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Original Research Article

Study of metformin in polycystic ovary syndrome

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ABSTRACT

Background: Objective of the study was to measure the efficacy and safety of insulin sensitizing drug metformin in reversing the metabolic and endocrine disturbances in fifty women with polycystic ovarian disease.
Methods: The study was performed on 57 women with polycystic ovarian syndrome (PCOS) in the outpatient department of obstetrics and gynaecology, V. S. General Hospital, Ahmedabad. Metformin 500 mg thrice daily was given until the cysts disappeared which was taken as the end point of the study. Follicular studies were done to check the effect of metformin on ovulation. Significance was tested by paired t test and p value calculated.
Results: Metformin was found effective in regressing polycystic changes in ovary, regularization of menstrual cycles and improving ovulation.
Conclusions: The present study shows that metformin has a beneficial role in effective management of PCOS.

Keywords: PCOS, Cysts, Metformin

INTRODUCTION

Polycystic ovary syndrome (PCOS), also called hyperandrogenic anovulation (HA), or Stein–Leventhal syndrome, is one of the most common endocrine disorders among women.[1,2] Symptoms and signs of PCOS are very heterogenous. The disease presents with any of the following combination features like menstrual irregularities (irregular menstrual cycles, and amenorrhoea), signs of hyperandrogenism (hirsutism, acne, and alopecia), a characteristic polycystic appearance of ovaries on ultrasound examination and endocrine disturbances involving high serum concentration of luteinizing hormones and androgens.[3-6] A link between disturbed insulin action and PCOS was first highlighted in 1980.[3] Insulin resistance and compensatory hyperinsulinemia play an important role in pathophysiology of PCOS. Insulin resistance is the lack of cellular sensitivity with respect to glucose metabolism. The endocrine manifestations of hyperinsulinemia are of hyperandrogenaemia leading to anovulation, subfertility and skin stigmata (acne, alopecia, and hirsutism).[7-10] In addition hyperinsulinemia is associated with metabolic disturbances like type 2 diabetes mellitus, dyslipidaemia, hypertension, and elevated plasma plasminogen activator-1 concentrations, all of which are risk factors for cardiovascular disease.[11-13] Regression of the symptoms of PCOS is achieved by reducing hyperinsulinaemia.[13] Hence recognition of this hyperinsulinemia has led to the intervention of insulin sensitizing drugs to play a key role in the management of PCOS. Among the available insulin sensitizing agents metformin is widely used drug. Clinical trials with metformin have recorded a wide range of benefits.

Objectives

Objective of the study was to study the efficacy and safety of metformin in regularization of menstrual cycles and regression of cysts in PCOS.

METHODS

The type of study was a prospective study. The study was conducted at the V. S. Hospital, Ahmedabad, Gujarat, India. The duration of the study was of 6 months from January 2019 to June 2019.

Inclusion criteria

The study included patients with age of 15-30 years and women with irregular menstrual cycles and evidence of polycystic ovaries on ultrasound.

Exclusion criteria

Patients with other causes of chronic anovulation e.g. hyperprolactinemia, hypothyroidism, congenital adrenal hyperplasia were excluded from the study.

The study was performed on 57 women with PCOS. Written and informed consent was obtained from each patient. Patients were selected as per standard diagnostic assessments.

History

History was taken specifically for menstrual pattern (oligomenorrhoea and amenorrhoea); and features of hyperandrogenism (hirsutism and acne).

Gynaecologic ultrasonography

According to Rotterdam 12 or more follicles should be seen in an ovary on ultrasound examination. The follicles are oriented in the periphery giving the appearance of "string of pearls". Polycystic ovaries are defined as 12 or more follicles in at least 1 ovary measuring 2-9 mm volume of >10 cm^3.

Biochemical tests

Serum level of luteinizing hormone (LH) is elevated. The elevated level of LH:FSH ratio >1.5-3 is an indicator of PCOS. Estrone level, sex hormone binding globulin, and adrostenedione are also elevated while estradiol: estrone ratio is reversed. 2-hour oral glucose tolerance test (GTT) in women with risk factors (obesity, family history, and history of gestational diabetes) may indicate impaired glucose tolerance (insulin resistance) in 15–33% of women with PCOS. Frank diabetes can be seen in 65–68% of women with this condition. Insulin resistance can be observed in both normal weight and overweight people. 50–80% of people with PCOS may have insulin resistance at some level.

Procedure

A total of 57 women who had polycystic ovaries on ultrasound were selected for the study. Detailed menstrual history regarding age of menarche, menstrual cycle and period of infertility were obtained from every patient. Each patient was questioned about past and family history of diabetes mellitus and hypertension. Body weight and height were estimated to calculate body mass index. Clinical examination with special reference to hirsutism was done. Investigations like ultrasound, fasting blood glucose, and thyroid stimulating hormone levels were done. From the 57 women selected, seven women discontinued due to non-compliance. So, 50 women were taken into study. These 50 women were given metformin 500 mg once daily for one week, followed by twice daily in the second week, and then thrice daily from third week to avoid non-compliance.

Ultrasound examination was done every month to note the disappearance of cysts and evidence of ovulation was seen by follicular study from day 11 to day 21 alternately.

RESULTS

Age

Metformin was well tolerated by all patients. Among 50 patients 18 patients were between 15-25 years and 32 patients were between 26-32 years (Table 1).

So, the incidence of PCOS is more at the age of 15-25 years.

Table 1: Age wise distribution of patients with PCOS.

Age (in years)	No. of patients
15-25	18
26-35	32

Mean body mass index

The body mass index (BMI) mean±SD before treatment was 26.42±2.52 kg/m^2 and after treatment it reduced to 25.1±2.59 kg/m^2 ($p>0.05$) (Table 2).

Table 2: Effect of treatment on the BMI of patients.

BMI (kg/m^2)	Before treatment	After treatment
Mean±SD	26.42±2.52	25.1±2.59

Menstrual cycle

So, among 50 (100%) patients who had irregular periods (88%) patients showed improvement in the menstrual cycles (Table 3).

Fasting blood glucose

So, the fasting blood glucose mean±SD before treatment was 88.56±8.59 mg/dl and after treatment it reduced to 79.58±6.92 mg/dl ($p<0.001$, highly significant) (Table 4).

Table 3: Effect of metformin in menstrual irregularities.

No of patients who took metformin	Patients with improved menses	No effect on menstrual irregularities
50	44	6

Table 4: Effect of treatment on the FBS of patients.

Fasting blood glucose (mg/dl)	Before treatment	After treatment
Mean±SD	88.6±8.59	79.6±6.92

Table 5: Month wise effect of treatment on cysts of PCOS in patients.

Cyst	Before treatment	After treatment						
	(n=50)	1 month (n=50)	2 months (n=47)	3 months (n=24)	4 months (n=13)	5 months (n=9)	6 months (n=9)	Total number of patients at the end of the study
Cyst present	50	47	24	13	9	9	9	9
Cyst absent	0	3	23	11	4	0	0	41

Table 6: Month wise effect of treatment on ovulation in PCOS patients.

Ovulation	Before treatment	After treatment						
	(n=50)	1 month (n=50)	2 months (n=47)	3 months (n=25)	4 months (n=16)	5 months (n=11)	6 months (n=11)	Total number of patients at the end of the study
Ovulation absent	50	47	25	16	11	11	11	11
Ovulation present	0	3	22	9	5	0	0	39

Cysts

So, among 50 patients 41 patients (82%) patients showed disappearance of cysts. At the end of 1st month out of 50 patients' cysts disappeared in 3 patients. At the end of 2nd month out of 47 patients' cysts disappeared in 23 patients. At the end of 3rd month out of 24 patient's cysts disappeared in 11 patients. At the end of 4th month out of 13 patient's cyst disappeared in 4 patients.in patients cyst did not disappear at the end of 6 month (Table 5).

Ovulation

So, among 50 patients' ovulation was seen in 39 (78%) patients. At the end of the first month out of 50 patient's ovulation was seen in 3 patients, at the end of the second month out of 47 patient's ovulation was seen in 22 patients, at the end of the third month out of 25 patient's ovulation was seen in 9 patients, at the end of 4th month out of 16 patient's ovulation was seen in 5 patients in the 11 patients there was no ovulation at the end of 6 months (Table 6).

DISCUSSION

The results in the present study suggested that metformin has an effective role in the management of PCOS. In the study metformin improved the regularization of menstrual cycles in 88% of previously ammenorrhic women with PCOS.[14] These results were consistent with those of Glueck et al who concluded in their study that metformin resumed normal menses in 91% of previously ammenorrhic women.[15]

The cycles became ovulatory after metformin treatment in 78% women with previous anovulatory cycles. These results were consistent with that of Moghetti et al.[16] In their study they concluded that metformin showed 79% improvement in ovulation. The above results show that metformin has a promising role with regression of polycystic ovarian menstrual cycles and resumption of ovulation in the management of PCOS.

Limitations

Many patients could not be tracked in the study due to noncompliance. Reasons for noncompliance included regular weekly and monthly follow up, travel expenses, and poor understanding of the issue due to illiteracy.

CONCLUSION

Insulin resistance plays a key role in the pathogenesis of PCOS by altering the endocrine and metabolic disturbances. In this regard insulin sensitizing drugs like metformin show promising results in reversing this endocrinopathy and improvement in the metabolic

disturbances. In conclusion metformin has a beneficial role in the management of PCOS.

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