

Original Article

A Study of the Effect of Metformin Versus Myo-Inositol in the Management of PCOS — A Randomised Controlled Trial

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Of the common hormonal disorders in females of childbearing age-group, polycystic ovary syndrome (PCOS) is the most important. It is associated with various morbidities like type-II diabetes mellitus, obesity, insulin-resistance, cardiovascular dysfunctions and is characterised by reproductive and psychological manifestations, resulting in an enormous impact on health. The objective of our study was to compare the efficacy of metformin and myo-inositol on certain parameters such as BMI reduction, LH/FSH ratio (suggesting insulin resistance) and HOMA-IR Index in PCOS patients. In our study, both metformin and myo-inositol significantly reduced the BMI. Metformin also significantly reduced the insulin resistance and improved insulin-sensitivity. It also significantly improved menstrual pattern in the women with PCOS. These changes were not observed when treated with myo-inositol. The sample size calculation was done with n Master 2.0 Christian Medical College, Vellore.

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Key words : Polycystic Ovary Syndrome, PCOS, Metformin, Myo-inositol.

An approximate 10-20 percent of ladies in the reproductive age-group are affected by polycystic ovary syndrome (PCOS). PCOS is the commonest cause of anovulatory infertility and is also called hyperandrogenic anovulation. Insulin-sensitizing agents are amongst the recommended treatment options for the hyperinsulinemia induced ovarian dysfunction, resulting in improved response to gonadotropin PCOS. This in turn, helps in restoration of normal menstrual cycle and ovulation, and thus increases the chance of spontaneous pregnancy. In 2003, the Rotterdam Consensus of the European Society of Human Reproduction and Embryology (ESHRE) & the American Society for Reproductive Medicine (ASRM) reached a general agreement on the diagnostic criteria for this syndrome. Metformin and myo-inositol are the main treatment options available in the management of PCOS (Fig 1).

MATERIALS AND METHODS

The present study was an open-label randomised controlled trial which was carried out at the department of obstetrics and gynaecology, IPGME&R & SSKM Hospital, Kolkata. Our study was conducted during a

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Editor's Comment :

- Polycystic ovary syndrome (PCOS) is a common cause of menstrual irregularity and infertility
- Diagnosis of the disease is commonly done with the help of Rotterdam criteria
- Metformin and Myo-inositol are the main drugs used in therapy
- Weight loss is also an important component of management
- Confounding factors like hypothyroidism needs to be ruled out before diagnosing PCOS

period of 2 years. It comprised of 306 PCOS patients (as per the Rotterdam Criteria), of whom 153 belonged to the group treated with Metformin and the remaining 153 belonged to the group treated with Myo-inositol. Patients who presented to the Gynaecology OPD in IPGME&R with suggestive symptoms of oligo-anovulation (amenorrhoea, oligomenorrhoea, polymenorrhoea, menorrhagia), hyperandrogenemia (example hirsutism, acne, infertility) and USG features suggestive of PCOS were included. Patients less than 18 years of age and the post-menopausal women were excluded in the study. Other criteria for exclusion from the study were patients with uncorrected hypothyroid status, or pregnant patients, or those who were diagnosed with CAH (congenital adrenal hyperplasia), prolactin secreting adenoma or diabetes mellitus. Patients who were already on treatment for PCOS were also excluded from our study.

The parameters such as height (in metre), weight (in kilogram) were recorded and BMI (Basal Metabolic

Index) was calculated. A detailed history including patients' menstrual history (such as amenorrhea, oligomenorrhea and irregular cycles), infertility, features of hyperandrogenemia (such hirsutism, acanthosis nigricans) were noted. Investigations such as assessment of LH (luteinizing hormone), FSH (follicle-stimulating hormone), serum prolactin and serum insulin were done.

The two groups were subjected to the following treatment schedule (all medicines were supplied free of cost from the hospital pharmacy) -

Metformin group : Metformin (500mg) thrice daily for 3 months.

Myo-inositol group : Myo-inositol (2 gram) twice daily for 3 months.

After three months of treatment, the following parameters were analysed and compared statistically between the two groups: BMI reduction, LH/ FSH ratio (suggesting insulin resistance) and HOMA-IR Index (Homeostatic Model Assessment of Insulin Resistance). HOMA-IR Index is used for quantifying IR (Insulin Resistance) and beta cell function. It is calculated by: $HOMA-IR = \frac{\text{glucose} \times \text{Insulin}}{405}$ (glucose in mg/dl).

Appropriate standard statistical tools were applied for analysis of the observed data.

RESULTS

The total number of PCOS patients in our study was 306. Of them 153 patients were advised metformin (500mg) thrice daily for 3 months (Metformin group) and the remaining 153 patients were advised myo-inositol (2 gram) twice daily for 3 months (Myo-inositol group).

In the Metformin group, the mean BMI was 28.12 before treatment. It reduced to 26.05 after 3 months of treatment. This was a statistically significant finding. The mean HOMA-IR index was 4.65 before treatment. It was reduced to 2.23 after treatment, i.e., statistically significant. The mean LH/ FSH ratio, which denoted insulin-resistance, was 2.36 before commencing treatment. It decreased to 1.6 post-treatment. This observation was also statistically significant.

In the Myo-inositol group, the mean BMI was 24.45 before treatment and it was decreased to

23.05 after completion of treatment. This observation was statistically significant. The mean HOMA-IR index was 2.02 before treatment. It was reduced to 2.00 after treatment. This finding was not statistically significant. The mean LH/FSH ratio was 2.02 before starting treatment. It diminished to 2.00 after three months of treatment, i.e., which was not statistically significant.

DISCUSSION

In our study, it was observed that the mean BMI, LH/ FSH ratio and HOMA-IR index grossly improved in the PCOS patients who were treated with metformin (Metformin group). These findings were statistically significant. In the patients who were treated with myo-inositol (Myo-inositol group), although the mean BMI reduced significantly, the mean LH/ FSH and mean HOMA-IR index failed to show any change. Thus, it was apparent in our study, that myo-inositol was ineffective in reducing insulin-resistance in the PCOS patients.

Numerous studies have been conducted in the past to analyse the efficacy of metformin in the management of PCOS. Velazquez *et al*¹ were amongst the first to show a 35% reduction in the area under insulin curve and a 31% decrease in insulin area to glucose area ratio, thus indicating the improved insulin-sensitivity in PCOS patients treated with metformin. Lord *et al*² in their meta-analysis, revealed that metformin was effective in decreasing fasting insulin levels and hence

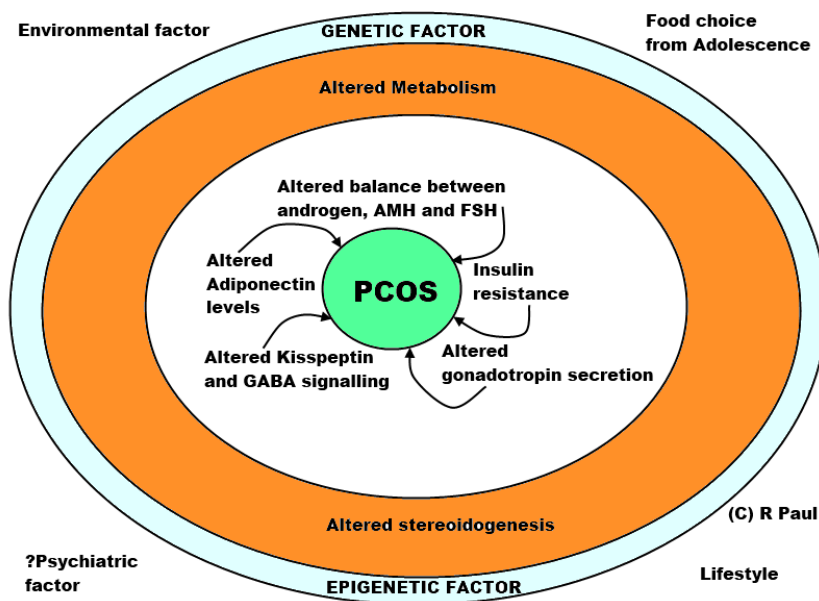


Fig 1 — The Pathophysiology of PCOS : schematic representation

was an effective treatment option for anovulation in PCOS.

Although in our study, myo-inositol did not show any improvement in the insulin-sensitivity in the PCOS patients, but some studies have demonstrated the contrary. For instance, Galazis *et al*⁶, showed that treatment with myo-inositol improved insulin-resistance in PCOS patients. In another study by Constantino *et al*⁴, 42 PCOS patients were treated with myo-inositol. It was found that the fasting serum insulin and glucose levels remained unchanged. About 69.5% had their ovulation restored. Teede *et al*⁵ recommended that inositol (in any form) should be considered an experimental remedy for treating PCOS. In a study by Gerli *et al*⁶, the BMI significantly improved in the patients treated with myo-inositol, but the waist-to-hip ratio remained unchanged.

A randomized, placebo-controlled, double-blinded study by Tang *et al*⁷ on obese PCOS patients treated with metformin alone or combined with lifestyle modifications, assessed the effects on anthropometry, metabolism, and menstruation. They concluded that metformin alone did not improve weight loss or menstrual regularity in the concerned patients. Significant improvement in menstrual health was achieved by weight loss alone through lifestyle changes.

CONCLUSION

From our study, it is evident that metformin is an excellent choice in the treatment of PCOS. It effectively reduced BMI and insulin-resistance in the PCOS patients. It also concluded that myo-inositol was effective in significantly reducing the mean BMI. However, in the myo-inositol group, there was no effect

on HOMA-IR index or mean LH/ FSH ratio thus suggesting its ineffectiveness in improving insulin-sensitivity in the patients with PCOS. So myo-inositol can be a good treatment option for reducing BMI or it may be used in combination with an insulin-sensitising agent like metformin in the treatment of PCOS, but not used alone.

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Conflict of Interest : None

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