

A PILOT STUDY ON EFFECT OF METFORMIN IN POLYCYSTIC OVARY SYNDROME

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ABSTRACT

The objective of the study was to evaluate the efficacy of Metformin in women with polycystic ovary syndrome. A Prospective study was performed in Infertility and Gynaecology Clinic. A total of 50 patients were recruited for the study, of which 8 patients were excluded due to insufficient data and 42 overweight patients with polycystic ovary syndrome was included for the study based on inclusion and exclusion criteria. Metformin 500 mg trice daily was given to each patient. The result of the study shows that 24 patient had oligomenorrhea, of which 18 patients had regular menstrual cycle after treatment with Metformin. 8 patient had amenorrhea, of which 4 patient got regular

menstrual cycle after treatment. The Mean \pm SD of fasting glucose, fasting insulin and glucose/insulin ratio were 96.6 \pm 14.2, 22.1 \pm 5 and 4.3 \pm 0.6. After treatment, it was found to be reduced to 93.6 \pm 10.2, 18.7 \pm 4 and 5.5 \pm 1.2. Significantly decreased concentration in hormonal parameters like LH, FSH, LH:FSH and testosterone were also observed. It was concluded that Metformin was found to be effective treatment for polycystic ovary syndrome.

KEYWORDS: Polycystic ovary syndrome, Metformin, Fasting glucose.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age, affecting about 6.5–6.7% of all premenopausal women ^[1, 2]. The disorder originally described as cystic disease of the ovaries by Stein & Levanthal ^[3] is now considered to be associated with a barrage of endocrine and metabolic disturbances such as hypertension, impaired glucose tolerance (IGT), type 2 diabetes mellitus, coronary artery

disease, increased risk of endometrial and perhaps breast cancer ^[4]. In the European Society of Human Reproduction and Embryology and the American Society of Reproductive Medicine ^[5] consensus, at least two of the following features are needed to make the diagnosis such as oligo/anovulation, hyperandrogenism, and polycystic features on ultrasound scan. The Androgen Excess Society recommended that androgen excess should remain a constant feature of PCOS irrespective of the ovulatory status and morphological features of the ovaries ^[6]. In young women with PCOS, insulin resistance (IR) may occur with high frequency. It is generally acceptable that IR plays a significant role in PCOS either directly or through obesity and represents a clinical concern to physicians and patients. Insulin acts by interacting with its own receptor and by the insulin growth factor (IGF) receptor type I, which have been detected in human models throughout all ovarian compartments, as granulosa, thecal and stromal tissues ^[7]. It has also been definitively proved that insulin is able to stimulate ovarian steroidogenesis. Insulin plays a direct role in the pathogenesis of hyperandrogenemia in PCOS, acting synergistically with luteinizing hormone to enhance the androgen production of theca cells ^[8].

Metformin was the first insulin sensitising drug used in PCOS to investigate the role of insulin resistance in the pathogenesis of the syndrome ^[9]. Metformin works by improving the sensitivity of peripheral tissues to insulin ^[10], which results in a reduction of circulating insulin levels. Metformin inhibits hepatic gluconeogenesis and it also increases the glucose uptake by peripheral tissues and reduces fatty acid oxidation ^[11]. Metformin plays its role in improving ovulation induction in women with PCOS through a variety of actions, including reducing insulin levels and altering the effect of insulin on ovarian androgen biosynthesis, theca cell proliferation, and endometrial growth ^[12]. The main objective of the study was to evaluate the efficacy of Metformin in women with PCOS.

MATERIALS AND METHODS

A Prospective study was performed in Infertility and Gynaecology Clinic. Institutional ethical committee approval was obtained for the study. Inclusion Criteria like women between 18 to 35 years of age with PCOS defined by Rotterdam criteria. Exclusion criteria like adrenal hyperplasia, thyroid dysfunction, hyperprolactinemia, known diabetes mellitus, severe hepatic or kidney diseases. The patients were enrolled into the study based on inclusion and exclusion criteria. A total of 50 patients were recruited. Informed consent was obtained from the patients. Demographic details and details like body mass index (BMI), hirsutism,

alopecia, acne, and menstrual history were collected. On second day of menstrual cycle, tests like fasting blood glucose, fasting insulin, free testosterone, follicle stimulating hormone (FSH), luteinizing hormone (LH), LH:FSH ratio, serum testosterone were performed after overnight fasting. Transabdominal ultrasonography was performed to assess the polycystic ovaries. Metformin 500 mg thrice daily was given to the patient. After three months of treatment, the above mentioned parameters were measured once again and the efficacy was assessed using student's t test.

RESULTS AND DISCUSSION

A total of 50 patients were recruited, of which 8 patients were excluded from the study due to insufficient data. Forty two women were enrolled into the study. Of the 42 patients, 9 patients had family history of PCOS. 12 patients were in the age group of 18-25 years, 22 patients were in the age group of 25-30 years and 8 were in the age group of 30-35 years. Maximum numbers of patients were seen in the age group of 25-30 years. Table 1 shows the demographic details of patient. It was clear that there was significant changes in weight and menstrual regularity were seen after treatment. Out of 42 patients, 24 patients experienced oligomenorrhea, of these 22 patients presented monthly menstruations during the followup period. Out of 42 patients, 8 patients experienced amenorrhea, 4 of these patients got regular menstrual cycle after treatment. Out of 42 patients, 39 patients had hirsutism and it was reduced in 6 patients after treatment. 24 patients had acne, significant changes were seen in 5 patients. 10 patients had alopecia, significant changes were observed in 1 patients after treatment with Metformin.

Table 1: Demographic details of the patient

Variables	Before treatment	After treatment
BMI (kg/m^2)	26.5 \pm 3	24.5 \pm 4
Oligomenorrhea	24	6
Amenorrhea	8	4

Table 2 shows Mean \pm SD of laboratory investigations

Parameters	Before treatment	After treatment
Fasting glucose (mg/dl)	96.6 \pm 14.2	90.6 \pm 10.2
Fasting Insulin (mIU/ml)	24.1 \pm 5	18.7 \pm 4
Glucose/Insulin ratio	3.8 \pm 0.6	5.5 \pm 1.2

LH (mIU/ml)	13.4±3.4	10.3±3.2
FSH (mIU/ml)	7.2±1.9	6.3±0.7
LH:FSH	1.52±0.5	1.24±0.3
Serum Testosterone (nmol/l)	2.6±0.4	1.1±0.2

The Mean±SD of fasting glucose, fasting insulin and glucose/insulin ratio were 96.6±14.2, 24.1±5 and 3.8±0.6. After treatment, fasting glucose was reduced to 90.6±10.2 which was considered to be statistically significant ($P=0.02$), fasting insulin was reduced to 18.7±4 ($P<0.0001$) and glucose/insulin ratio was reduced to 5.5±1.2 ($P<0.0001$). It was clear that significant changes were seen in biochemistry parameters like fasting glucose, fasting insulin and glucose/insulin ratio. Significantly decreased concentration in hormonal parameters like LH ($P<0.0001$), FSH ($P=0.0058$), LH:FSH ($P=0.0027$) and serum testosterone ($P<0.0001$) were also observed after treatment. Velazquez *et al.*, 1994 reported in an observational study that Metformin shows significant improvement in menstrual regularity and reduction in circulating androgen levels as well as a significant reduction in body weight^[9]. Harborne *et al.*, 2005 concluded that Metformin shows significant decrease in BMI in obese and morbidly obese women independent of lifestyle modification^[12].

CONCLUSION

Metformin was a simple and effective treatment for PCOS and it was able to restore spontaneous ovulation in most patients with PCOS.

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