

Comparative Study on Efficacy of Myoinositol over Metformin in Polycystic Ovary Syndrome Patients

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Abstract

Introduction: Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, prevalent across different populations around the world. PCOS prevalence worldwide is estimated to be 6-10% or even 15% when the diagnosis is based on Rotterdam criteria. Studies of PCOS in India carried out in convenience samples reported a prevalence of 3.7% to 22.5%, with 9.13% to 36% prevalence in adolescents only. **Materials and Methods:** A study during January 2020 to December 2020 was done on patients attending the department of Gynaecology & Obstetrics of Govt Medical College, Ananthapur. A total of 50 women with PCOS and infertility were selected and their reports generated according to Rotterdam classification. Out of 50 patients 25 were recommended Myoinositol 2000 mg thrice a day and Folic acid 200 µg twice a day and continued for at least 3 months. Another 25 patients were treated with Metformin 1500 mg/ day in three divided dosages. **Results:** The data of 50 women with PCOS were evaluated. Baseline characteristic like age and BMI were almost similar in both groups. According to obtained records, 37 women experienced an improvement of their menstrual cycle towards ovulatory cycles. A total number of 13 women became pregnant. This result could be achieved in the form of pregnancy after the intake of 2-3 months of Myoinositol and Folic acid. No relevant side effects were reported in the patients taking Myoinositol and Folic acid. **Conclusion:** This confirms that myoinositol is not only an effective alternative in the treatment of PCOS patients but also a safe and secure drug as no side effects could be observed in the standard dosages. On the other side easy compliance results in the better outcome in the management of ovulation, hyperandrogenism and metabolic parameters on patients with PCOS.

Keywords: PCOS, Metformin, Myoinositol, PCOD.

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Introduction

Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, prevalent across different populations around the world. PCOS prevalence worldwide is estimated to be 6-10% or even 15% when the diagnosis is based on Rotterdam criteria[1]. Studies of PCOS in India carried out in convenience samples reported a prevalence of 3.7% to 22.5% [2,3] with 9.13% to 36% prevalence in adolescents only [4,5]. This syndrome was first described by Stein and Leventhal in 1931. It is a disorder characterized by excessive secretion of androgens by the ovaries, oligomenorrhoea, anovulation/oligoanovulation and insulin resistance and with variable clinical manifestations that include irregular menstrual cycles, hirsutism, alopecia and acne [1]. PCOS increases woman's risk of infertility, dysfunctional uterine bleeding, endometrial carcinoma, as well as insulin resistance, dyslipidemia and hypertension [all risk factors for cardiovascular disease (CVD)]. The potential increased risk of CVD may be related to the higher incidence of metabolic syndrome in this population [6]. The pathogenesis of PCOS has not been completely elucidated and is multifactorial, with genetic and environmental factors being implicated. Insulin resistance is presumed to be caused by defects in

the insulin receptor and post receptor components of the insulin signaling pathway [7,8].

Elevated insulin levels cause abnormal functioning of hypothalamic-pituitary-ovarian axis that lead to PCOS. Women with PCOS experience an increased frequency of hypothalamic GnRH pulses, which in turn results in an increase in the LH/FSH ratio [9]. Insulin resistance is main causative factor for all these consequences & morbidity. Failure of the target cells to respond to normal or ordinary levels of insulin is regarded as insulin resistance irrespective of the body mass index (BMI). Hyperinsulinaemia due to insulin resistance occurs in approximately 80% of PCOS Women with central obesity and 30%-40% of lean PCOS women. Hyperinsulinemia is the main causative factor in PCOD women both obese and lean and cause hyperandrogenism [10].

Insulin directly promotes ovarian steroidogenesis, and inhibits liver release of the sex hormone binding globulin (SHBG) and production of insulin-like growth factor binding protein 1 (IGFBP-1). Increased concentrations of IGF-1 additionally promote ovarian release of androgens [9]. Metformin is a hepato-selective insulin sensitizer. It has beneficial properties of weight loss, lipid reduction and modulator of endothelial function. It also improves ovarian function in insulin-resistant women. It does not cause hyperinsulinaemia or hypoglycaemia. Myo-inositol (MI) is a naturally occurring substance produced in the human body that belongs to the vitamin B complex group. MI is one of the nine different types of inositol and can be found naturally in many foods. Of the nine different types of inositol, two have insulin-sensitizing capabilities: MI and d-chiro-inositol. PCOS has been linked to a deficiency in myo-inositol. MI can be

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synthesized by the body from food, but when we are already deficient, the lack of MI can impact the ability of the body to be sensitive to insulin. Women with PCOS are also known to have a defect in their insulin-signaling pathways, which are heavily dependent upon inositol-containing substances (phosphoglycan mediators). During certain conditions like periconceptional periods in PCOS women, the physiological requirements of MI increases. MI plays an important role as the structural basis for a number of secondary messengers including synthesis of phosphatidylinositol 3-kinase (PI 3-kinase), a key messenger to improve insulin sensitivity and thereby reducing insulin resistance. Supplying extra MI appears to temporarily correct the impaired insulin pathways and reduce the signs and symptoms of insulin resistance.

Materials and Methods

A study during January 2020 to December 2020 was done on patients attending the department of Gynaecology & Obstetrics of Govt

Medical College, Ananthapur. A total of 50 women with PCOS and infertility were selected and their reports generated according to Rotterdam classification. Out of 50 patients 25 were recommended Myoinositol 2000 mg thrice a day and Folic acid 200 µg twice a day and continued for at least 3 months. Another 25 patients were treated with Metformin 1500 mg/ day in three divided dosages. The primary outcome of the study was to determine the restoration of ovulatory function and the pregnancy rate following treatment. The secondary outcome was to evaluate the compliance rate and side effects reported in both groups of the patients receiving treatment. In our study the pregnancy outcome was also studied.

Results

The data of 50 women with PCOS were evaluated. Baseline characteristic like age and BMI were almost similar in both groups.

Table 1: Age distribution

S.No	Age group in years	Group A (N=25)	Group B (N=25)
1	15-20	5 (20%)	4 (16%)
2	21-25	3 (12%)	3 (12%)
3	26-30	7 (28%)	6 (24%)
4	31-35	5 (20%)	5 (20%)
5	36-40	2 (8%)	3 (12%)
6	41-45	3 (12%)	4 (16%)
7	Total	25 (100%)	25 (100%)

Table 2: BMI Distribution

S.No	Age group in years	Group A (N=25)	Group B (N=25)
1	<24.9	6 (24%)	6 (24%)
2	25-29.9	14 (56%)	13 (52%)
3	30-34.9	5 (20%)	6 (24%)
4	Total	25 (100%)	25 (100%)

Table 3: Effect on insulin levels

S.No	Fasting insulin	Group A (N=25)	Group B (N=25)
1	Before treatment (micro U/ml)	14.34	14.35
2	After treatment (micro U/ml)	7.01	8.89

In group A, serum fasting insulin level decreased by 51% but not so in group B (38%).

Table 4: Glucose insulin ratio

S.No	Glucose insulin ratio	Group A (N=25)	Group B (N=25)
1	Before treatment	7.85	7.82
2	After treatment	14.14	10.15

Table 5: Hormonal data before and after treatment with Myoinositol and Metformin.

Hormonal data	For Myo inositol (Group A)		For Metformin (Group B)	
	Before treatment	After treatment	Before treatment	After treatment
Total Testosterone ng/ml	98.56	37.26	99.41	50.20
Estradiol pg/ml	85.23	92.32	88.13	81.43
DHEAS µg /dL	361.64	186.2	363.16	257.19
LH mIU/ml	15.13	8.86	15.76	7.5
FSH mIU/ml	6.90	4.86	6.89	6.34
LH : FSH Ratio	2.36	1.7	2.35	2

According to obtained records, 37 women experienced an improvement of their menstrual cycle towards ovulatory cycles. A total number of 13 women became pregnant. This result could be achieved in the form of pregnancy after the intake of 2-3 months of Myoinositol and Folic acid. No relevant side effects were reported in the patients taking Myoinositol and Folic acid.

Discussion

This study could show that a new treatment option for women with PCOS and infertility is available. 70% of the patients restored ovulation following treatment with Myoinositol 2000 mg thrice a day and Folic acid 200 µg twice a day for at least three months. The

administration of this molecule improves the glucose uptake by acting as a direct Insulin signaling messenger. It thus improves the insulin resistance and hormonal status, thereby restoring the ovulation process. There is also marked difference in safety and compliance between myoinositol and metformin as found in this study. The patients on Metformin have reported mild to severe gastro-intestinal side effects like abdominal pain, nausea, anorexia and diarrhoea. Myoinositol seems to be a safe and well tolerated drug with comparable efficacy as Metformin. Poor compliance and side effects of Metformin makes it less acceptable. The efficacy, absence of significant side effects, and the fact that myoinositol is a natural

component of human diet makes it an attractive insulin sensitizer in PCOS. In recent years many studies have demonstrated that an improvement in ovulation rate and regulation of menstrual cycles was obtained by the combined use of 4 grams of Myoinositol and 400 µg of Folic acid. Also in another study, Treatment with 1200 mg/d of myoinositol for 12 weeks was effective in reducing hormonal, metabolic and oxidative abnormalities in patients with PCOS by improving insulin resistance. Gerli et. al [11] could show in a prospective study that the group of patients receiving myo inositol and folic acid experience ovulation in 82% of the cases whereas in placebo group, it was only 63%. He also reported a regular menstrual cycle in 70% of cases with myo inositol and folic acid after 16 weeks of treatment as only 13% case in placebo group. In a study by Raffone et al [12], used Myoinositol 2000 mg and folic acid 200 µg twice daily vs Metformin 1500 mg /day and found that number of pregnancies was clearly higher in group A. Costantino et. al in his double blinded placebo controlled study found that after 16 weeks of Myoinositol treatment improved the blood pressure, triglyceride, cholesterol, glucose and insulin values after a 75 gram oral GTT significantly [9] The evaluated hormonal values were significantly decreased. Total and free Serum testosterone and Progesterone levels as a marker of ovulation were increased significantly in the group receiving Myoinositol. Kamenov et al [13] studied ovulation induction with Myoinositol alone and with combination with Clomiphene citrate in PCOS patients with insulin resistance. He also found significant improvement in ovulation induction with Myoinositol alone.

Conclusion

PCOS is the most common endocrine problem affecting the women from menarche to premenopausal age. As PCOS is an emerging disorder during adolescence, early intervention is necessary to improve the reproductive health of adolescents and to prevent future complications. A variety of treatment strategies have been developed based on the patient symptomology and need. Insulin PCOS is the most common endocrine problem affecting the women from menarche to premenopausal age. As PCOS is an emerging disorder during adolescence, early intervention is necessary to improve the reproductive health of adolescents and to prevent future complications. A variety of treatment strategies have been developed based on the patient symptomology and need. Insulin. This confirms that myoinositol is not only an effective alternative in the treatment of PCOS patients but also a safe and secure drug as no side effects could be observed in the standard dosages. On the other side easy compliance results in the better outcome in the management of ovulation, hyperandrogenism and metabolic parameters on patients with PCOS.

Conflict of Interest: Nil

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