B (n=60)	P Value
Weight	Base line 12 weeks 24 Weeks	65.86 ± 0.80 64.30 ± 0.78 63.10 ± 0.68	65.98 ± 0.99 64.35 ± 1.11 63.20 ± 1.45	0.85
BMI	Base Line 12 weeks 24 Weeks	26.45 ± 0.41 25.78 ± 0.42 25.31 ± 0.40	27.56 ± 0.60 26.58 ± 0.32 26.43 ± 0.70	0.69
Waist Hip Ratio (WHR)	Base Line 12 weeks 24 Weeks	0.77 ± .005 0.78 ± .005 0.76 ± .005	0.78 ± .008 0.77 ± .010 0.77 ± .012	0.92

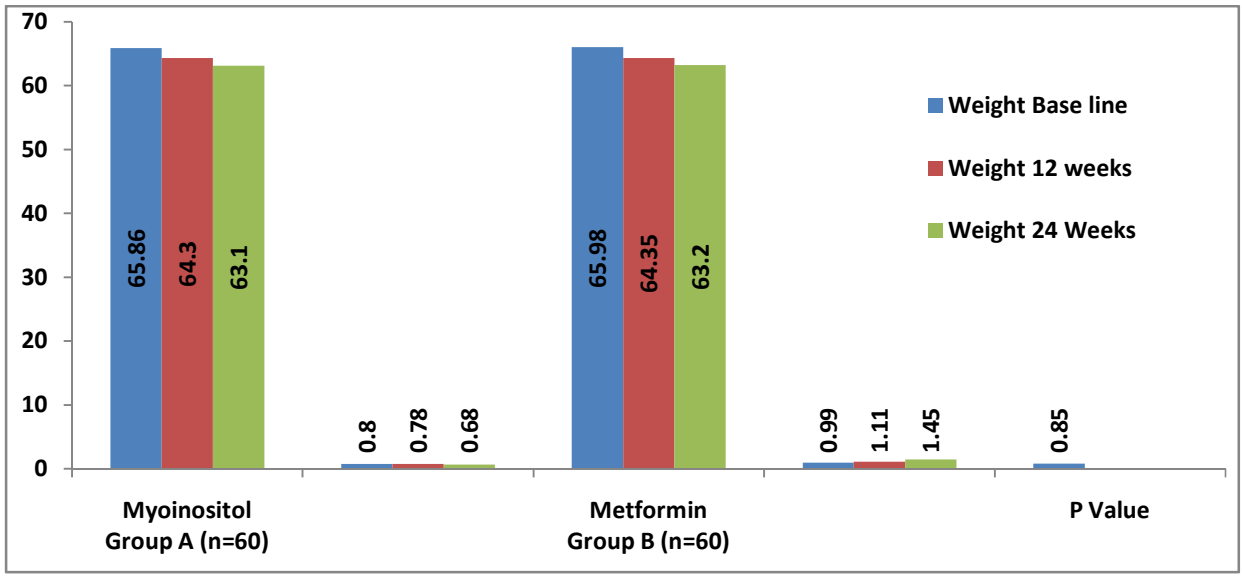

Fig 1: changes in BMI

DISCUSSION

PCOS is the most common endocrine disorder among women of reproductive age, is considered to be not only a reproductive endocrinopathy but also a metabolic disorder. Insulin resistance occurs in around 50% to 80% of women with PCOS, **[15]** primarily in the more severe National Institute of Health (NIH) diagnosed PCOS and in those who are overweight. The risk of gestational diabetes mellitus (GDM) is increased and is further exacerbated by obesity **[9, 16]**. There is a close association between insulin resistance (IR) and obesity. In PCOS, obesity worsens insulin resistance and exacerbates reproductive and metabolic features. The gyneoid type of fat distribution develops during female puberty and persists during the fertile phase of adult life **[17]**. Peripheral fat tissue, especially in the lower body region is an important source of extra ovarian estrogen synthesis because aromatization from androgens to estrogens takes place there **[17]**. The major endocrine symptom of PCOS, hyperandrogenicity is clearly associated with a preponderance of fat localized in the upper body sites. This sex-specific fat distribution, commonly called android fat distribution, Study associated with obesity and a variety of metabolic characteristics as well as an indicator of reduced reproductive capability of the woman **[17]**. Upper-body obesity is a key component of the IR syndrome. Abdominal fat distribution is measured by Waist-hip ratio (WHR) which gets altered in insulin resistance. 5% to 10% weight loss has significant clinical benefits improving psychological outcomes, reproductive features (menstrual cyclicity, ovulation and fertility) and metabolic features (insulin resistance and risk factors for cardiovascular disease and type II DM).) **[18]** More than 50% of PCOS patients are obese. These women are at the risk of diabetes, atherosclerosis, and cardiovascular diseases. Since obesity is the most common cause of insulin resistance and hyperandrogenism, weight reduction might be the first recommendation for PCOS women. Weight loss up to 5-7% during 6 mo can restore ovulation and fertility in more than 75% women. In our study, there was a statistically significant reduction in BMI at 12 and 24 w compared to baseline values in both the groups. Mean decrease in BMI was 0.67 and 0.56 respectively at the end of 12 w with myoinositol and metformin respectively. In myoinositol group mean reduction in BMI was from 26.45 (baseline) to 25.31 (24 w), showed a decrease of 1.14.

In metformin group mean reduction in BMI was from 26.09 (baseline) to 24.96 (24 w), showed a decrease of 1.13. In a study done by Awalekar *et al*., in which 102 patients were randomized into three groups i.e. metformin (500 mg tds), myoinositol (2 g bd) plus folic acid (5 mg od) and lifestyle modification group for a period of 12 w. BMI decreased by 2.51 and 1.00 with metformin and myoinositol respectively **[19]**. The findings of our study are similar to above-quoted study as BMI was reduced with both the drugs at the end of 12 w in both the studies. But the decrease was more with metformin in a study done by Awalekar et al. as compared to the present study (2.51 vs 0.56). The decrease in BMI was also more with myoinositol in above-quoted study as compared to our study (1 vs 0.67). In a study done by Genazzani et al., in 20 PCOS patients, who were randomly assigned to receive either myoinositol 2000 mg plus folic acid 200 µg daily or folic acid 200 µg daily for a period of 12 w changes in BMI were observed. BMI decreased by 0.70 with myoinositol, whereas increased by 0.10 with folic acid **[20]**. The findings of our study are similar to above-quoted study as BMI was reduced with myoinositol at the end of 12 w in both the studies. The decrease in BMI in a study done by Genazzani et al. is in concordance with the present study (0.70 vs 0.67). In another study done by Genazzani *et al*., 34 patients were given a combination of alpha-lipoic acid (400 mg) and myoinositol 1g every day for 12 w. BMI decreased by 0.50 at the end of 12 w **[21]**. The findings of our study are similar to above-quoted study as BMI reduced with myoinositol at the end of 12 w in both the studies. However the decrease in BMI in a study done by Genazzani et al. is less as compared to the present study (0.50 vs 0.67). This could be due to the fact that dose of myoinositol given in above study (1g) was less than our study (2 g). There was a slight reduction in WHR at the end of 12 w (0.01), which was maintained over a period of 24 w compared to baseline values in myoinositol group. In metformin group, there was no reduction in WHR at the end of 12 and 24 w. In a study done by Angik *et al*., in which metformin and myoinositol were compared to observe their effects on WHR, 100 patients were randomly allocated to treatment with either myoinositol or metformin. Myo-inositol group received 1g twice daily while metformin group received 500 mg twice daily for 6 mo, in which metformin and myoinositol were compared to observe their effects on WHR. The WHR increased by 0.10 in myoinositol

group whereas decreased by 0.03 with metformin at the end of 24 w, however changes in WHR were not significant in both the groups **[22]** The findings of our study differ from above-quoted study in the context that slight better response was observed with myoinositol in our study whereas that was with metformin in above-mentioned study. However, the similarity is that no statistically significant change was observed in WHR over a period of 24 w with both the drugs. In a study done by Gerli *et al*., 45 PCOS patients were given myoinositol combined with folic acid 2 g bd and 47 were given folic acid as placebo and observed after 14 w. There was no change seen in both the groups at the end of 14 w **[13]**. The findings of our study are in concordance with the above-mentioned study as no significant change was observed in WHR with myoinositol. The results of present study indicate that both metformin and myoinositol led to improvement in anthropometric parameters over the period of 24 w. As the difference in all these parameters found to be statistically non-significant when compared, hence myoinositol can be considered comparable to metformin in the treatment of PCOS. Though the sample size and study duration were small in this study, further research with larger groups and longer study period is required to support these findings.

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. As an improvement in insulin resistance helps in weight reduction and vice versa. Metformin and myoinositol being insulin sensitizers improved anthropometric parameters in PCOS. Both the drugs were found to be equally efficacious. Hence, myoinositol can be a new addition in the armamentarium for the treatment of PCOS. As insulin resistance is the underlying pathology in PCOS, insulin sensitizers along with lifestyle modification should be considered as a new integrative strategy which can lead to weight reduction and improvement in symptoms of PCOS.

CONFLICT OF INTERESTS

All the authors declare that there is no conflict of interest.

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