

DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20214648>

Original Research Article

Role of oral inositol supplementation in women with polycystic ovarian syndrome

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Received: 11 September 2021

Revised: 24 October 2021

Accepted: 25 October 2021

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ABSTRACT

Background: PCOS is one of the most common endocrine disorder in women of reproductive age, it affects about 5-10% of women of reproductive age. It is characterized by chronic anovulation, hyperandrogenism, and insulin resistance. 30-40% of PCOS women have impaired glucose tolerance.

Methods: This was prospective observational study carried out on 100 patients of PCOS visiting outpatient Department of Obstetrics and Gynecology, BRD Medical College, Gorakhpur from 1st July 2018 to 30th June 2019. Patients were diagnosed as PCOS on basis of Rotterdam criteria. In these 100 patients, oral inositol 2 gm twice daily was given for 3 months to 6 months depending upon the response of the patient and patients were examined every 4 week for menstrual regularity, acne improvement, hirsutism, spontaneous ovulation and pregnancy.

Results: With inositol supplementation, menstrual abnormality corrected in 80% cases, 45% cases having acne improved. Ovulation occurred in 75.5% cases and 66.6% cases conceived with inositol supplementation.

Conclusions: Insulin resistance is the basic pathophysiology for PCOS hence inositol supplementation is supposed to be very good medicine for management of PCOS to improve insulin sensitivity. Inositol leads to improvement in regularity of menstrual cycle, insulin resistance, hyperandrogenic features like hirsutism, acne, restores ovulation and improves oocyte quality.

Keywords: Inositol, Insulin resistance, Myoinositol, PCOS

INTRODUCTION

PCOS is one of the most common endocrine disorder in women of reproductive age, it affects about 5-10% of women of reproductive age who suffer from obesity, hyperandrogenism, ovarian dysfunction and menstrual irregularities.

Both aetiology and diagnosis of the syndrome is controversial. According to Rotterdam criteria developed in 2003, PCOS is diagnosed when there is presence of two of the following three conditions- 1) oligomenorrhea and/or anovulation, 2) clinical and/or biochemical signs of hyperandrogenism that may be associated with hirsutism, 3) polycystic ovaries on ultrasonography.¹

Although not included as criteria, insulin resistance and hyperinsulinemia are important etiologic factors associated with typical clinical signs and hormonal disorders of PCOS. Insulin resistance along with hyperinsulinemia affects 40-50% of PCOS patients both lean and obese.²

The exact cause of insulin resistance observed in PCOS women is unknown, although a post receptor defect that could affect glucose transport has been proposed.³⁻⁴ Further studies have suggested that impairment in the insulin pathway could be due to a defect in the inositolphosphoglycans (IPGs) second messenger.⁵⁻⁶ In PCOS women a defect in tissue availability or altered metabolism of inositol or IPGs mediators may contribute

to insulin resistance.⁷ Hyperinsulinemia could induce an excess of androgen production in PCOS women through two different ways: first one is direct stimulation of ovaries to produce androgens and the other one is the reduction of sex hormone binding globulin (SHBG) serum level.⁸ Isoforms of inositol belongs to the vitamin B complex. Epimerization of the six hydroxyl group of inositol leads to formation of 9 stereo isomers including myoinositol (MI) and D-chiroinositol. D-chiroinositol (DCI) is involved in insulin mediated androgen synthesis, whereas MI mediate glucose uptake and follicular stimulating hormone (FSH) signalling. Reduced intraovarian myoinositol adversely affect glucose uptake and

metabolism of both oocyte and follicular cells. Since oocyte are characterized by high glucose consumption, this would compromise oocyte quality. MI and DCI are intracellularly incorporated in to inositolphosphoglycan (IPGs) which are second messengers of insulin and some actions of insulin are mediated by these IPGs mediators. Epimerase conversion of MI to DCI is under insulin control. The excess insulin enhanced action of the epimerase in the ovary, resulting in excessive conversion of MI to DCI which results in increased DCI and reduced MI in ovary, leading to lack of second messenger. A ratio of 40:1 (MI:DCI) is thought to be physiological for most tissues.⁹

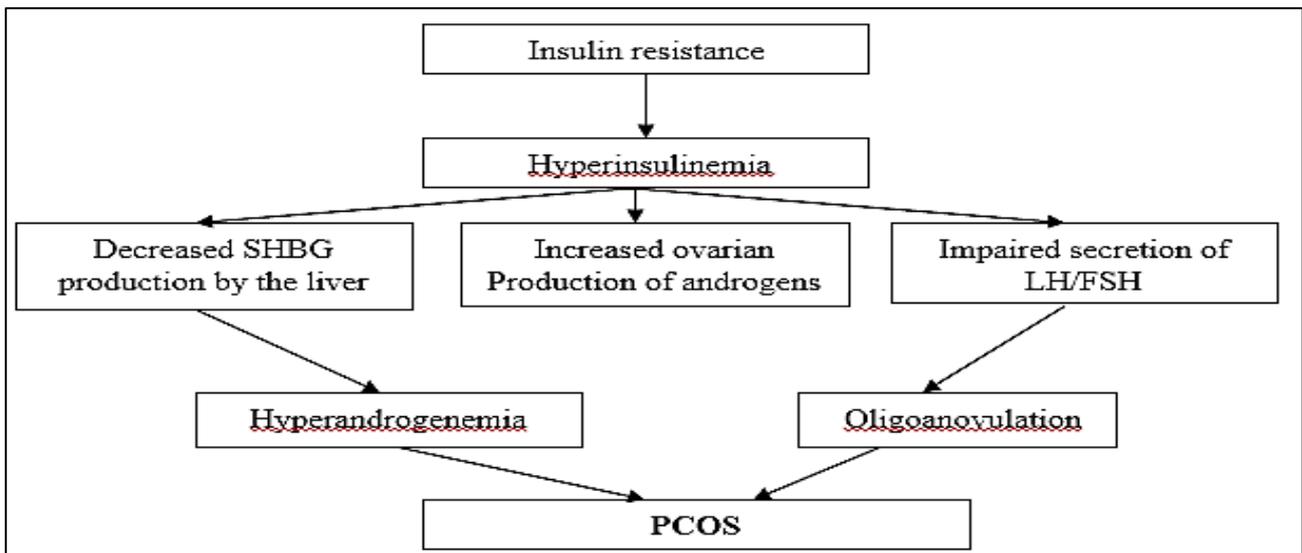


Figure 1: Insulin resistance and development of PCOS.

Due to association between PCOS and insulin resistance, insulin sensitizers have been used in the therapy of PCOS. Previous studies have shown the use of metformin, troglitazone or myoinositol reduces serum androgens and improves ovulation in women with PCOS. Several clinical studies have highlighted the usefulness of inositol supplementation in PCOS. Also it has been proven to be

safe even after high dose consumption.¹⁰

The aim of this study was to observe the effectiveness of oral myoinositol supplementation in PCOS women for menstrual irregularities, cutaneous hyperandrogenic resolution and for the effectiveness on ovulation and pregnancy rate.

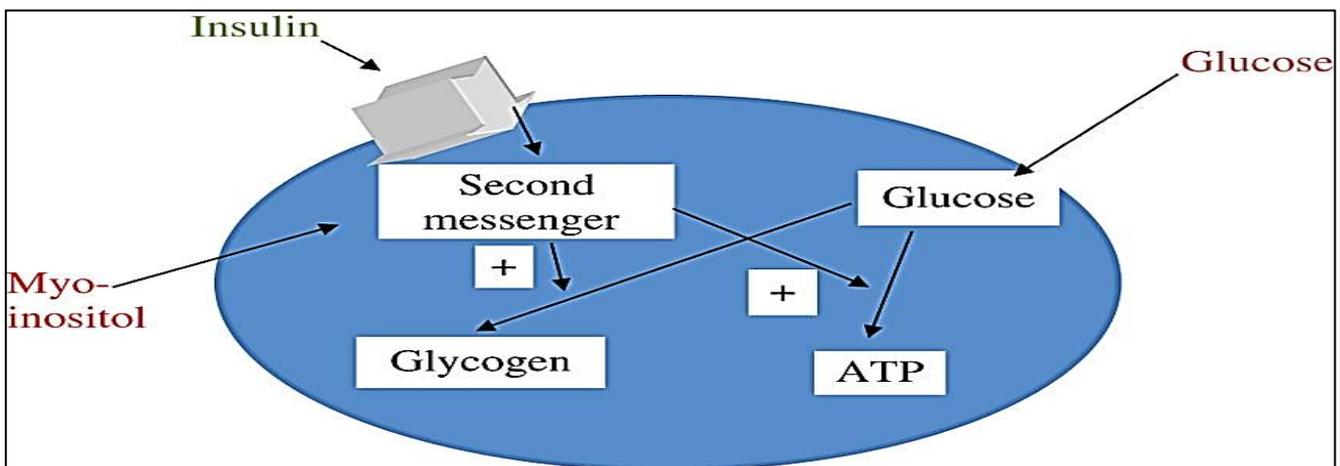


Figure 2: Mechanism of action of myoinositol in the cell.

METHODS

This study was prospective observational study carried out on 100 patients of PCOS visiting outpatient Department of Obstetrics and gynaecology, BRD Medical College, Gorakhpur from 1st July 2018 to 30th June 2019.

Detailed history of all patients taken and physical examination done after taking informed consent. Patients were diagnosed as PCOS if two out of the three following features were present (Rotterdam's criteria 2003)- 1) oligomenorrhea and/or anovulation, 2) polycystic ovaries on ultrasonography, 3) clinical and/or biochemical sign of hyperandrogenism that may be associated with hirsutism.

All routine investigations including 75 gm oral glucose tolerance test (GTT), Hba1c and lipid profile done. Along with this hormonal profile like serum levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), testosterone (total and free), thyroid stimulating hormone (TSH) done. Ultrasonography (transabdominal/transvaginal) was done to see polycystic ovarian morphology.

Inclusion criteria

Patients of PCOS in the reproductive age group (15-49) visiting to Obstetrics and Gynecology outpatient department, BRD Medical College, Gorakhpur.

Exclusion criteria

Patients having menstrual irregularities, hyperandrogenic features, ovulatory dysfunctions and infertility due to other pathologies apart from PCOS were not included in this study.

After confirmation of diagnosis and taking consent from these patients, they were advised oral myoinositol 2 gm twice daily for 3 months to 6 months depending upon the response of the treatment. Patients were examined every 4 week for menstrual regularity, acne improvement, hirsutism, spontaneous ovulation and pregnancy.

Data analysis

Data analysis was done using statistical package for the social statistics (SPSS) 16 software. Data was summarized in tables. Results are presented in percentage. No statistical test was applied.

RESULTS

Socio-demographic profile of PCOS patients shows maximum no. of cases (37%) belonged to 21-25 years of age followed by 15-20 years of age (33%). Unmarried women/girls having PCOS were 55%. 60% cases belonged to upper class and from urban area. Only 40% women were

having normal weight rest 60% were of higher weight (Table 1).

Table 1: Distribution of cases on basis of demographic characteristics.

Variables	No. of cases	Percentage
Age group (years)		
15-20	33	33
21-25	37	37
26-30	25	25
31-35	05	05
Socioeconomic status		
Lower	10	10
Middle	30	30
Upper	60	60
Education		
Illiterate	10	10
Literate	90	90
Residence		
Urban	60	60
Rural	40	40
Marital status		
Married	45	45
Unmarried	55	55
BMI (kg/m²)		
Normal (<24.9)	40	40
Overweight (25.0-29.9)	55	55
Obese (30 or more)	5	5

Most common symptom was menstrual abnormality found in 100 (100%) cases followed by infertility 45 (45%) cases and hyperandrogenic feature like acne and hirsutism were present in 35 (35%) cases (Table 2).

Oligomenorrhoea was most common menstrual irregularity found in 70% of women. 10% women having combination of oligomenorrhoea and hypomenorrhoea, rest 20% come with history of irregular menstrual cycles (Table 3).

Table 2: Distribution of cases according to symptoms.

Symptoms	No. of cases	Percentage
Menstrual abnormality	20	20
Menstrual abnormality + acne	08	08
Menstrual abnormality + hirsutism	15	15
Menstrual abnormality + hyperandrogenic features (acne + hirsutism)	12	12
Menstrual abnormality + infertility	45	45
Total	100	100

Table 3: Distribution of cases according to type of menstrual abnormality.

Menstrual abnormality	No. of cases	Percentage
Oligomenorrhoea	70	70
Oligomenorrhoea + hypomenorrhoea	10	10
Irregular menstruation	20	20
Total	100	100

Table 4: Average weight loss in patient after taking inositol.

BMI (kg/m ²)	Weight loss (kg)/month	
	Min. (kg)	Max. (kg)
In over weight (25.0-29.9)	0.25	0.5
In obese (30 or more)	0.5	0.75

In our study average weight loss after taking inositol in overweight patients was 0.25-0.5 kg/month while in obese patients it was 0.5-0.75 kg/month (Table 4).

Table 5: Results after myoinositol treatment.

	No. of cases/total no. of cases	Percentage
Menstrual abnormality corrected with inositol supplementation	80/100	80
Acne improved with inositol supplementation	9/20	45
Ovulation occurred with inositol supplementation	34/45	75.5
Infertile cases conceived with inositol supplementation	30/45	66.6

Table 5 shows results after 3-6 months therapy with myoinositol. Menstrual abnormality corrected in 80% cases, 45% cases having acne improved. Ovulation occurred in 75.5% cases and 66.6% cases conceived with inositol supplementation.

DISCUSSION

PCOS is a common endocrine disorder affecting women of reproductive age group. In our study we found 95% of cases were below age 30 years and only 5% above 30 years (mean age was 22.98±4.43 years). Mean age among PCOS patients was 27±7.7 in study done by Murlidhara et al in KMC Mangalore. Monika et al and Spandana et al also observed PCOS is more common in this age group.¹¹⁻¹³

Insulin resistance is a key factor in the pathogenesis of anovulation and hyperandrogenism in PCOS patients and

insulin resistance is significantly exacerbated by obesity.

We observed that 55% patients were overweight, 5% obese and rest 40% were of normal weight in our study. After giving myoinositol the average weight loss in overweight patients was 0.25-0.5 kg/month. Rim et al compared the effect of inositol (ovacure) alone to inositol and metformin (ovacure+metformin). They found 2.7 kg weight loss in inositol group compared to 4.64 kg in inositol+metformin group after 6 month of treatment. Reduction in weight was more in group using combined myoinositol and metformin.¹⁴

Our study showed 100 (100%) of PCOS patients suffering from various kind of menstrual irregularities along with other features of PCOS. Menstrual regularity was achieved in 80 (80%) cases within 3 to 6 month of inositol supplementation who were having oligomenorrhoea±hypomenorrhoea. In study done by Genazzani et al, all patients under myoinositol 2 gm with folic acid 200 µg administration reported menstrual cycles during 12 week treatment.¹⁵ Similarly Venturella et al and Le Donne et al had shown significant improvement in menstrual abnormality in their studies.^{16,17}

Being a insulin sensitizer myoinositol improves insulin sensitivity thereby reduces androgen levels.

So its use benefits in cutaneous disorder of hyperandrogenism (acne, hirsutism). Out of 20 women having acne, 9 (45%) cases improved with inositol supplementation. In study of Monika et al. 2017 only 33.3% (5/15) had improvement in acne.¹² In studies of Minozzi et al and Zacche et al they found significant reduction in problem of hirsutism.^{18,19}

Ovulatory dysfunction is very common in PCOD women Raffone et al compared the effects of metformin and myoinositol on PCOS patients, total 120 patients were recruited, 60 patients were treated with metformin and 60 patients were treated with myoinositol. Among the patients treated with myoinositol spontaneous ovulation restored in 65% patients which is higher than metformin (50%).²⁰

Pedro-Antonio et al observed after 2-3 month of inositol supplementation among 3602 patients with PCOS 70% of women restored ovulation.²¹ These results were similar to our study, ovulation occurred in 75.5% cases within 3-6 months of inositol supplementation.

Many studies demonstrated myoinositol improves the pregnancy rate in PCOS women suffering from infertility. It might be due to decreasing insulin resistance leads to improved oocyte quality and development of mature oocytes. This effect of MI can be supported by our own study data as out of 45 infertile women, 30 (66.67%) women conceived within 3-6 months of MI supplementation. In study of Raffone et al, it could be shown that the number of pregnancies was clearly higher in the myoinositol group than in the metformin group of

patients.²⁰ While in study of Papaleo et al and Riju Angik et al the conception rate was 40% and 36.84%.^{22,23}

Limitations of the study are though the sample size and study duration was small, further research with larger samples and longer study periods is required to support the role of myoinositol treatment for PCOS. HOMA-IR (homeostatic model assessment for insulin resistance) not used to test insulin resistance due to unavailability of this test at our institution. Ferriman-Gallaway (FG) score not used to quantify hirsutism because most of unmarried patients did not gave consent. We assess hirsutism only on exposed areas like face and arms.

CONCLUSION

Insulin resistance is the basic pathophysiology for PCOS, hence inositol supplementation is supposed to be a very good medicine for management of PCOS to improve insulin sensitivity. Myoinositol lead to improvement in regularity of menstrual cycle, insulin resistance, hyperandrogenic features like hirsutism, acne, polycystic ovarian morphology, hormonal parameter and reproductive axis (restores ovulation and improves oocyte quality). MI is a safe and simple treatment that is able to restore spontaneous fertility in most PCOS patients with infertility. Most of infertile women on inositol do not require ovulation induction drug. Along with diet control and exercise (obese PCOS), myoinositol must be used as a first line drug for treatment of various complaints in PCOS patients.

ACKNOWLEDGMENTS

Authors would like to thank all study participants for their cooperation and providing the necessary information.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Malik N, Dubey N. Role of oral inositol supplementation in women with polycystic ovarian syndrome. *Int J Reprod Contracept Obstet Gynecol* 2021;10:4493-8.