

Comparison of Metformin and Myoinositol for the Treatment and Improvement of Clinical, Metabolic, and Hormonal Parameters in Women with Polycystic Ovary Syndrome

Uditi Merchant¹, Ashwini Desai²

^{1,2}Choithram Hospital & Research Centre, 14, Manik Bagh Road, Indore, Madhya Pradesh, 452014, India

¹Corresponding Author Email ID: [uditi.naidu.un\[at\]gmail.com](mailto:uditi.naidu.un[at]gmail.com)

MOB NO: - +91 – 8319469499

Abstract: *The study demonstrates that treatment with both Metformin and Myoinositol improves clinical, hormonal, and metabolic profiles in women with polycystic ovary syndrome PCOS. After 6 months of therapy, both groups showed regular menstrual cycles, reduced mFG scores, decreased BMI, serum testosterone, LHFSH ratio, and improved polycystic ovarian morphology. Both drugs were found to be safe and effective in PCOS patients. When comparing the treatment groups, Myoinositol showed comparable efficacy to Metformin, except for a more significant decrease in serum testosterone levels by Metformin, reducing signs of hyperandrogenism. Myoinositol can be considered as a viable treatment option for PCOS with comparable effectiveness. Myo - inositol may counteract the etiopathologies responsible for PCOS - related symptoms and serve as an alternative to treatments associated with side effects, particularly in adolescents*

Keywords: Metformin, Myoinositol, insulin resistance

1. Introduction

Polycystic ovarian syndrome (PCOS) is a common female endocrine disorder. It is characterized by irregular periods, obesity, excessive facial/body hair, male pattern baldness, decreased sex drive, skin tags, infertility, depression, weight gain and multiple ovarian cysts. Insulin resistance is one of the most common features of PCOS, and a condition in which the cells of the body become resistant to the effects of insulin. The root cause of PCOS is unknown but genetic predisposition, insulin resistance, excess androgen production, and obesity all play a role. ^[1]Conventional treatment options include drug treatments for hirsutism and acne; drugs such as clomiphene, tamoxifen and gonadotropins to induce ovulation for infertility; surgery i. e. laparoscopic ovarian drilling ^[2] to induce ovulation by reducing androgen levels, and promising insulin - sensitizing drugs such as metformin. Emerging evidence suggests that lifestyle choices such as weight reduction and exercise, along with specific nutraceuticals like myoinositol targeted to safely and effectively deal with symptoms, underlying causes and associated risk factors, might help reduce the incidence and severity of PCOS. The most important aspect of long term care of PCOS is managing cardiovascular risks such as obesity, insulin resistance, diabetes, coronary artery disease, hypertension and elevated blood cholesterol. These patients are 7 times more likely to have myocardial infarction. ^[3] Early recognition and intervention are considered to be the cornerstones of PCOS treatment.

Metformin: Metformin therapy decreases hyperandrogenism and ovarian volume in women with PCOS. ^[4]It reduces hyperinsulinemia, reverse the endocrinopathy of PCOS and normalize endocrine,

metabolic and reproductive functions, leading to the resumption of menstrual cyclicity and ovulation. ^[5]

Myoinositol: In women with the PCOS, insulin resistance may be related to a deficiency in Myo - inositol containing mediator of insulin action and thus the administration of the Myo - inositol improves insulin sensitivity. Myo - inositol decreases serum androgen concentrations, reduces circulating insulin and improves glucose tolerance and other altered metabolic values associated with insulin resistance in women affected by PCOS. ^[6]Metformin and Myo - inositol being insulin sensitizers improve hyperandrogenic and reproductive features of PCOS in women. There are very limited studies available on the comparative efficacy of Metformin and Myoinositol.

2. Purpose & Significance

The purpose of the study is to compare the effectiveness of two drugs (Metformin and Myoinositol) in treatment and improvement of clinical, metabolic and hormonal parameters in women with polycystic ovary syndrome. The main objectives are:

- 1) To determine the prevalence of PCOS in our hospital on the basis of Rotterdam's criteria (2003).
- 2) To evaluate the efficacy of Metformin and Myoinositol in their respective groups.
- 3) Evaluation of following clinical parameters - weight, BMI, irregular cycles, hypomenorrhoea, acne, hirsutism, infertility.
- 4) Evaluation of following metabolic parameters – fasting blood sugar, fasting insulin and insulin resistance using HOMA2 - IR.
- 5) Evaluation of IR following hormonal parameters – serum

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LH, serum FSH, serum testosterone.

3. Methodology

Study Area and Population

Patients between 18 - 40 years of age with signs and symptoms of PCOS who attended the Outpatient Department of Obstetrics and Gynaecology at CHRC.

Study Design

Prospective, non - randomized, & comparative study.

Study Period

October 2014 to September 2016

Sample Size and Sampling Technique

According to the study done by **Unfer et al (2012)** [7] had reported the incidence of PCOS as 5 - 10% in reproductive age group women. Accordingly we have considered 7% and calculated the sample size. The sample size was calculated using the following formula:

The sample size n and margin of error E are given by

$$x = Z (c/100) 2r (100 - r)$$

$$n = N x / ((N - 1) E^2 + x)$$

$$E = \text{Sqrt} [(N - n) x / n (N - 1)]$$

where N is the population size, r is the fraction of responses that you are interested in, and $Z (c/100)$ is the critical value for the confidence level c . With this we got sample size as 100.

In our study we had included 100 patients. The convenient sampling technique was used in the study.

Grouping

Group 1: Women in this group received metformin.

Group 2: Women in this group received myoinositol.

The distribution to the groups was done on consecutive basis. First woman was allocated to Group 1, the next woman was allocated to Group 2, the third woman was allocated to Group 3 and so on so forth till each group had 50 women each.

The women were enrolled into the study on the basis of the below mentioned inclusion and exclusion criteria.

Inclusion Criteria

- Women between age of 18 - 40 years with signs and symptoms of PCOS diagnosed with PCOS according to the Rotterdam criteria were included in the study.
- Women willing to give voluntary written informed consent for participation in the study.

Exclusion Criteria

- Other hormonal dysfunction (hypothalamic, pituitary, thyroid or adrenal causes for the clinical signs);
- Neoplasms;
- Mental illness;
- Women not willing to provide voluntary written informed consent for participation in the study.

Women and/or her legally acceptable representative were

explained in detail about the study, its risks/benefits, procedures, etc. After getting their verbal approval for participation in the study, a voluntary written informed consent was obtained from them. Only after obtaining this voluntary written informed consent, the study related procedures were initiated.

Women were divided in group 1 and group 2 on consecutive basis.

Group 1 patients were allocated to treatment with metformin.

Group 2 patients were allocated to treatment with myoinositol.

Group 1 received 500 mg metformin twice daily while Group 2 received 1 g myoinositol twice daily for 6 months.

Efficacy assessment was done by observing the clinical signs and symptoms i. e. regularity of menstrual cycle, hirsutism (using modified Ferriman Gallwey score - a score of 0 (none) to 4 (severe) in nine areas of the body is assigned with maximum possible score of 36), acne and changes in weight. Metabolic & hormonal effects will be assessed by doing investigations like FBS, fasting insulin, HOMA2 - IR, FSH, LH, testosterone, etc. Pelvic USG was also done. These findings were reassessed at 3 & 6 months.

The clinical findings and investigations mentioned in study proformawere repeated after 3 months and 6 months and were compared with the baseline values.

The outcome was assessed after analyzing the efficacy of the two drugs in patients of PCOS.

HOMA2IR

HOMA - IR index used as a marker of insulin resistance, based on measurements of fasting glucose and fasting insulin levels, is the homeostatic model assessment of insulin resistance (HOMA - IR). [8] The original model HOMA1 - IR, first published by Matthews and cols. in 1985, [9] has been widely used, especially in epidemiological and clinical studies. Recently, the model was updated with some physiological adjustments to a computer version (HOMA2 - IR) providing a more accurate index. [10] The HOMA2 - IR index was obtained by the program HOMA Calculator v2.2.2. [11] The HOMA2 - IR is a more accurate representation of the metabolic process because it models the feedback relationship between insulin and glucose in the various organs in the body. [12]

The HOMA2 - IR is a non - linear equation, hence there is no formula mentioned in the text, but this value needs to be calculated using the online calculator by inputting the fasting glucose and fasting insulin values. This calculator is available from <https://www.dtu.ox.ac.uk/homacalculator/download.php>. Hence, HOMA2 - IR was used for the present study.

Statistical Analysis Used

Data was collected and analyzed for descriptive statistics using the mean, standard deviation and percentage values. For comparison of mean values between the groups unpaired 't' test was applied and for comparison of mean values within the group, paired 't' test was applied. A P value of <

0.05 was taken as statistically significant. Final data was presented in the form of tables and graphs.

study, hence, there was no additional burden on the patient. Also the present study was not funded by any of the pharmaceutical company or institution.

Financial Inputs and Funding

The women were managed as per the hospital protocol for the management. Routine investigations were done. No additional tests were undertaken for the requirement of the

4. Observations and Results

Comparison of BMI between metformin and myoinositol groups at baseline, 3 months and 6 months (N=100)

BMI	Metformin Group (n=50)		Myoinositol Group (n=50)		't' Value	P Value
	No.	Mean±SD	No.	Mean±SD		
At baseline	50	27.83 ± 4.08	50	27.28 ± 2.56	0.799, df=98	0.426, NS
At 3 months	50	26.94 ± 4.09	50	26.25 ± 2.55	1.008, df=98	0.316, NS
At 6 months	50	26.02 ± 4.04	50	25.12 ± 2.57	1.330, df=98	0.187, NS

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Comparison of hirsutism (mFG score) between metformin and myoinositol groups at baseline, 3 months and 6 months, (N=100)

Hirsutism (mFG score)	Metformin Group (n=50)		Myoinositol Group (n=50)		't' Value	P Value
	No.	Mean±SD	No.	Mean±SD		
At baseline	50	8.08 ± 3.51	50	7.16 ± 4.09	1.207, df=98	0.230, NS
At 3 months	50	6.30 ± 3.11	50	6.34 ± 3.70	- 0.058, df=98	0.953, NS
At 6 months	50	5.30 ± 2.98	50	5.58 ± 3.49	- 0.432, df=98	0.667, NS

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Comparison of fasting blood sugar between metformin and myoinositol groups at baseline, 3 months and 6 months, (N=100)

Fasting Blood Sugar	Metformin Group (n=50)		Myoinositol Group (n=50)		't' Value	P Value
	No.	Mean±SD	No.	Mean±SD		
At baseline	50	96.50 ± 6.59	50	94.62 ± 5.61	1.536, df=98	0.128, NS
At 3 months	50	93.20 ± 5.62	50	91.18 ± 5.25	1.858, df=98	0.066, NS
At 6 months	50	89.84 ± 5.91	50	88.58 ± 5.22	1.130, df=98	0.261, NS

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Comparison of fasting insulin between metformin and myoinositol groups at baseline, 3 months and 6 months (N=100)

Fasting Insulin	Metformin Group (n=50)		Myoinositol Group (n=50)		't' Value	P Value
	No.	Mean±SD	No.	Mean±SD		
At baseline	50	15.48 ± 3.96	50	15.49 ± 4.53	- 0.022, df=98	0.982, NS
At 3 months	50	13.19 ± 3.46	50	13.20 ± 3.99	- 0.013, df=98	0.989, NS
At 6 months	50	10.84 ± 3.13	50	11.03 ± 3.55	- 0.284, df=98	0.777, NS

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Comparison of HOMA2 - IR between metformin and myoinositol groups at baseline, 3 months and 6 months (N=100)

HOMA2 - IR	Metformin Group (n=50)		Myoinositol Group (n=50)		't' Value	P Value
	No.	Mean±SD	No.	Mean±SD		
At baseline	50	2.02 ± 0.52	50	2.01 ± 0.58	0.090, df=98	0.928, NS
At 3 months	50	1.71 ± 0.45	50	1.70 ± 0.52	0.103, df=98	0.918, NS
At 6 months	50	1.39 ± 0.41	50	1.42 ± 0.46	- 0.210, df=98	0.834, NS

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Comparison of Day2 - LH between metformin and myoinositol groups at baseline, 3 months and 6 months (N=100)

Day2 - LH	Metformin Group (n=50)		Myoinositol Group (n=50)		't' Value	P Value
	No.	Mean±SD	No.	Mean±SD		
At baseline	50	5.91 ± 1.50	50	5.89 ± 2.01	0.056, df=98	0.955, NS
At 3 months	50	5.39 ± 1.27	50	5.51 ± 1.98	- 0.354, df=98	0.724, NS
At 6 months	50	5.09 ± 0.99	50	5.06 ± 1.69	0.087, df=98	0.931, NS

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Comparison of LH/FSH ratio between metformin and myoinositol groups at baseline, 3 months and 6 months (N=100)

LH/FSH Ratio	Metformin Group (n=50)		Myoinositol Group (n=50)		't' Value	P Value
	No.	Mean±SD	No.	Mean±SD		
At baseline	50	1.71 ± 0.73	50	1.64 ± 0.95	0.387, df=98	0.699, NS
At 3 months	50	1.47 ± 0.60	50	1.28 ± 0.65	1.492, df=98	0.139, NS
At 6 months	50	1.30 ± 0.43	50	1.11 ± 0.56	1.959, df=98	0.053, NS

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Comparison of serum testosterone between metformin and myoinositol groups at baseline, 3 months and 6 months (N=100)

Serum Testosterone	Metformin Group (n=50)		Myoinositol Group (n=50)		‘t’ Value	P Value
	No.	Mean±SD	No.	Mean±SD		
At baseline	50	1.38 ± 0.65	50	1.35 ± 0.78	0.238, df=98	0.812, NS
At 3 months	50	1.17 ± 0.55	50	1.27 ± 0.62	- 0.826, df=98	0.411, NS
At 6 months	50	0.93 ± 0.43	50	1.20 ± 0.46	- 3.047, df=98	0.003*

Unpaired ‘t’ test applied. P value < 0.05 was taken as statistically significant

At baseline, 3 months & 6 month, The difference statistically not significant (P > 0.05), showing that all above parameters were comparable between the two groups

Distribution of women according to mean ovarian volume in the metformin and myoinositol group, (N=100)

Ovarian Volume	Metformin Group (n=50)		Myoinositol Group (n=50)		‘t’ Value	P Value
	No.	Mean±SD	No.	Mean±SD		
At baseline	50	15.28 ± 1.94	50	14.50 ± 1.97	1.993, df=98	0.049*
At 3 months	50	12.45 ± 1.65	50	11.82 ± 2.02	1.711, df=98	0.090, NS
At 6 months	50	9.47 ± 1.75	50	9.10 ± 2.08	0.965, df=98	0.337, NS

Unpaired ‘t’ test applied. P value < 0.05 was taken as statistically significant

The above table shows the mean comparison of mean ovarian volume at baseline, 3 months and 6 months between metformin and myoinositol groups.

At baseline, the mean ovarian volume in metformin group was 15.28 ± 1.94, while in myoinositol group it was 14.50 ± 1.97. The difference was found to be statistically significant (P < 0.05), with a higher ovarian volume in metformin group in comparison to the myoinositol group.

At 3 months, the mean ovarian volume in metformin group was 12.45 ± 1.65, while in myoinositol group it was 11.82 ± 2.02. The difference was found to be statistically not significant (P > 0.05), showing the mean ovarian volume was comparable between the two groups.

At 6 months, the mean ovarian volume in metformin group was 9.47 ± 1.75, while in myoinositol group it was 9.10 ± 2.08. The difference was found to be statistically not significant (P > 0.05), showing the mean ovarian volume was comparable between the two groups.

There is a significant decrease in both the metformin and myoinositol group at 3 months and 6 months from baseline value, but there was no statistically significant difference in the mean ovarian volume between the two groups at 3 months and 6 months (P>0.05), while it was significant with a lower ovarian volume in myoinositol group (P<0.05) in comparison to the metformin group.

Comparison of number of follicles between metformin and myoinositol groups at baseline, 3 months and 6 months, (N=100)

Number of Follicles	Metformin Group (n=50)		Myoinositol Group (n=50)		‘t’ Value	P Value
	No.	Mean±SD	No.	Mean±SD		
At baseline	50	14.80 ± 1.39	50	14.70 ± 1.82	0.309, df=98	0.758, NS
At 3 months	50	12.00 ± 1.67	50	11.76 ± 1.89	0.678, df=98	0.499, NS
At 6 months	50	8.84 ± 1.88	50	8.82 ± 1.77	0.055, df=98	0.956, NS

Unpaired ‘t’ test applied. P value < 0.05 was taken as statistically significant

The difference was found to be statistically not significant (P > 0.05), showing that mean number of follicles was comparable between the two groups.

Comparison of acne between metformin and myoinositol group at baseline, 3 months and 6 months (N=100)

Acne	Metformin Group (n=50)		Myoinositol Group (n=50)	
	No.	%	No.	%
Baseline	14	28.0	14	28.0
At 3 months	14	28.0	13	26.0
At 6 months	6	12.0	6	12.0

At baseline in both the groups, acne was present in 14 (28%) women. At 3 months slightly lower number of women 13 (26%) of myoinositol group were having acne in comparison to 14 (28%) women in the metformin group.

While at 6 months in both the groups only 6 (12%) women were having acne.

Comparison of conception in infertile women between metformin and myoinositol group at the end of the study period (N=100)

Conception	Metformin Group (n=8)		Myoinositol Group (n=5)	
	No.	%	No.	%
Conception	3	37.5	2	40.0
Z value	- 0.09			
P value	0.928, NS			

Z test for two sample proportion applied. P value < 0.05 was taken as statistically significant

Out of 5 infertility patients in the myoinositol group, 2 (40%) conceived and out of 8 patients in metformin group, 3 (37.5%) conceived. The results in the two groups were comparable but it was not significant statistically (P>0.05).

5. Discussion

Prevalence:

In our hospital, over the last 2 years there were

approx.15321 women presented to the gynaecology OPD. Of these nearly 309 women were diagnosed to have PCOS. Hence, the prevalence in our institute was 2.02%. In our study, women between 18 - 40 years were included of which, in the metformin as well as in myoinositol group, majority of the women were between age group of 21 - 30 years which is Similar to studies done by **Mohamed et al (2015)**, [¹³Awalekaret al, (2015) [¹⁴ and **Angik et al (2015)**. [¹⁵

Regularity of Cycles: In our study, After 6 months of treatment in metformin group 37 (74%) women had regular cycles & in myoinositol group 39 (78%) women had regular cycles. Similar results were seen in a study by **Angik et al (2015)**, [¹⁵Nehra et al (2016), [¹⁶ and **De Leo et al (2013)**. [¹⁷

BMI: In our study there is a significant decrease in the BMI in both groups at 3 months and at 6 months in comparison to the baseline and at 6 months in comparison to 3 months ($P < 0.05$), showing that metformin & myoinositol decreases the BMI in women. But on comparing the 2 groups, the difference was not significant statistically. Similar results were seen in a study by **Awalekar et al (2015)** [¹⁴ and **Nehra et al (2016)**. [¹⁶

Hirsutism (Modified Ferriman Galleway Score): In our study, a significant decrease in the hirsutism in both groups at 3 months and at 6 months in comparison to the baseline and at 6 months in comparison to 3 months ($P < 0.05$), showing that metformin & myoinositol decreases hirsutism in women. Similar results were seen in study by **De Leo et al (2013)**, [¹⁷Nehra et al (2016) [¹⁶ and **Angik et al (2015)**. [¹⁵

Fasting Blood Sugar: Our study showed a significant decrease in the FBS in both groups at 3 months and at 6 months in comparison to the baseline and at 6 months in comparison to 3 months ($P < 0.05$), showing that metformin & myoinositol decreases the FBS in women. Similar to the study by **De Leo et al (2013)**. [¹⁷

Fasting Insulin: A significant decrease in both groups in the fasting insulin at 3 months and at 6 months in comparison to the baseline and at 6 months in comparison to 3 months ($P < 0.05$), showing that metformin & myoinositol decreases the fasting insulin in women. Similar to study by **De Leo et al (2013)**, [¹⁷ and **Artini et al (2013)** [¹⁸

HOMA2 - IR: a significant decrease in the HOMA2 - IR in both groups at 3 months and at 6 months in comparison to the baseline and at 6 months in comparison to 3 months ($P < 0.05$), showing that metformin & myoinositol decreases the HOMA2 - IR in women. Similar results were seen in the study by, **De Leo et al (2013)**, [¹⁷ and **Mohamed et al (2015)** [¹³

Luteinizing Hormone (LH): Our study shows a significant decrease in the Day2 - LH in both groups at 3 months and at 6 months in comparison to the baseline and at 6 months in comparison to 3 months ($P < 0.05$), showing that metformin & myoinositol decreases the Day2 - LH in women. The difference was found to be statistically significant ($P <$

0.05), with a higher Day - 2LH in myoinositol group in comparison to the metformin group. Similarly **Genazzani et al (2012)**, [¹⁹ investigated the efficacy on insulin sensitivity and hormonal parameters of 8 weeks treatment with myo - inositol (MYO) & after treatment interval found a significant decrease in mean LH levels.

LH/FSH Ratio: Our study showed a significant decrease in the Day2 - LH/FSH in both groups at 3 months and at 6 months in comparison to the baseline and at 6 months in comparison to 3 months ($P < 0.05$), showing that metformin & myoinositol decreases the Day2 - LH/FSH in women similar to study by **Angik et al (2015)**, [¹⁵ and **De Leo et al (2013)**. [¹⁷

Serum Testosterone: Our study showed a significant decrease in both groups in the mean serum testosterone at 3 months and at 6 months in comparison to the baseline and at 6 months in comparison to 3 months ($P < 0.05$), showing that metformin & myoinositol decreases the mean serum testosterone in women. The difference was found to be statistically significant ($P < 0.05$), with a higher serum testosterone in myoinositol group in comparison to the metformin group. Similar to the study by **De Leo et al (2013)**. [¹⁷

Mean (Right & Left) Ovarian Volume: There is a significant decrease in both the metformin and myoinositol group at 3 months and 6 months from baseline value, but there was no statistically significant difference in the mean ovarian volume between the two groups at 3 months and 6 months ($P > 0.05$), while it was significant at baseline with a lower ovarian volume in myoinositol group ($P < 0.05$) in comparison to the metformin group similar to study by, **Sanoee et al (2011)**, [²⁰ **Angik et al (2015)**, [¹⁵ and **Nehra et al (2016)**. [¹⁶

Number of Follicles: Our study showed a significant decrease in the mean number of follicles in both groups at 3 months and at 6 months in comparison to the baseline and also at 6 months in comparison to 3 months ($P < 0.05$), showing that both the drugs decreases the mean number of follicles in women, Similar results were seen in a study by **Angik et al (2015)**, [¹⁵ and **Nehra et al (2016)**. [¹⁶

Acne: At baseline, acne was present in 14 (28%) women, after metformin, at 3 months acne was still present in 14 (28%), but at 6 months it was present in 6 (12%) women. At baseline, acne was present in 14 (28%) women, after myoinositol, at 3 months acne was still present in 13 (26%), but at 6 months it was present in only 6 (12%) women. There was a decrease in percentage of acne in the both the groups. At 3 months slightly lower number of women 13 (26%) of myoinositol group were having acne in comparison to 14 (28%) women in the metformin group. While at 6 months in both the groups only 6 (12%) women were having acne. Similar results were seen in a study by **Zacche et al (2009)**, [²¹ **Nehra et al (2016)**. [¹⁶

Infertility: In our study, out of 5 infertility patients in the myoinositol group, 2 (40%) conceived and out of 8 patients in metformin group, 3 (37.5%) conceived. The results in the two groups were comparable but it was not significant

statistically ($P>0.05$) Similar to study by Angik et al (2015).
[15]

6. Conclusion

Taking into consideration the complexity of the syndrome, the best therapy for PCOS should include a 360° approach to the problem. Therefore, besides the need for changing their lifestyle, a nutraceutical and/or pharmacological treatment should be initiated as soon as the correct diagnosis is made, to avoid long term complications.

In the present study, we demonstrated that treatments with Metformin & Myoinositol improved patient's clinical, hormonal and metabolic profiles. After 6 months of therapy both study groups have demonstrated regularity of menstrual cycles, lower mFG scores, decreased BMI, decreased serum testosterone, decreased LH/FSH ratio & decreased HOMA2 - IR & improvement of polycystic ovarian morphology. Both Myoinositol and Metformin were found to be safe and efficacious in patients suffering from PCOS. On comparing the above mentioned treatment groups, the results of Myoinositol were comparable with Metformin except that Metformin decreased the serum testosterone levels more significantly as compared to Myoinositol, thus reducing signs of hyperandrogenism.

Hence, Myoinositol can be used for the treatment of PCOS with comparable efficacy.

Myo - inositol may oppose the etiopathologies responsible for the onset and deterioration of PCOS related symptoms, and may represent a reasonable alternative to other treatments modalities. Moreover this natural choice is much more accepted by patients and clinicians who consider metformin only an antidiabetic drug.

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