

# Myo-inositol as a Safe and Novel Approach in the Treatment of Infertile PCOS Women: An Observational Study

Yasmin N<sup>1</sup>, Afreen S<sup>2</sup>, Kamrunnaher<sup>3</sup>, Ferdous JA<sup>4</sup>, Shewly NR<sup>5</sup>, Ferdous M<sup>6</sup>

### Abstract

**Conflict of Interest:** None

**Received:** 30.07.2019

**Accepted:** 08.10.2019

www.banglajol.info/index.php/JSSMC

**Background:** Adjunctive therapies to have a baby and widespread perception is that dietary supplementation such as myo-inositol are associated with only benefit, not with harm in case of PCOS women. The use of 2×1000mg myo-inositol +2×200microgram folic acid per day is a safe and promising tool in the effective improvement of symptoms and infertility for patients with a PCOS.

**Objectives:** To evaluate the effectiveness and safety of oral supplementation of inositol for reproductive outcomes among subfertile women with PCOS who are trying to conceive.

**Materials and methods:** Using questionnaire an observational study was performed in ShSMCH of outdoor infertility clinic and routine clinical practiced. In this observational study Thirty-five PCOS women of childbearing age with oligo or amenorrhea were enrolled in the study. Ovulatory disorder due to PCOS was apparently the only cause of infertility; no tubal defect or deficiency of male semen parameters was found. Myo-inositol combined with folic acid 2g twice a day was administered continuously. During an observation period of 6 months from July,2018 to December, 2018, ovulatory activity was monitored with ultrasound scan and hormone profile and the number of spontaneous menstrual cycles and eventually pregnancies were assessed.

**Results:** Twenty eight out of 35 (80%) patients restored their spontaneous menstrual cycle during treatment. A total of 10 singleton pregnancies (28.5% of patients) were obtained. Nine clinical pregnancies were assessed with fetal heart beat at USG scan. One pregnancies evolved in spontaneous abortion.

**Conclusion:** Myo-inositol is a simple and safe treatment that is capable of restoring spontaneous ovarian activity and consequently fertility in most patients with PCOS. This therapy did not cause multiple pregnancy.

### Key Words:

Myo-inositol, Polycystic ovary syndrome, Sub-fertility

[J Shaheed Suhrawardy Med Coll 2019; 11(2): 115-118]

DOI: <https://doi.org/10.3329/jssmc.v11i2.48961>

### Introduction

The PCOS is the most common cause of irregular menstrual cycle, chronic anovulation, and infertility of women often manifested as an androgen excess, with the typical ultrasound features. Observational studies postulate

that up to 15% of women suffer under this condition during their reproductive life. However its pathogenesis is still poorly understood.

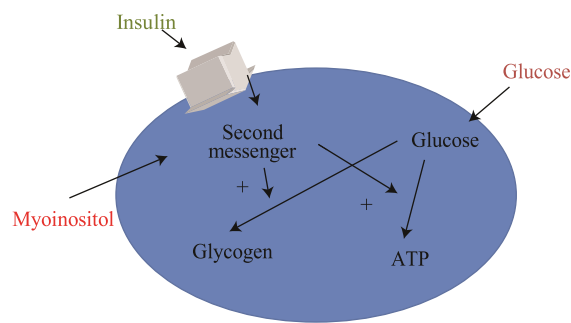
Recently it has been found that insulin resistance plays a key role in the clinical development of PCOS in almost all the women.<sup>1</sup> The hyperinsulinemia could induce an excess of androgens production in PCOS women through two different ways: first one is direct stimulation of ovaries to produce androgens, and the other one is the reduction of sex hormone binding globulin (SHBG) serum levels.<sup>2</sup> Due to the key role of insulin in the syndrome etiopathology, for many years, insulin sensitizers such as metformin, have been considered as possible therapeutic options in the management for the improvement of ovarian dysfunction with consecutive anovulation, irregular menstrual cycles.<sup>3,4</sup> Metformin, when used in the therapeutic dose range, was shown to have several side effects such as flatulence, diarrhea, and nausea, so that many patients are unable to use this treatment option in

1. Dr. Nilofar Yasmin, Associate Professor (Obs & Gyn), Shaheed Suhrawardy Medical College & Hospital
2. Dr. Shabeen Afreen, Asst. Professor (Obs & Gyn), Kurmitola General Hospital
3. Dr. Kamrunnaher, Asst. Professor (Obs & Gyn), Mymensingh Medical College & Hospital
4. Dr. Jannat Ara Ferdous, Associate Professor (Obs & Gyn) Shaheed Suhrawardy Medical College & Hospital
5. Dr. Naznin Rashid Shewly, Associate Professor (Obs & Gyn) Shaheed Suhrawardy Medical College & Hospital
6. Dr. Menoka Ferdous, Associate Professor (Obs & Gyn), Shaheed Suhrawardy Medical College & Hospital

**Correspondence to:** Dr. Nilofar Yasmin, Associate Professor (Obs & Gyn), Shaheed Suhrawardy Medical College & Hospitals. Phone: 01819147555, E-mail: nilofar71@gmail.com

gynecology for a longer period of time.<sup>5,6</sup> Therefore, in parallel to the common use of metformin and other insulin sensitizer agents for the treatment of PCOS, in the recent years, other therapeutic alternatives have been investigated. Myoinositol is one of the most interesting molecules that have been studied for the treatment of PCOS. The substance inositol is a *chemical compound* with the formula  $C_6H_{12}O_6$  or  $(-CHOH)_6$ , a sixfold *alcohol (polyol)* of *cyclohexane*, with five equatorial and one axial hydroxyl group. It is widely found in nature.<sup>7</sup> Inositol was defined in the past as “myometrial sugar,” Defining inositol as a vitamin-B In fact, several studies have proved that the inositol molecule is directly involved in the insulin cellular signaling. Regarding PCOS, several studies have shown that one of the mechanisms of insulin deficiency has its rise from the inositolphosphoglycan (IPG) mediator and that a deficiency of inositol in the inositolphosphoglycans is responsible for insulin resistance.<sup>8</sup> (see Figure 1).

Indeed, the action of myoinositol in a PCOS pathway would be related to an improved insulin sensitivity and a



**Fig-1:** Mechanism of action of myoinositol in the cell.

sequent increased intracellular glucose uptake.<sup>9</sup> Elevated concentration of myoinositol in human follicular fluid appears to play a role in follicular maturity and provide a marker of good quality oocytes.<sup>10</sup> Thus we hypothesized that the administration of myoinositol, would improve insulin activity and restore ovulatory function and fertility in amenorrhic women with PCOS.

## Methodology

*Study Type:* Non comparative observational study,

*Study population:* 35 subfertile women with PCOS defined by oligo or amenorrhea (six or fewer menstrual cycles during a period of 1 year), hyperandrogenism (hirsutism, acne or alopecia) and typical ovarian features on ultrasound scan attending in infertility clinic in Shaheed Suhrawardi Medical College Hospital and routine clinical practice were enrolled in the study. All women started with an intake of myoinositol and folic acid in a dosage of  $2 \times 2000$  mg myoinositol +  $2 \times 200$   $\mu$ gm folic acid per day and used it for at least 6 months. Study period: 6 month (July, 2018-December, 2018)

Their is not considered any patients with significant prolactinemia or hypothyroidism or androgen excess such as adrenal hyperplasia or Cushing’s syndrome .All women underwent assessment of tubal patency and all male partners were evaluated with two different semen analyses without finding any defect.

The primary outcome of the study was to determine the ovulatory function restoration and the pregnancy rates after treatment. Restoration of ovulation was determined by day 12 ultrasound scan and day 21 progesterone test. The pregnancies were documented by the obstetrician and confirmed by a positive test for plasma beta-human chorionic gonadotropin and ascertainment of a fetal heart beat on ultrasound scan.

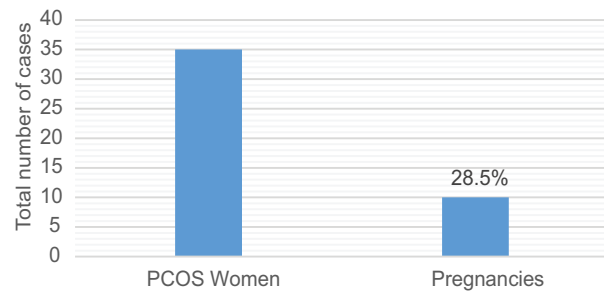
## Result

Baseline clinical and biochemical features of the PCOS patients are reported in table 1. The outcome of treatment is shown in figure 1. The data of 35 patients with PCOS with infertility were evaluated. According to the obtained data after 2-3 months of intake myoinositol and folic acid 28 women (80%) experienced an improvement of their menstrual cycle. 70% of them maintained spontaneous ovulation activity, documented by follicular growth and increased serum progesterone concentration in the luteal phase (mean  $10.5 \pm 1.8$  ng/ml). During the observational period of 6 months a total 10 pregnancy occurred. All were singletons pregnancies documented at us Scan, while one of them was abortion. This means a ratio of 28.5% of the investigated women becomes pregnant during the observational study. No twin pregnancies were documented. No relevant side effects have been reported in the patients taking myoinositol and folic acid product.

**Table-1**

*Shown clinical and biochemical features of the patients.*

Particulars	Baseline	After myo-inositol
Age (years)	32±4	
Body mass index (kg/m <sup>2</sup> )	28.5±2.4	
Follicle stimulating hormone (mUI/ml)	4.5±2.8	
Leutinizing hormone TSH (mUI/ml)	6.3±3.1	
Prolactin	19.1±2.7	
Serum progesterone (ng/ml)		10.5±1.8



**Fig.-1:** Number of patients and pregnancy rates.

### Discussion

PCOS is one of the most common endocrine disorders affecting women. Insulin resistance and hyperinsulinemia are strictly inherent to the phenotype of a high proportion of women with PCOS. A defect in insulin action had been suspected, particularly as consequence of a deficiency of DCI a competent of inositol phosphoglycan.

MI administration increases in patients with PCOS, thereby improving ovulatory function and decreasing testosterone concentration.

Despite the clear limitations of the observational study, there are reliable available data, since a wide range of patents can be analyzed. This study could show that a new treatment option for patients with a PCOS and infertility is available. Seventy percent of the patients restored ovulation after the treatment. Furthermore, the achieved pregnancy rates are at least in a range equivalent to or even superior to those reported by the use of the insulin sensitizer metformin. Kaimzaden and Javedani<sup>11</sup> described pregnancy rate of 14% in a cohort of 90 women and Legro et al of 12.3% in a cohort of 75 women with PCOS

In a study of Raffone et al. where a comparison between the administration of (myo-inositol 2 x 2000 gm + folic acid 200 micro gram per day)<sup>12</sup> and the administration of metformin (1500 mg per day) in women with a PCOs was performed. It could be shown that the number of pregnancy was clearly higher in the myo-inositol group than in the metformin group of patient.

The important evidence is related to the difference of myo-inositol and metformin in term of safety profile & compliance for patient. Side effect of metformin have been commonly reported in particularly for mild to severe Gastro Intestinal Side effects such as abdominal pain nausea & diarrhea. Only in some cases, very severe side effects on lactic acidosis have been found. On the other side, myo-inositol seems to be a safe and well tolerated approach.

Many studies like Gerli et al. Could show in a prospective study that the group of patients receiving myo-inositol and folic acid experienced in 82% of the cases an ovulation when the was only observed in 63% of the cases in the group of patients which received placebo.

By the same way 70% of the patients of the myo-inositol group developed regular menstrual cycle of 16 wks treatment whereas only 13% of the women did it in the placebo group.

Many study have been shown that the progesterone level as a marker of ovulation, experience as significant rise in the group that received myo-inositol. This data can be supported by our own data as progesterone a value of  $10.5 \pm 1.8$  mg/ml. could be observed.

### Conclusion

Myo-inositol is not only as effective alternative in the treatment of PCOS patients but also a secure one as no side effects could be observed in the standard dosage. It is a simple and safe treatment that is able to restore spontaneous fertility in most patients with PCOS.

### References

1. A. D. Genazzani, C. Lanzoni, F. Ricchieri, and V. M. Jasonni, "Myo-inositol administration positively affects hyperinsulinemia and hormonal parameters in overweight patients with polycystic ovary syndrome," *Gynecological Endocrinology*, vol. 24, no. 3, pp. 139–144, 2008.
2. M. L. Croze and C. O. Soulage, "Potential role and therapeutic interests of myo-inositol in metabolic diseases," *Biochimie*, vol. 95, no. 10, pp. 1811–1827, 2013.
3. J.-P. Baillargeon, M. J. Iuorno, and J. E. Nestler, "Insulin sensitizers for polycystic ovary syndrome," *Clinical Obstetrics and Gynecology*, vol. 46, no. 2, pp. 325–340, 2003.
4. A. D. Genazzani, C. Battaglia, B. Malvasi, C. Strucchi, F. Tortolani, and O. Gamba, "Metformin administration modulates and restores luteinizing hormone spontaneous episodic secretion and ovarian function in nonobese patients with polycystic ovary syndrome," *Fertility and Sterility*, vol. 81, no. 1, pp. 114–119, 2004.
5. A. M. Strugaru, G. Botnariu, L. Agoroaei, I. C. grigoriu, and E. Butnaru, "Metformin induced lactic acidosis—particularities and course," *Revista Medico-Chirurgicala a Societatii de Medici si Naturalisti din Iasi*, vol. 117, no. 4, pp. 1035–1042, 2013.
6. C.-H. Kim, K.-A. Han, H.-J. Oh et al., "Safety, tolerability, and efficacy of metformin extended-release oral antidiabetic therapy in patients with type 2 diabetes: an observational trial in Asia," *Journal of Diabetes*, vol. 4, no. 4, pp. 395–406, 2012.
7. R. S. Clements Jr. and B. Darnell, "Myo-inositol content of common foods: development of a high-myo-inositol diet," *The American Journal of Clinical Nutrition*, vol. 33, no. 9, pp. 1954–1967, 1980.
8. J.-P. Baillargeon, J. E. Nestler, R. E. Ostlund, T. Apridonidze, and E. Diamanti-Kandarakis, "Greek hyperinsulinemic women,

- with or without polycystic ovary syndrome, display altered inositols metabolism,” *Human Reproduction*, vol. 23, no. 6, pp. 1439–1446, 2008.
9. N. M. Hooper, “Glycosyl-phosphatidylinositol anchored membrane enzymes,” *Clinica Chimica Acta*, vol. 266, no. 1, pp. 3–12, 1997.
  10. N. M. Hooper, “Glycosyl-phosphatidylinositol anchored membrane enzymes,” *Clinica Chimica Acta*, vol. 266, no. 1, pp. 3–12, 1997.
  11. S. Gerli, E. Papaleo, A. Ferrari, and G. C. Di Renzo, “Randomized, double blind placebo-controlled trial: effects of Myoinositol on ovarian function and metabolic factors in women with PCOS,” *European Review for Medical and Pharmacological Science*, vol. 11, no. 5, pp. 347-354, 2007
  12. M. A. Karimzadeh and M. Javedani. “An assessment of lifestyle modification versus medical treatment with clomiphene citrate metformin and clomiphene citrate-metformin in patients with polycystic ovary syndrome.” *Fertility and Sterility*, vol. 94, no. 1, pp. 216-220, 2010
  13. E. Raffone, P. Rizzo, and V. Benedetto, “Insulin sensitiser agents alone and in co-treatment with r-FSH for ovulation induction in PCOS women,” *Gynecological Endocrinology*, vol. 26, no. 4, pp. 275–280, 2010.