

## Myoinositol In Restoring Spontaneous Ovarian Activity in Patients with Polycystic Ovarian Syndrome (PCOS)

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### Abstract

**Objective:** To assess the efficacy of myoinositol in the management of patients with Polycystic ovarian syndrome (PCOS)

**Methods:** It was quasi experimental study conducted in Department of Obstetrics and Gynecology Services institute of Medical Sciences, Services Hospital, Lahore from 30-6-2018 to 31-12-2018. 140 sub fertile patients with PCOS were selected through random sampling. Patients were given 2gram of myoinositol/day. The effect was assessed after 3 and 6 months of treatment by monthly menstrual cycle regularity and ovulation. All this information was recorded in proforma.

**Results:** The mean age of patients was  $26.90 \pm 5.52$  years. The mean BMI of patients was  $37.38 \pm 4.08$  kg/m<sup>2</sup>. After 3 months of treatment, menstrual cycle become regular in 34 (24.3%) patients and ovulation occurred in 54 (38.6%) cases. After 6 months of treatment, menstrual cycle become regular in 75 (53.6%) patients and ovulation occurred in 101 (72.1%) cases.

**Conclusion:** The myoinositol is an effective treatment in terms of regularity of menstrual cycle and ovulation induction in subfertile women with PCOS.

**Keywords:** Myoinositol, Polycystic ovarian syndrome, Menstrual irregularity, Ovulation

### Introduction

Polycystic ovarian syndrome (PCOS) is a multifactorial disorder. The worldwide incidence of polycystic ovarian syndrome (PCOS) is 5-10% of women of reproductive age.<sup>1</sup>

The clinical feature of PCOS varies from oligomenorrhea, signs of hyperandrogenism such as acne, hirsutism, alopecia, infertility and seborrhea, along with sonographic picture of polycystic ovaries.<sup>2</sup> It is associated with long term metabolic abnormalities such as obesity, insulin resistance, acanthosis nigricans, type II diabetes mellitus, hypertension and dyslipidemia.<sup>3</sup> Almost 50-70% of patients have

insulin resistance and hyperinsulinemia.<sup>4</sup> As a result of insulin resistance, hyperinsulinemia alters the FSH to LH shift, insulin increase the production of androgens from the ovary by stimulating cytochrome P450c17 $\alpha$ , and this increased production of androgens leads to anovulatory infertility. There is increase production of testosterone because ovarian theca cells in PCOS affected women are more capable to convert androgens precursors to testosterone.<sup>5</sup> The insulin sensitizing agent can solve the hyperinsulinemia induced dysfunction of ovarian response to endogenous gonadotrophins, leading to reestablishment of menstrual cyclist, ovulation and increasing pregnancy rates.

Inositol is a chemical compound and nutrient discovered in 1936 and is commonly found in such foods as legumes, meat, citrus fruit, and whole grains in the most common form of Myo-inositol. Myoinositol (a part of vitamin B complex) has a role in both nuclear and cytoplasmic oocyte development, so higher myoinositol level in follicular fluid is an indicator of good oocyte quality.<sup>6</sup> Inositol phosphate can has a role in activating enzymes that control glucose metabo-

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Submission Date:	09-09-2020
1st Revision Date:	30-09-2020
Acceptance Date:	24-10-2020

lism. The altered metabolism of inositol phosphate can mediators in PCOS women contribute to insulin resistance. Insulin sensitizing agent such as Myoinositol reduces production of androgens from theca cells and also reducing testosterone concentration<sup>7</sup>. Myo-inositol is one stereoisomer of a C6 sugar alcohol that belongs to the inositol family. It is the precursor of inositol triphosphate, acting as an intracellular second messenger and regulating a number of hormones such as thyroid-stimulating hormone, FSH and insulin.<sup>8</sup>

Systematic review of randomized trials have shown its efficacy in improving insulin sensitivity of target tissues, restores ovulation and hormonal functions, reduces clinical and biochemical hyperandrogenism and dyslipidemia through reduction of plasma insulin level with success in achieving pregnancy.<sup>9,10</sup>

The rationale of my study is to observe the effect of myoinositol in improving metabolic, hormonal and clinical features in patients with PCOS. Although literature is available in studies conducted in other population but there is no local study available in this topic in Pakistan and there are genetic differences from one population to another so the effect of my drug may also vary accordingly and the study results may not be consistent with already existent literature. It may help in improvement of clinical features such as acne, hirsutism and obesity in patients with PCOS, also help in increasing conception rate by restoring spontaneous ovarian activity.

### Operational Definitions

Polycystic ovarian syndrome: in 2003, the European society of human reproduction and Embryology (ESHRE) and American society of reproductive medicine (ASRM) recommends at least 2 of the 3 following features are to be present to diagnose PCOS

1. oligo-ovulation or anovulation manifested by oligomenorrhea or amenorrhea for 6-9 cycles/yr
2. Hyperandrogenism assessed clinically by acne, obesity, hirsutism or hyperandrogenemia assessed biochemically by raised level of testosterone i.e.; >70ng/dl.
3. Polycystic ovaries (peripheral arrangement of >8 follicles of size <10mm in one or both ovaries) assessed by ultrasound.

### Efficacy

It was assessed on 3rd and 6th months post treatment in terms of:

Restoration of normal menstrual cycle: Normal menstrual cycle ranges from 3-7/21-35 days for 3-6 months assessed by history of the patient

**Ovulation:** It was the event of de-Graaf's follicle rupturing and releasing secondary oocytes. The normal ovulation day in mostly 14th day of 28 day menstrual cycle. Ovulation was assessed by day 21 progesterone level ranging from 16-28nmol/l.

### Methods

It was quasi experimental study conducted in Department of Obstetrics and Gynecology Services institute of Medical Sciences, Services Hospital, Lahore from 30-6-2018 to 31-12-2018. After getting permission from IRB, 140 sub fertile patients with PCOS were selected through Non-probability consecutive sampling. Inclusion criteria was 18 to 35 years of age, married women.

Sub-fertile women assessed by history i.e. not able to conceive after at least one year of regular, unprotected sex.

Patients selected with PCOS according to Rotterdam criteria as per operational definition. Patients known allergic myoinositol and non-complaint patients were excluded. A detailed history was taken regarding menstrual cycle, infertility, weight gain, acne, hirsutism, clinical examination including weight, height, blood pressure were noted and investigation such as transvaginal ultrasound was performed assessment of ovulation was done by measuring day 21 progesterone level ranges from 16 to 28nmol/l.

Patients were given 2gram of myoinositol/day. The effect was assessed after 3 and 6 months of treatment by monthly menstrual cycle regularity and ovulation. All this information was recorded in proforma.

### Data Analysis

SPSS version 21.0 was used for data analysis. Quantitative variables like patient's age, hormonal profile were presented by mean and standard deviation. Qualitative variables like ovulation, mens-

trual cycle regularity were presented by calculating frequency and percentages. Data was stratified for age, duration of PCOS and BMI. Post-stratification, chi-square test was used taking P-value  $\leq 0.05$  as significant.

## Results

The mean age of patients was  $26.90 \pm 5.52$  years. The mean BMI of patients was  $37.38 \pm 4.08$  kg/m<sup>2</sup>. Table 1

After 3 months of treatment, menstrual cycle become regular in 34 (24.3%) patients while irregular in 106 (75.7%) patients and ovulation occurred in 54 (38.6%) cases while did not occurred in 86 (61.4%) cases. After 6 months of treatment, menstrual cycle become regular in 75 (53.6%) patients and ovulation occurred in 101 (72.1%) cases. Table 2

**Table 1:** Descriptive Statistics of Patients

	140
Age (years)	$26.90 \pm 5.52$
BMI	$37.38 \pm 4.08$

Data was stratified for age of patients. After 3 months, in patients aged 18-25 years, menstrual cycle become regular in 16 (26.2%) cases and ovulation occurred in 20 (32.8%). After 3 months, in patients aged 26-35 years, menstrual cycle become regular in 18 (22.8%) cases and ovulation occurred in 34 (43.0%). The difference was insignificant in both age strata

**Table 2:** Distribution of outcome at 6th Month

		Frequency	Percent
Menstrual cycle	Regular	75	53.6
	Irregular	65	46.4
Ovulation	Yes	101	72.1
	No	39	27.9

( $p > 0.05$ ).

Data was stratified for age of patients. After 6 months, in patients aged 18-25 years, menstrual cycle become regular in 34 (55.7%) cases and ovulation occurred in 44 (72.1%). After 6 months, in patients aged 26-35 years, menstrual cycle become regular in 41 (51.9%) cases and ovulation occurred in 57 (72.2%). The difference was insignificant in both age strata ( $p > 0.05$ ). Table 3

Data was stratified for BMI of patients. After 3 months, in normal BMI patients, menstrual cycle become regular in 15 (32.6%) cases and ovulation

occurred in 19 (41.3%). After 3 months, in overweight patients, menstrual cycle become regular in 17 (33.3%) cases and ovulation occurred in 27

**Table 3:** Comparison of Outcome in Age Strata at 6th Month

		Age (years)		Total	P-value
		18-25	26-35		
Menstrual cycle	Regular	34	41	75	0.652
		55.7%	51.9%	53.6%	
	Irregular	27	38	65	0.998
		44.3%	48.1%	46.4%	
Ovulation	Yes	44	57	101	0.998
		72.1%	72.2%	72.1%	
	No	17	22	39	0.998
		27.9%	27.8%	27.9%	

(52.9%). After 3 months, in obese patients, menstrual cycle become regular in 2 (4.7%) cases and ovulation occurred in 8 (18.6%). The difference was significant in all BMI strata ( $p < 0.05$ ). Table 4

Data was stratified for BMI of patients. After 6 months, in normal BMI patients, menstrual cycle become regular in 33 (71.7%) cases and ovulation occurred in 38 (82.6%). After 6 months, in overweight patients, menstrual cycle become regular in 25

**Table 4:** Comparison of Outcome in BMI Strata at 3rd Month

		BMI			Total	P-value
		Normal	Over-weight	Obese		
Menstrual cycle	Regular	15	17	2	34	0.001
		32.6%	33.3%	4.7%	24.3%	
	Irregular	31	34	41	106	0.001
		67.4%	66.7%	95.3%	75.7%	
Ovulation	Yes	19	27	8	54	0.003
		41.3%	52.9%	18.6%	38.6%	
	No	27	24	35	86	0.003
		58.7%	47.1%	81.4%	61.4%	

(49.0%) cases and ovulation occurred in 37 (72.5%). After 6 months, in obese patients, menstrual cycle become regular in 17 (39.5%) cases and ovulation occurred in 26 (60.5%). The difference was significant in all BMI strata ( $p < 0.05$ ) for menstrual regularity while insignificant for ovulation ( $p > 0.05$ ). Table 5

## Discussion

PCOS is a metabolic disorder that is associated with wide range of hormonal and biochemical dysfunc-

tion. It has a high prevalence among Pakistani women

**Table 5:** Comparison of Outcome in BMI Strata at 6th Month

		BMI			Total	P-value
		Normal	Over-weight	Obese		
Menstrual cycle	Regular	33	25	17	75	0.007
		71.7%	49.0%	39.5%	53.6%	
Ovulation	Irregular	13	26	26	65	0.066
		28.3%	51.0%	60.5%	46.4%	
Ovulation	Yes	38	37	26	101	0.066
		82.6%	72.5%	60.5%	72.1%	
Ovulation	No	8	14	17	39	0.066
		17.4%	27.5%	39.5%	27.9%	

(52%) as compared to Caucasians(20-25%)<sup>11</sup>. The main reason for associated infertility is that the eggs in the ovaries are unable to mature efficiently and cannot be released, resulting in small cyst formations and ovarian inflammation. In fact, the presence of PCOS puts an individual at a significantly higher risk of developing type II diabetes, hypertension, gynecologic carcinomas, certain psychological conditions and low quality of life.<sup>12</sup>

In our study, the mean age of patients was 26.90± 5.52 years. Data was stratified for age of patients. After 6 months, in patients aged 18-25years, menstrual cycle become regular in 34 (55.7%) cases and ovulation occurred in 44 (72.1%). In patients aged 26-35years, menstrual cycle become regular in 41 (51.9%) cases and ovulation occurred in 57 (72.2%). The difference was insignificant in both age strata (p>0.05). The patients with subfertility belong to reproductive age group. Myoinositol was effective in older age group as well. Myoinositol has shown to improve metabolic dysfunction in postmenopausal women as well.<sup>13</sup>

In our study, myoinositol was found effective in inducing menstrual cycle regularity in 75 (53.6%) patients and ovulation occurred in 101 (72.1%) cases after 6 months of treatment. Similar results have been shown in other studies where 61.7% to 65.5% female had ovulation.<sup>8,14,15</sup> It is a very important finding for subfertile women with PCOS. Subfertility is a curse for women of Sub continent. They are subject to all sorts of emotional harassment and stigmatized but also face threats of divorce and physical violence.<sup>16</sup>

Improved pregnancy rates have been reported in various studies as well but we did not follow patients

for pregnancy. No moderate to severe side effects were observed when myo-inositol was used at a dosage of 2000 mg per day in our study.

The use of 2000 mg myo-inositol per day is well tolerated by patients in other studies as well.<sup>16,17</sup> PCOS is also associated with the failure of in vitro fertilization as these patients suffer from poor quality oocytes. Myoinositol has been found to improve quality of oocytes as it improves insulin sensitivity and decrease hyperandrogenism.<sup>18</sup>

In our study, the mean BMI of patients was 37.38± 4.08kg/m<sup>2</sup>. Increased BMI is itself associated with insulin resistance and decreased chances of fertility. Data was stratified for BMI of patients. After 6 months, in normal BMI patients, menstrual cycle become regular in 33(71.7%) cases and ovulation occurred in 38 (82.6%). In overweight patients, menstrual cycle become regular in 25 (49.0%) cases and ovulation occurred in 37(72.5%). In obese patients, menstrual cycle become regular in 17(39.5 %) cases and ovulation occurred in 26 (60.5%). The difference was significant in all BMI strata (p<0.05) for menstrual regularity while insignificant for ovulation (p>0.05). Myoinositol has been found to facilitate weight loss in PCOS patients in addition to improving biochemical and endocrine parameters<sup>19,20</sup>. Inositols have emerged as important component of endocrine modulation especially linked to insulin signalling<sup>21</sup>. More research is needed to generate local data so that national guidelines can be formulated.

## Conclusion

The myoinositol is found to be effective in inducing ovulation and menstrual cycle regularity in sub fertile PCOS patients.

## Author's Contribution

**IU:** Conceptualized and design the study.

**NS:**Data Maintenance

**QJ, SZ:** Data entry, Statistical Analysis

**TW:** Approved the final version and Data review Data

**AK:** Data Collection

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