



**EFFECT OF MYO INOSITOL VERSUS METFORMIN ON QUALITY OF LIFE IN
POLYCYSTIC OVARIAN SYNDROME IN WOMEN**

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Article Received on 30/08/2016

Article Revised on 19/09/2016

Article Accepted on 09/10/2016

ABSTRACT

Introduction: In polycystic ovary syndrome (PCOS), changes in physical appearance i.e. weight gain and body hair, menstrual disturbances and infertility result in psychological distress and reduced quality-of-life. Metformin and Myo-inositol being insulin sensitizers improve biochemical, clinical and reproductive parameters in PCOS in women. This study was done to compare the quality of life of Myo-inositol versus Metformin in PCOS in women. **Material & Methods:** A prospective, open labeled, randomized, comparative, clinical study was conducted on 60 patients. The patients were randomly divided in two groups of 30 each to receive either of the following two treatments: Group A: Tab Myo-inositol 1g twice daily. Group B: Tab Metformin 500mg thrice daily for 24 weeks. QOL assessment was done by HRQOL questionnaire by Cronin et al. at week 0, 12 and 24. Five domains i.e. emotions, body hair, weight, infertility and menstrual problems were assessed. **Results:** There was significant improvement in QOL parameters, in all the five domains in both the groups over a period of 24 weeks. However, on comparing both the groups at 24 weeks, there was no significant difference in all the five domains. **Conclusion:** Metformin and Myo-inositol are used for the treatment of PCOS. These drugs improve insulin resistance, menstrual irregularities, hyperandrogenism and infertility. QOL which is reduced in PCOS, was assessed by the administration of both of these drugs. Although there was a definite improvement in QOL with both types of treatment in PCOS in women but on comparing both the groups no significant difference was observed.

KEYWORDS: HRQOL, Metformin, PCOS, Myo-inositol, Insulin sensitizers.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in reproductive-aged women.^[1] Clinical presentations associated with PCOS, such as overweight/obesity, hirsutism, acne, hair loss/androgenic alopecia, oligomenorrhea, amenorrhea and infertility, can lead to mood disturbances, affect the emotional well being as well as sexual satisfaction of women and cause a reduction in the health related quality of life (HRQOL) of patients.^[2,3] Obesity, clinical signs of hyperandrogenism (i.e., acne, hair loss), and infertility are the main contributors to psychological morbidity.^[4-6] The HRQOL of women with PCOS has been investigated in several studies for some countries.^[1,7,8] However, data on the HRQOL of Indian women with PCOS is limited.

PCOS is strongly associated with reproductive and metabolic implications affecting patient's psychological functioning and satisfaction with life. Psychological implications entail challenges in depression, physical

appearance/ feminine identity, eating habits and psychosexual dysfunction with significant impact on quality of life (QOL).^[9] Increased rate of depressive symptoms compared to non-BMI matched controls^[10,11] with prevalence ranging from 28 to 64% (for depression) and 34 to 57% (for anxiety) have been reported in women with PCOS.^[12] Also, a lower health related QOL and increased risk of mental depression are reported in women with PCOS. In Indian women, a 54% prevalence of depression was reported, of whom 72% were obese, 70% had hirsutism, 61% had acne and 56% were infertile indicating a considerable effect on QOL of these women.^[13] The Patient Health Questionnaire 9 (PHQ-9) can be used to measure the severity of depression whereas the generic Short Form-36 (SF-36) and disease-specific polycystic ovary syndrome questionnaire (PCOSQ) are used to assess the health related QOL in women with PCOS.

Clinical interventions in PCOS women that influence obesity, hirsutism, acne or menstrual disturbances would

be expected to improve overall HRQOL. Insulin sensitizing drugs such as metformin and glitazones have been shown to improve all these somatic problems in PCOS patients.^[14-16] Metformin and myo-inositol are insulin sensitizers. This study is done to compare the effect of these two drugs on quality of life in PCOS women.

MATERIAL AND METHODS

This was a prospective, open label, randomized, comparative clinical study conducted by the Department of Pharmacology and Obstetrics & Gynaecology, Pt.B.D.Sharma PGIMS, Rohtak, India on 60 patients. Study was in accordance with the principles of good clinical practice (ICH-GCP) and declaration of Helsinki. An informed consent was obtained from all the patients enrolled for the study. The study was approved by the PG Board of study, Pharmacology and Dean Faculty in Para-clinical sciences, University of Health Sciences, Rohtak.

An adequate number of patients were screened and selected as per the inclusion and exclusion criteria for the study. The eligible patients were randomly divided into two study groups i.e. Group A (Myo-inositol) and Group B (Metformin) with the help of computer generated random numbers. Each study group had minimally 30 patients who completed the study as per the protocol. During the study, patients were not permitted to take any non-study drugs.

The inclusion criteria included females of reproductive age group (15-45 yrs), diagnosed with PCOS according to AES (Androgen Excess Society)/2006 criteria: Presence of hyperandrogenism (clinical and/or biochemical), Oligo or anovulation, PCOM (Polycystic ovarian morphology) - 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. The Exclusion criteria were: women suffering from any neoplastic disease, hyperprolactinemia, Cushing's disease, Hypothyroidism/Hyperthyroidism, Pregnant and nursing mothers, active liver disease, renal impairment, established type 1 or type 2 diabetes mellitus, any history of drug intake of anti diabetic or oestrogen and progesterone, history of any treatment taken in last 3 months, smokers and alcoholic subjects and patients who were unable to come for regular follow ups.

Patients who were diagnosed with PCOS according to the AES (Androgen excess society) 2006 criteria were included in the study. The patients were randomly divided in two groups of 30 each to receive either of the following two treatments: Group A: Tab Myo-inositol 1g twice daily. Group B: Tab Metformin 500 mg thrice daily for 6 months.

Quality of life was measured using PCOSQ. PCOSQ is 26 items, multi-dimensional, self report questionnaire

given by Cronin *et al*^[17], for the quality of life assessment among PCOS women. Its validity and reliability has been demonstrated previously. The PCOSQ evaluates five domains of the patient's quality of life, i.e. emotions, body hair, weight, infertility problems and menstrual problems.^[17] Patients were asked to choose the response option that best suited their feelings during the past 2 weeks. Scores range 1-7 for each item in which, the higher score represents better function. By adding the scores of the individual items that comprise the domain and dividing by the number of questions in that domain, individual domain scores were obtained. There were 8 questions related to emotions, 5 each for body hair and weight, and 4 each for the infertility and menstrual problem domains. The composite score was obtained by adding the five domain scores.

Data was expressed as Mean \pm SEM. Both intragroup and intergroup statistical analysis was done. Intragroup analysis for repeated measures was done using ANOVA for parametric data and pairwise comparison was done. Intergroup analysis was done using unpaired 't' test for parametric data. A p-value <0.05 was considered as statistically significant.

RESULTS

A total of 79 patients with symptoms of PCOS were screened for this study. Out of this, 8 patients were excluded, as 6 patients did not fulfill the predefined inclusion criteria of the study and 2 were not willing to give informed consent. Rest of the 71 patients, enrolled in the study were randomized with the help of computer generated random numbers and were allocated to either of the two treatment groups. Patients in Group A received Myo-inositol 1gm BD while Group B received Metformin 500 mg TDS for 24 weeks. Of the 71 patients enrolled in the study, 35 were allocated to MI 1gm BD Group A and 36 allocated to Metformin 500 mg TDS group. 5 patients in Group A and 6 patients in Group B were lost to follow-up and were dropped from the study and the remaining 30 patients in either group completed the treatment successfully. The baseline characteristics of the patients are tabulated in Table I.

Table-1: Comparison of Study Population Characteristics In Both the Groups.

Variables	Group A (n=30)	Group B (n=30)	'p' value
Age in years	23.8±.69	23.26± 1.03	0.669
Weight (Kgs)	63.96±.90	63.58 ± 1.88	0.856
BMI (kg/m ²)	26.45 ± .41	26.09 ± .76	.679
Marital Status			
Married	19	22	-
Unmarried	11	8	
Education			
Literate	26	28	-
Illiterate	4	2	
Age at menarche	11.8±.29	11.1±.21	0.06
Number of patients with Irregular cycle	25	24	-
mFG score of Hirsutism	9.03 ± .32	9.06 ± .46	.954

- Age, weight, BMI, mFG score are expressed as Mean±SEM
- Group A: MI 1000 mg BD
- Group B: Metformin 500 mg TDS

Assessment of QOL was divided into five domains i.e. emotional domain, body hair domain, weight domain, infertility problem domain and menstrual problem domain. The composite score of QOL was recorded in all the patients of either group before drug administration (baseline) and at end of 12 and 24 weeks. Table 2 shows the changes in domain scores with the treatment. At the end of 24 weeks there was statistically significant improvement in the scores of all the domains of QOL i.e. emotional domain, body hair domain, weight domain, infertility domain and menstrual domain with both the drugs. In myo-inositol

group, improvement in scores of these domains was 13.85%, 21.66%, 20.96%, 15.76% and 31.57% respectively at the end of 24 weeks as compared to baseline values. At the end of 24 weeks, improvement in composite QOL score was 20.30% as compared to baseline values. In metformin group, improvement in the scores of these domains was 12.69%, 14.0%, 21.58%, 21.22% and 32.44% respectively as compared to baseline values. At the end of 24 weeks, improvement in composite QOL score was 20.31% as compared to the baseline values.

Table- 2: Comparison of Changes In Scores of Various Domains of Qol In Both The Groups.

PCOSQ domains		Myo-inositol (Group A)		Metformin (Group B)		p value (inter-group)
		Mean ± SEM	Improvement from baseline	Mean ± SEM	Improvement from baseline	
Emotions domain	Baseline	4.62 ± .08	-	4.57 ± .08	-	.679
	12 weeks	4.94 ± .06 *	0.32 (6.92%)	4.83 ± .06*	0.26 (5.68%)	.244
	24 weeks	5.26 ± .05 [#]	0.64 (13.85%)	5.15±.05 [#]	0.58 (12.69%)	.150
Body hair domain	Baseline	4.20±.12	-	4.50 ±.14	-	.120
	12 weeks	4.67 ± .09*	0.47 (11.19%)	4.71 ±.12*	0.21 (4.66%)	.833
	24 weeks	5.11 ± .08 [#]	0.91 (21.66%)	5.13±.09 [#]	0.63 (14%)	.833
Weight domain	Baseline	4.15±.09	-	4.17±.12	-	.88
	12 weeks	4.54±.08*	0.39 (9.39%)	4.61±.09*	0.44(10.55%)	.636
	24 weeks	5.02±.06 [#]	0.87 (20.96%)	5.07±.08 [#]	0.90 (21.58%)	.630
Infertility problems domain	Baseline	4.44 ± .09	-	4.24±.09	-	.138
	12 weeks	4.82±.07*	0.38 (8.55%)	4.68±.07*	0.44 (10.37%)	.197
	24 weeks	5.14±.05 [#]	0.70 (15.76%)	5.14±.06 [#]	0.90 (21.22%)	1.00
Menstrual problem domain	Baseline	3.80±.12	-	3.76±.12	-	.817
	12 weeks	4.46±.11*	0.66 (17.36%)	4.29±.10*	0.53 (14.09%)	.247
	24 weeks	5.00±.08 [#]	1.20 (31.57%)	4.98±.08 [#]	1.22 (32.44%)	.838

- All values are expressed as Mean±SEM
- Group A: Myo-inositol 1000 mg BD
- Group B: Metformin 500 mg TDS

[#] Comparison of values at end of week 24 with baseline values: showing statistical significance ($p < 0.05$).

INTRAGROUP ANALYSIS:

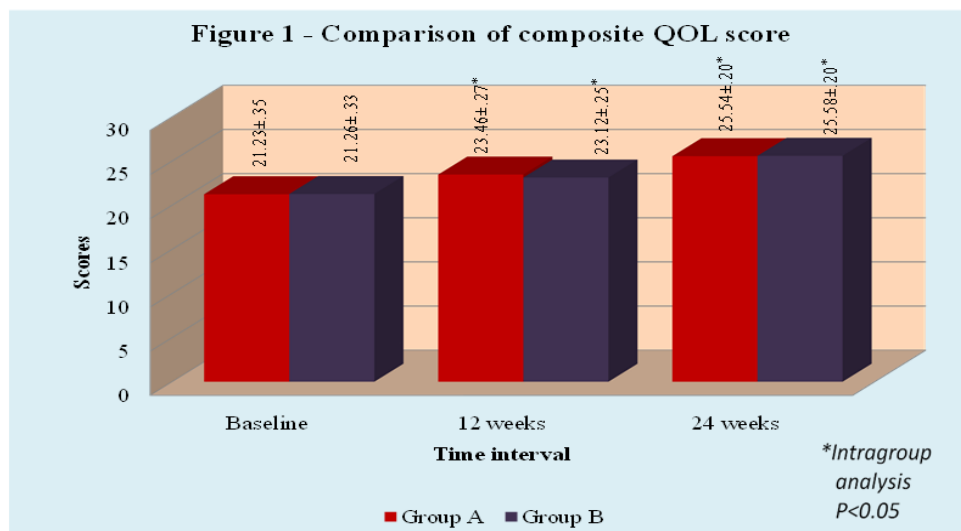
* Comparison of values at end of week 12 with baseline values: showing statistical significance ($p < 0.05$).

INTERGROUP ANALYSIS:

Comparison of values between Group A and B is not statistically significant ($p > 0.05$).

Figure 1 shows the changes in composite QOL score over period of 24 weeks in both the groups. In myo-inositol group there was 10.50% improvement in composite quality of life score whereas, improvement in metformin group was around 8.74 % at end of 12 weeks compared to their baseline values ($p < 0.05$). At the end of

24 weeks improvement in composite QOL score with myo-inositol and metformin was 20.30% and 20.31% respectively as compared to baseline values. Although there was improvement in composite QOL score with both the drugs but there was no difference observed.



DISCUSSION

Polycystic ovary syndrome (PCOS) is a common endocrine disorder characterized by chronic anovulation and hyperandrogenism. Its pathophysiology, most likely a combination of genetic disposition and environmental factors, is not completely understood.^[18,19] PCOS is one of the leading causes of infertility and is also characterized by hirsutism, acne, seborrhea, hair loss, and obesity.^[20,21] A significant proportion of PCOS patients has been found to suffer from defective insulin secretion and insulin resistance.^[22] Accordingly, PCOS patients may be expected to have a higher morbidity and mortality from the sequelae of the metabolic syndrome.^[23,24]

PCOS women suffer from marked reductions in quality-of-life, impaired emotional well-being. WHO defined Quality of life as “the concept of an individual of his status in life in relation to the culture and the system of values in which he lives, and in relation to the goals, standards and needs”.^[25] The definition comprises six large areas, namely physical health, emotional status, level of independence, social relations, environmental characteristics and spiritual needs. In 1990, Spilker described the assessment of quality of life by means of three interrelated parameters: global assessment of well-being, comprehensive domains (e.g., physical, psychological or social domains) and the individual components of each domain.^[26] These components classified the multidimensional character of quality of life. In the present study assessment of QOL was divided into five domains i.e. emotional domain, body hair domain, weight domain, infertility problem domain and

menstrual domain on the basis of validated questionnaire given by Cronin *et al.*^[17]

At the end of 24 weeks improvement in scores of emotional domain, body hair domain, weight domain, infertility domain and menstrual domain in myo-inositol group versus metformin group was 13.85% vs 12.69%, 21.66% vs 14.0%, 20.96% vs 21.58%, 15.76% vs 21.22% and 31.57% vs 32.44% respectively as compared to baseline values. At the end of 24 weeks improvement in composite QOL score with myo-inositol and metformin was 20.30% and 20.31% respectively as compared to baseline values. Although there was improvement in composite QOL score with both the drugs but there was no difference observed.

Although exact similar studies were not available in which similar treatment groups were compared for observing the effects on QOL using PCOSQ. In spite of our best efforts, we couldn't find a study in which effect of myo-inositol was studied on QOL in PCOS. However after literature search, we could get the study in which effect of metformin on QOL was observed.

In a study done by Hahn *et al.*, after 6 months of treatment, changes in clinical and endocrine parameters, quality-of-life, psychological disturbances and sexuality were assessed in 64 PCOS patients using validated questionnaires (SF-36, SCL-90-R) and visual analogue scales. During this treatment, HRQOL, particularly the psychosocial aspects (indicated by significant increases in SF-36 scales Vitality, Social Function, Emotional Role Function, Mental Health, Psychological Sum scale) and

emotional well-being (reflected by significant lowering of SCL-90-R scales) improved after 6 months.^[27]

The findings of our study are quite similar to the above mentioned study as there was improvement in QOL in PCOS women in both the studies with metformin, but the scale used was different in above mentioned study than from our study.

In a study by Ou *et al.*, 109 participants (56 % were overweight, 80 % had hyperandrogenism) were recruited. Among the domain scores of WHO Quality of Life (WHOQOL-Bref), the psychological domain score was the lowest one (12.64 ± 2.2 , range 4–20). In Chinese version of health-related quality-of-life questionnaire (Chi-PCOSQ), weight (3.25 ± 1.59) and infertility (3.38 ± 1.93) domain scores were relatively low. Overweight and hyperandrogenic patients had significantly lower HRQOL as compared with those of normal weight and non-hyperandrogenic patients, respectively. Metformin significantly improved the physical domain of WHOQOL-Bref ($p=0.01$) and the infertility ($p = 0.043$) and acne and hair loss aspects ($p = 0.008$) of PCOS-specific HRQOL. In the subgroup analysis, significantly improved HRQOL following metformin treatment appeared for only overweight and hyperandrogenism subgroups.^[28]

The findings of our studies are similar to above mentioned study as there was improvement in both the domains i.e. weight domain and body hair domain with metformin in our study.

In another study done by Prabhu *et al.* where 100 patients were enrolled equally into without metformin group and with metformin group, based on their pharmacotherapy for their PCOS management. Results indicated significant positive differences in the mean score of anxiety, depression, self-esteem, social anxiety and QOL of respondents in metformin group. The change in mean score was highest in QOL, showing a higher score of 90.60 ± 17.60 in metformin group compared to score of 80.40 ± 15.45 without metformin. Except for self-esteem ($p>0.05$), significant differences in the anxiety, depression, social anxiety and QOL ($p<0.05$) are observed in comparison with both groups. The odds ratio was conducted and results indicated that with metformin group QOL is 5.4176 times better than without metformin group QOL.^[29]

The findings of our study are in concordance with the above mentioned study as metformin significantly improved the emotional component of QOL.

Both the drugs led to improvement in QOL over the period of 24 weeks. As the difference in all these parameters after 6 months of respective treatment in both the groups was found to be statistically non-significant, thus, myo-inositol may be considered comparably effective to metformin in treatment of PCOS. Though the sample size and study duration was small in this study,

further research with larger groups and longer study periods is required to support these findings.

CONCLUSION

PCOS causes a major reduction in quality of life and psychological well-being and severely limits sexual satisfaction and self-worth in affected women. Changes in outer appearance, particularly obesity and excessive body hair were significantly associated with specific negative aspects of quality of life and sexual satisfaction. Considering the array of treatments (insulin sensitizers) available to offer symptomatic relief to women with PCOS, more studies observing the affect of treatment on HRQOL would be beneficial in order to provide guidance in clinical decision making to prescribing physicians. In addition, further studies are required to explore the impact of PCOS upon HRQOL and the effect of drugs improving the HRQOL.

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