

Two Years Experience of Myo-Inositol Use in Women Presented with Polycystic Ovarian Syndrome

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Myo-Inositol Use
in Women with
Polycystic
Ovarian
Syndrome

ABSTRACT

Objective: To determine the two years' experience of myo-inositol use in women presented with polycystic ovarian syndrome at a tertiary care hospital.

Study Design: Observational / cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynaecology Unit-II, Chandka Medical College Hospital Larkana from January 2017 to December 2018.

Materials and Methods: A total of 65 patients with polycystic ovarian syndrome were included. Detailed history was taken and myo-inositol was administered to assess the outcomes i.e. conceiving of women, weight loss and menstrual regularity.

Results: The mean age was 31.98±4.615 years. The results were 25 patients (38.5%) conceived after treatment, 15 (23.1%) had weight loss and menstrual regularity was noted in 20 patients (30.8%).

Conclusion: The treatment of females with PCOS with myoinositol has showed considerable amount of improvements in terms of increasing fertilization along with omitting menstrual cycle irregularities and weight loss of the patients.

Key Words: Myo-inositol, Polycystic ovarian syndrome, Infertility

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INTRODUCTION

According to the definition of polycystic ovary syndrome (PCOS), it can be defined as a gynecological disease which is of heterogeneous nature which shows polycystic ovaries on the ultrasound and most of the times causes irregular bleedings, excess of androgen levels and long term anovulation.¹ As per research it is thought to be as the most common reason for making females of reproductive age infertile by number of 5 percent to 10 percent.² However, strong genetic association along with lifestyle and gestational environment are thought to be as an important factor though exact etiopathology of PCOS is still not known. In a meeting which was held in Rotterdam 2003, American society for Reproductive medicine and European society of Human reproduction and

Embryology has clearly defined the criteria for how to define PCOD.³ Moreover, insulin resistance was discovered as one of the factors behind the clinical causation of PCOS in women recently. Especially obese PCOS patients with having severe insulin sensitivity disorders with hyperinsulinemia compensatory mechanisms along with in females having normal basal metabolic index as well. It also indicates that weight is not directly associated with the development of insulin resistance at all.⁴ Scientifically androgen production can be initiated by two different ways with the stimulus of hyperinsulinemia as firstly by inducing ovaries to produce androgens or lessening the binding of globulin related to sex hormones in serum.⁵

Furthermore, as per our literature review it was found that for a long period of time drugs like metformin, troglitazone or pioglitazone which are also termed as insulin sensitizers thought to be as vital choice for management therapy due to the important role of insulin in its etiopathology. Moreover, for menstrual cycle irregularities or the improvement in ovarian dysfunction along with consecutive anovulation metformin is being given as a treatment in patients with hyperinsulinemic condition.⁶ It was also reported that metformin use will result in a few side effects like nausea, diarrhea, flatulence making it as difficult to use in a longer run.⁷ However, in very recent times alternatives of management therapy drugs for PCOS, compounds cyclohexane with five equatorial and one axial hydroxyl group and most frequent form found in

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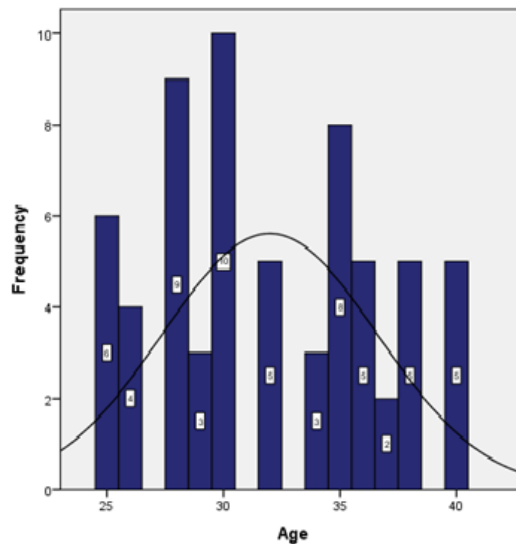
nature in relative to other nine different stereoisomer forms, have been under the investigation.⁸ Plenty of researches have been conducted for PCOS which collectively suggests that, insulin resistance is a net result of inositol insufficiency in the inositolphosphoglycans so insulin deficiency will be rise from the inositolphosphoglycan (IPG) mediator. Furthermore, many researches have also stated that if D-chiro-inositol which is converted from myo-inositol intracellularly, administrated to the affected patients can decrease insulin resistance⁹ while as a second messenger, myo-inositol can play very important role in cells for various signal pathways which enhance the sensitivity for insulin which will ultimately show remarkable increase of glucose uptake intracellularly.¹⁰ So, the researchers have proved myoinositol as a potential nontoxic drug option for an effective management of women with PCOS by improving the metabolic processes following induction of ovulation activity especially in infertile women and also paved the way for researchers to take experimental interest in to it. Moreover, myoinositol dose up to 12 grams per day is termed as the safest dose with slight gastrointestinal adverse effects, have also been reported by the various researches.¹¹ So, the main aim of this study was to assess the rates of pregnant women under the administration of myoinositol and folic acid in combination therapy for the PCOS in Germany, and secondly to institute this notion if this can be opted for the improvement of the patients with infertility.

MATERIALS AND METHODS

This cross-sectional study was carried out at Department of Obstetrics & Gynaecology Unit-II, Chandka Medical College Hospital Larkana from 1st January 2017 to 31st December 2018. A total of 65 patients with polycystic ovarian syndrome were included. Detailed history was taken and myo-inositol was administrated to assess the outcomes i.e. conceiving of women, weight loss and menstrual regularity. The patients of age 25 to 40 years, who were diagnosed cases of polycystic ovarian syndrome (PCOS) were included. Patient’s name, age, marital status, body mass index (BMI) and patients complains like infertility and scanty menses was recorded. Exclusion criteria were firmly followed to avoid confounding variables. Myo-inositol was started and continued for 2 years. After 2 years outcome/results were assessed in terms of conceived after treatment, weight loss and menstrual cycle regularity after treatment. Patients with presence of other causes of hyperandrogenism or infertility, such as hypothyroidism, congenital adrenal hyperplasia, cushing’s syndrome, hyperinsulinaemia or endometriosis were excluded. Data was entered and analyzed in SPSS 22.

RESULTS

The mean age was 31.98+4.615 years and frequency of age is presented in Figure 1. The mean BMI was 27.044+3.555 kg/m² (Table 1). There were 15 (23.1%) single while 50 (76.5%) patients married. The infertility was noticed in 40 (61.53%) patients and scanty menses in 35 (53.8%). Twenty five patients (38.5%) conceived after treatment, 15 (23.1%) had weight loss and menstrual regularity was noted in 20 patients (30.8%) [Table 2].



Graph No.1: Frequency distribution of age (years)

Table No.1: Descriptive statistics of age & BMI

Statistics	Age (years)	BMI (kg/m ²)
Minimum	25	18
Maximum	40	35
Mean±SD	31.98+4.615	27.044+3.5550

Table No.2: Frequency of marital Status, complain of patients (infertility & scanty menses) and Results (conceived after treatment, weight loss, menstrual regularity)

Variable	No.	%	
Marital status			
Single	15	23.1	
Married	50	76.9	
Complain	Yes	No	Total
Infertility	40(61.53%)	25(38.46%)	65(100%)
Scanty menses	35(53.8%)	30(46.2%)	65(100%)
Results			
Conceived a	25(38.5%)	40(61.5%)	65(100%)
Weight loss	15(23.1%)	50(76.9%)	65(100%)
Menstrual reg	20(30.8%)	45(69.2%)	65(100%)

Majority of the patients who conceived after treatment were 33-40 years of age group (p=0.005), had BMI of 28.1-36 kg/m² (p=0.539), majority of patients had complain of infertility (p=0.000) & significant

association was noted with complain of scanty menses (p=0.005). Weight loss after treatment was commonly noted in age group of 25-32 years (p-value=0.719), BMI of 28.1-36 kg/m² (p=0.070), also commonly noted in patients with complain of infertility (p=0.041) and no significant association was noted with complain of

scanty menses (p=0.220). Menstrual regularity after treatment was commonly noted in age group of 25-32 years (p-value=0.263), BMI of 20-28 kg/m² (p-value=0.200), with significantly associated complain of infertility (p-value=0.000) and scanty menses (p-value=0.000) [Tables 3-4].

Table No.3: Stratification of conceived after treatment, weight loss, menstrual regularity according to Age, BMI (n=65)

Variable	Conceived after treatment		Weight loss		Menstrual regularity	
	Yes	No	Yes	No	Yes	No
Age (years)						
25-32	7(10.76%)	30(46.15%)	10(15.38%)	27(41.53%)	16(24.61%)	21(32.30%)
33-40	18(27.69%)	10(15.38%)	5(7.69%)	23(35.38%)	4(6.15%)	24(36.92%)
P value	0.005		0.719		0.263	
BMI (kg/m²)						
20-28	11(16.92%)	28(43.07%)	3(4.61%)	36(55.38%)	14(21.53%)	25(38.46%)
28.1-36	14(21.53%)	12(18.46%)	12(18.46%)	14(21.53%)	6(9.23%)	20(30.76%)
P-value	0.539		0.070		0.200	

Table No.4:Result (conceived after treatment, weight loss, menstrual regularity) according to Age, BMI (n=65)

Variable	Conceived after treatment		Weight loss		Menstrual regularity	
	Yes	No	Yes	No	Yes	No
Infertility						
Yes	24(36.92%)	17(26.15%)	10(15.38%)	31(47.69%)	5(7.69%)	36(55.38%)
No	1(1.53%)	23(35.38%)	5(7.69%)	19(29.23%)	15(23.07%)	9(13.84%)
P value	0.000		0.041		0.000	
Scanty Menses						
Yes	8(12.30%)	27(41.53%)	6(9.23%)	29(44.61%)	20(30.76%)	15(23.07%)
No	17(26.15%)	13(20%)	9(13.84%)	21(32.30%)	0(%)	30(45.15%)
P-value	0.005		0.220		0.000	

DISCUSSION

Amongst many endocrinal diseases, PCOS is considered as the most frequently upsetting the health of women who are reproductively active. Moreover, credible number of women with PCOS have hyperinsulinemia along with developing resistance to insulin. So, myoinositol which is termed as the insulin lowering drug are known for the betterment in outcome of spontaneous ovulation because of the encouragingly positive consequence on meiotic division of human oocyte. Moreover, this course of treatment not only positively sway genesis of steroid hormones but will also lessening the ability of theca cells to produce androgens. Research has not only showed the diminishing of testosterone concentration in the serum but also increasing ovulation in females with PCOS by administrating inositol.¹² In this present study 25 patients which makes 38.5 percent of the total sample revived their ovulatory functions as previously done in a research study of Regidor et al.¹³ In which it was reported that 70 percent of the patients gained normality in their ovulatory functions. Though it was an observational study and this was the main limitation of it, but still reliable data

of the patients for analysis is present. Moreover, the rates of pregnancy were in a range equal or more than those stated after the administration of metformin which is insulin sensitizer. Another research study of Karimzadeh and Javedani¹⁴ also suggested that around 14.4 percent of pregnancy rates were reported in a cohort with the 90 female participants likewise, 12.3 percent in a cohort group of 75 females with having PCOS.¹⁵ Furthermore, it is also evident from the study that the safety profiles and patient compliance were slightly different between the myoinositol and metformin, and those are the observed side effects like mild to severe gastrointestinal upset which includes nausea, diarrhea and abdominal pain. While few patients reported with severe side effects as lactic acidosis. On the contrary myoinositol was proved as to be less harmful and nearly safe for the use and tolerated very well by the patients was equally capable in terms of efficacy as of metformin. So, on the whole it would be pertinent to say that myoinositol administration can increase glucose uptake intracellularly. Another prospective research study which is named as Gerli et al¹⁶ has clearly reported that, overall 82 percent improvement was observed by increasing ovulatory functions of females patients who were administrated

myoinositol along with the combination of folic acid and on the contrary patients who received placebo were observed the ovulatory function restoration by 63 percent. Likewise regular menstrual cycles were experienced by 70 percent of females taking myoinositol after 16 weeks of treatment and 13 percent regular cycles were found in a placebo group as compared to our study the percentage was 30.8 percent for menstrual cycle regularity and this was most commonly found in an age group of 25 to 32 years of age with p value of 0.263, Basal metabolic index of 20 to 28 kg/m² with p value of 0.200, with considerable infertility compliant with p value of 0.000 and scanty menstruation with the p value of 0.000. In this research study 23.1 percent of females showed considerable weight loss as well when given myoinositol meanwhile improvement in ovulatory functions were attained by the dose of 4 g myoinositol and 400 µg folic acid per day.

In another research study namely Raffone et al¹⁷, two groups were compared in one group was given myoinositol 2x 2000 gram along with the 200 µg per day administrated to the female patients with PCOS while other group was given 1500 mg per day. When analyzed the results then considerable improvements were noted in the ovulatory functions and rates of pregnancies were higher in myoinositol group relative to metformin group. However, in this research study the age group of 33 to 40 years successfully conceived after getting myoinositol treatment with p value 0.005 having basal metabolic index of 28.1 to 36 kg/m² with the p value 0.539. However, patients in majority had complained infertility with p value of 0.000 while scanty menses complains with p value of 0.005. Furthermore, plenty of other researches no doubt showed myoinositol efficacy with improving fertility in women with PCOS¹⁸⁻²⁰.

There have been copious research studies presenting that myoinositol treatment regime along with in combination of folic acid in the dosage 2 x 2000 g myoinositol and 200 µg of folic acid per day) positively affects hence ultimately improves hormonal and metabolic parameters. Furthermore, another important research study namely Costantino et al²¹ has showed that, after administration of myoinositol considerable amount of improvement after 75 mg oral glucose tolerance test was observed in triglycerides, cholesterol, blood pressure and level of insulin with 16 weeks of treatment period. Moreover, prominent decrease in free serum testosterone levels relative to increase progesterone levels because of increased ovulation was seen. It would be appropriate to conclude that myoinositol improves the metabolic profiles in females but also give them relieve from other skin and acne problems by suppressing androgen activity.

Similarly, author Unfer et al²² conducted a research meta-analysis and concluded that when the 4000 g of

myoinositol along with the combination of 400 milligram of folic acid given to the patients reported no any kind of adverse effects as compared to the treatment with 1500 mg of metformin were stated and improvement of ovulatory functions was observed in the former group. Kamenov et al²³ also endorsed the fact which means women who were taking myoinositol in combination with clomiphene citrate in females with PCOS who have developed resistance for insulin. Melatonin can contribute a further therapeutic benefit if more researches conducted²⁴

So, in the light our research study it is safe to conclude that myoinositol can be implemented as an effective treatment plan for patients with PCOS with little or no adverse effects of it as per the research. However, the importance of proper compliance to the treatment regime cannot be denied which in turn ensures the positive outcomes in terms of ovulatory function disturbances, along with hyperandrogenism and metabolic profiles of PCOS affected females. However, further detailed researches are required to be conducted in future as well just to observe the effect of myoinositol on developmental process of follicles and oocyte maturation along with results of pregnancy in IVF procedure.

CONCLUSION

The treatment of females with PCOS with myoinositol has showed considerable amount of improvements in terms of increasing fertilization along with omitting menstrual cycle irregularities and weight loss of the patients.

Author's Contribution:

Concept & Design of Study:	Basma Zia Isran
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Data Analysis:	Shaista Hifaz Abro
Revisiting Critically:	Basma Zia Isran, Shazia Shaikh
Final Approval of version:	Basma Zia Isran

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