

Effects of Myoinositol on Ovulation in Polycystic Ovarian Syndrome (PCOS) Women

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ABSTRACT

Introduction: Polycystic ovarian syndrome (PCOS), which is almost 5–10% among reproductive-age women, is the most commonly diagnosed female endocrine disease. PCOS has been defined as a disorder with irregular and/or prolonged menstrual cycle, extensive androgen level, and the hyperandrogenic symptoms of hirsutism, acne and/or alopecia, and multicystic ovaries. The study aims to explore the relation between myoinositol intake and mid-cycle ovulation in PCOS patients.

Methods: 110 Patients were recruited from a private clinic in Karbala city, Al-Hindiya district. Criteria for selecting patients: aged 20–35 years, history of infertility, PCOS. Patients comprised two groups (55 patients each), the first group treated with metformin 850mg, b.i.d, and placebo. The second group was treated with metformin 850mg twice-daily dosing (BID) and myoinositol oral supplementation 1000 mg/day for 4 months. Ultrasonography was performed monthly on day 13 to assess the follicular size. Data were based on one-way ANOVA and the Dunnett multi-comparison test.

Results: No significant difference was noticed [$p > 0.05$] when comparing the mid-cycle follicular size [mm] before and after metformin and placebo intake in a given dose. Mid-cycle follicular size significantly [$p < 0.05$] increased by 6 folds after metformin and myoinositol administration compared to a control group in a given dose and time. The addition of myoinositol to metformin was significantly [$p < 0.05$] increased mid-cycle follicular size by 3 folds compared to placebo and metformin in a given dose and time.

Conclusion: The important finding was that myoinositol supplementation might affect follicular maturation positively in PCOS patients.

Keywords: Myoinositol Supplementation, Ovulation, Polycystic Ovarian Syndrome (PCOS).

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INTRODUCTION

Polycystic ovarian syndrome (PCOS), which is almost 5–10% among reproductive-age women, is the most commonly diagnosed female endocrine disease.¹ The PCOS is defined as a disorder that included irregular and/or prolonged menstrual cycle, extensive androgen level, the hyperandrogenic symptoms of hirsutism, acne and/or alopecia, and multicystic ovaries.¹ PCOS has two criteria: androgenic hormone increase, irregular ovulation or lack of ovulation, and extensive ovaries with twelve follicles each.² PCOS also has various risks, such as insulin resistance (IR), obesity, increase in blood pressure, type 2 diabetes (T2DM), and metabolic syndrome (MS) associated with PCOS, as well as a range of heart risk factors.³ Moreover, women who suffer from PCOS, suffer from metabolic and IR disorders associated with a disorder in vitamin D metabolism.⁴ Myoinositol has been used primarily as a natural insulin sensitizer over the

last 10 years as an isomerized and dephosphorylated glucose 6-phosphate Precursor. Recent studies have focused on the role of myoinositol in PCOS pathophysiology. The deficiency in the myoinositol intracellular metabolites, D-chiro-inositol (DCI), and inositol-phosphoglycan (IPG), insulin mediators in women has been suggested to be induced to avoid insulin.⁵ Patients with PCOS have an additional urinary clearance of DCI⁶ has also been postulated. DCI functions as an intracellular messenger for insulin sensitivity in mammalian oocytes, plays a role in a follicular environment, meiotic recovery, and oocyte maturation.⁷ It would be helpful to study the possible additive advantage of combining lifestyle procedures with myoinositol. Myoinositol, a natural, reliable, and effective drug to improve insulin resistance, is recommended for PCOS and insulin resistance management in conjunction with other positive lifestyle modifications.

Aims of The Study

This study aims at exploring the relation between myoinositol intake and mid-cycle ovarian follicle maturation in PCOS patients.

METHOD

The present study was a clinical prospective observational study and was conducted on patients with PCOS, both suspected and already diagnosed, attending a private clinic in Karbala city / Al-Hindya district from 10th February 2019 to 4th September 2019. 60 Patients were recruited from a private clinic in Karbala city / Al-Hindya district.

Criteria for Selecting Patients

Inclusion criteria.

- All newly suspected and diagnosed cases of PCOS.
- Aged 20-35 years.
- History of infertility and PCOS
- No history of hypertension or any chronic disorder

Exclusion criteria

- Any diagnosed case of PCOS who had a history of myoinositol intake within one year.
- Diagnosed PCOS cases who were under treatment and recovered with treatment (medical and surgical).
- Patients who were not willing to take part in our study.

The selected patients were divided over 2 groups:

1. Group 1: (55 patients) treated with metformin 850 mg, b.i.d, and placebo.
2. Group 2: (55 patients) treated with metformin 850 mg, b.i.d and myoinositol oral supplementation 1000 mg/day for 3 months (single blind technique).

Patients Follow up Parameters

The mid-cycle follicular size was assessed monthly on day 13 using Ultrasonography.

Statistical Analysis

SPSS version 20 was used to conduct statistical analysis. Consistent variables (means \pm SD) have been presented. The mean between the two groups is compiled with independent t-test samples. The t-test paired has been used to compare readership methods. A p-value of up to 0.05 was considered

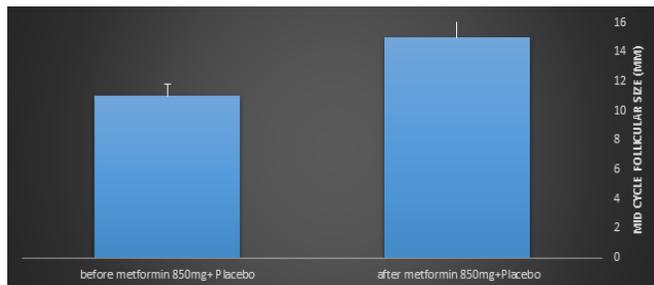


Figure 1: The effect of Metformin 850mg b.i.d and placebo on follicular size (mm) for 3 months. $P > 0.05$. Data is stated as the mean changes in follicular size (\pm SEM) (n =55 in each group). In addition, one-way ANOVA test stated Statistical significance after following by correction of Dunnett for multiple comparisons. * $p < 0.05$

significant. Data were subject to one-way ANOVA testing and multiple comparisons Dunnett testing.

RESULTS

Effect of metformin and placebo on mid-cycle follicular size in PCOS patients. No significant difference noticed [$p > 0.05$] when comparing the mid-cycle follicular size [mm] before and after metformin and placebo intake in a given dose.

Effect of metformin and D3 on mid-cycle follicular size in PCOS patients. Mid-cycle follicular size significantly [$p < 0.05$] increased by 6 folds after metformin and myoinositol administration in comparison to a control group in a given dose and time.

Comparison between effect of metformin+ placebo and metformin+ myoinositol 1000 mg/day on mid-cycle follicular size in PCOS patients. The addition of myoinositol to metformin was significantly [$p < 0.05$] increased mid-cycle follicular size by 3 folds in comparison to placebo and metformin in a given dose and time.

DISCUSSION

Myoinositol is a natural substance found in the B vitamin family. Research revealed that it helps the body to keep hormones in balance, promotes ovarian function, enhances follicular size quality, and preserves the menstrual cycle in a standard form. Specifically, studies depicted that myoinositol had positive effects on boosting reproductive function among women with PCOS, a disease more than 5 million women wrestled with Baillargeon JP, *et al.*⁸

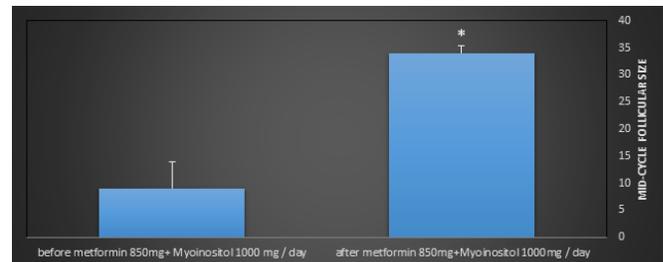


Figure 2: The effect of Metformin 850mg b.i.d and myoinositol 1000 mg / day on follicular size (mm) for 3 months. $P < 0.05$. Data is stated as the mean changes in follicular size (\pm SEM) (n =55 in each group). In addition, the One-way ANOVA test stated Statistical significance after following by correction of Dunnett for multiple comparisons. * $p < 0.05$

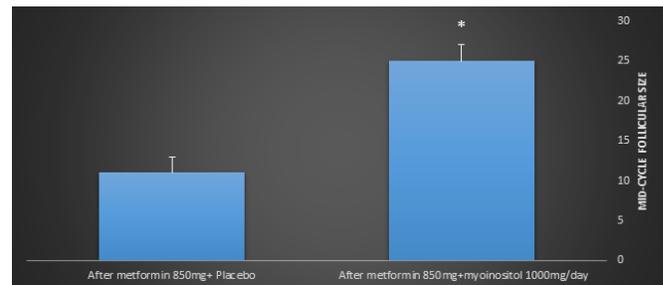


Figure 3: The effect of Metformin 850mg b.i.d + placebo and myoinositol 1000 mg/day on follicular size (mm) for 3 months. $P < 0.05$. Data is stated as the mean changes in follicular size (\pm SEM) (n =55 in each group). In addition, one-way ANOVA test stated Statistical significance after following by correction of Dunnett for multiple comparisons. * $p < 0.05$

Recently, a study of 3,602 women with PCOS who consumed myoinositol and folic acid for 2–3 months, 69% improved their ovulatory and menstrual cycles. In another article, researchers have depicted that “myoinositol treatment upregulates ovulation significantly in oligomenorrhea women and PCOS.”⁸

Myoinositol is not only a brilliant alternative in the treatment of PCOS patients but as well as a safe one. To our knowledge, no inositol adverse effects were seen or noticed at its standard dosage.

Several recent studies have shown myoinositol to help PCOS patients effectively, partially because it can increase insulin sensitivity, restore hormonal equilibrium, enhance menstrual regularity, decrease hyperandrogenism and affect ovarian functions. Research has shown that myoinositol improves fertility among PCOS people, and as the syndrome is the main cause of women’s infertility, these results are particularly very promising.⁹ And there is a continuing debate which is if the supplementation of myoinositol is effective PCOS therapy. Therefore, we conducted this study among PCOS patients. Mid-cycle ovarian follicular size on the 13th of ovulation has been evaluated after supplementing myoinositol intake 1000 mg/day for 3 months.

Currently, the evidence to support using myoinositol in PCOS is rapidly emerging and promising particularly concerning hormonal, ovulatory, and metabolic benefits. As with many aspects of nutrition-based interventions. However, the research is still considered to be limited by small study group sizes. Inositol in some way can be used as an experimental therapy in PCOS, according to the International PCOS Network, “such an agent is cheerfully obtainable, with low to moderate costs, and with a relatively limited side effect profile, and can be used regardless of small and inadequate quality evidence. People using this agent are advised, as with any other treatment or alternative therapy, to inform their health care team.”¹⁰

The present study demonstrated that daily myoinositol 1000 mg/day for 3 months in PCOS women who already on scheduled metformin 850 mg b.i.d for 3 months significantly ($p < 0.05$) increased the mid-cycle follicular size as compared to the placebo group.

The study by Karmenov *et al.* has shown that myoinositol improves insulin resistance and body weight and improves the ovarian activity of PCOS patients.¹¹ Papaleo E. *et al.* showed that myoinositol is a simple, safe treatment that can restore spontaneous ovarian activity and fertility in most PCOS patients.¹² Moreover, Pundir *et al.* demonstrated that the ovulation rate of Inositol and the hormone and metabolic profile in PCOS women appear substantially improved as compared to placebo.¹³

In a study of Raffone *et al.* where an assessment between the management of myoinositol ($2 \times 2000 \text{ g} + 200 \mu\text{g}$ per day) and the management of metformin (1500 mg per day) in females with a PCOS was done, it could be revealed that pregnant females were greater in the myoinositol group than in the metformin group of patients.¹⁴ Costantino *et al.* stated that myoinositol might lead to an exceedingly significant

development of the blood pressure, cholesterol, triglycerides, glucose, and insulin standards post a 75 mg oral glucose tolerance check.

These enhancements were assessed post a 1 weeks management program. The assessed hormonal standards presented a significant reduction in the whole plus-free S. testosterone levels plus progesterone levels, as an indicator of ovulation.¹⁵ Furthermore, additional studies in PCOS patients have explained the effectiveness of myoinositol in the development of fertility due to the enhancement of insulin resistance.¹⁶ Concerning PCOS, numerous studies have presented that one of the best significant procedures of insulin shortage has its increase from the inositolphosphoglycan (IPG) mediator and that a lack of inositol in the inositolphosphoglycans is in control of insulin resistance. Management of myoinositol might reduce insulin resistance.¹⁷ Myoinositol was found to produce a vital part in the signal trails of cells. Myoinositol action in a PCOS pathway would be connected to better insulin sensitivity and improved intracellular glucose uptake.¹⁸

CONCLUSIONS

The results from this study have strongly revealed that myoinositol oral supplementation in a given dose might help increase the follicular size maturity in PCOS women. Furthermore, myoinositol is considered a safe one as no adverse effects could be detected in the normal dose. Further studies recommended for hyperandrogenism, and metabolic parameters besides the management of ovulation, in patients with a PCOS.

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