

Efficacy of Metformin Therapy in Management of Polycystic Ovary Syndrome

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ABSTRACT

Background: Earlier analysis shows that metformin is beneficial clinically in treating polycystic ovary syndrome (PCOS) by reducing hyperinsulinemia.

Aim: The goal of this study was to determine the importance of metformin in modifying amenorrhea/ oligomenorrhea and anovulation within six months in women with polycystic ovary syndrome and hyperinsulinemia. Another goal was to evaluate hyperinsulinemia and weight loss with metformin in the studied people.

Methods: This randomized controlled trial was held at the Obstetrics and Gynecology department of the Jinnah Postgraduate Medical Centre Karachi for one-year duration from July 2020 to July 2021. The study included 160 women who met the biochemical and clinical conditions for hyperinsulinemia and PCOS. Two females stopped taking the drug due to abdominal cramps, diarrhoea and nausea. Other excluding factors were inadequate adherence in one female women and use of other medications in two women. One female had anomalous levels of serum creatinine and was omitted from the analysis. So, 154 total patients were studied. 500 mg / day metformin orally was started and was held at 500 mg for six-months. FSH, serum LH, fasting insulin, fasting glucose and creatinine were measured in addition to ultrasound and body weight. After 6 months: fasting insulin levels, menstrual cycles, body weight and serum progesterone on day 21 were measured. Serum androgen levels remains high in PCOS along with Prolactin levels and the LH/FSH ratio may be greater than 2 times. So, these parameters were assessed after six months of metformin to determine the improvement in symptoms of oligomenorrhea and amenorrhea in PCOS and clinically with improvement in menstrual cycle.

Results: Subsequently 6 months of treatment with metformin, 135 out of 154 (84%) women had regular periods, 24 of which were in the ovulation range of luteal progesterone (> 30 nmol / L). The average fasting insulin concentration among patients on metformin therapy reduced from 22.5 micro-U / ml to 21.01 micro-U / ml ($p = 0.00$).

Keywords: PCOS, Metformin, irregular periods

INTRODUCTION

Polycystic ovary syndrome, first described by Leventhal and Stein in 1905, is the most common disorder of endocrine system causing irregular periods in females of childbearing age; This is the most important clinical symptom of Polycystic ovary syndrome¹⁻². The resistance of insulin in combination with hyperinsulinemia as a compensatory mechanism causes hyperandrogenism that disrupts the pituitary-ovarian axis, resulting in elevated anovulation, LH levels, infertility and amenorrhea³⁻⁴. Thus, enhancement of sensitivity of insulin-by-insulin sensitizers may clinically important in the treatment of the clinical indices of hyper-androgenemia and hyperinsulinemia. To date, numerous treatments for the clinical symptoms of PCOS have been tried⁵⁻⁶. Antiandrogens, alone or in combination with oral contraceptives, are measured the 1st line of treatment for symptoms of Polycystic ovary syndrome, but there is no consensus on their effectiveness in metabolic changes such as hyperinsulinemia. It is currently believed that insulin sensitivity is improved by substances sensitizing to insulin, e.g. Metformin has therapeutic value, either direct or indirect, in the treatment of PCOS⁷⁻⁸. Metformin significantly improves the clinical symptoms of hyperandrogenism by increasing or decreasing insulin activity at the peripheral cell level⁹. The goal of this study was to determine the importance of metformin in modifying amenorrhea/ oligomenorrhea and anovulation within six months in women with polycystic ovary syndrome and hyperinsulinemia. Another goal was to evaluate hyperinsulinemia and weight loss with metformin in the studied people.

MATERIALS AND METHODS

This randomized controlled trial was held at the Obstetrics and Gynecology department of the Jinnah Postgraduate Medical Centre Karachi for six-months duration from July 2020 to July 2021. One-hundred Sixty women who reported amenorrhea or oligomenorrhea in outpatient's department were accepted for the study and were tested for hyperinsulinemia and PCOS. Two females stopped taking the drug due to abdominal cramps, diarrhoea and nausea. Other excluding factors were inadequate adherence in one female women and use of other medications in

two women. One female had anomalous levels of serum creatinine and was omitted from the analysis. So, 154 total patients were studied. The characteristic presence of numerous peripheral cysts 6-9 mm in the ovaries on ultrasound and the FSH: LH ratio > / = 1: 3 were diagnosed as having PCOS. Hyperinsulinemia was defined as fasting insulin concentration > / = 20 micro-U / ml. The fasting blood glucose and weight in kilograms were documented. Females with decreased renal function (> 1.5 serum creatinine) were omitted from the analysis due to the jeopardy of lactic acidosis following therapy with metformin. Oral metformin was recommended with food to evade side effects related with stomach. The metformin was given 500 mg daily for the 1st week, then two times daily for the 2nd week, and lastly three times daily (1500 mg) for six-months. After six months, the menstrual cycles, fasting blood sugar and insulin levels, mild to moderate progesterone (in women on regular cycles) and weight in kg were determined to assess ovulation. Serum androgen levels remains high in PCOS along with Prolactin levels and the LH/FSH ratio may be greater than 2 times. So, these parameters will be assessed after six months of metformin to determine the improvement in symptoms of oligomenorrhea and amenorrhea in PCOS and clinically with improvement in menstrual cycle.

Data were analyzed in SPSS 21.0 using paired t-test.

RESULTS

160 females finalised the study. The age range was between 13 and 39 years old.

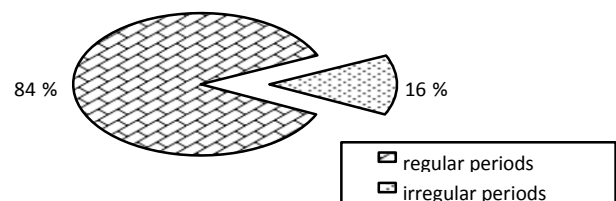


Fig 1: Regularity of Menstrual cycle after six months of therapy with metformin n=154

The age range was between 13 and 39 years old. Six months after receiving metformin, 135 women had regular menstrual cycles (Fig. 1), 24 of which were in the ovulation range of luteal progesterone (> 30 nmol / L). The average fasting insulin concentration among patients on metformin therapy reduced from 22.5 micro-U / ml to 21.01 micro-U / ml ($p = 0.00$) (Table 1).

Table 1: Statistical analysis of decrease in serum insulin levels with metformin

		Mean	95% CI for mean	Standard Deviation	Median	Average Absolute Deviation from Median	Result of paired t-test
Insulin treatment	before	22.5	24.10-25.10	0.92	22.9	0.67	T = -15.2 Degrees of freedom = 22 p=0.000
Insulin treatment	after	21.1	20.01-21.60	0.73	19.8	0.49	
Difference		-1.4	-4.09 thru-3.5	1.1	-3.1	0.76	

DISCUSSION

This analysis shows the benefit of metformin treatment in attaining the menstrual cycle within six months for the mainstream of females in this populace¹⁰⁻¹¹. The similar has been testified previously in few Western analysis¹². Antiandrogens and Oral contraceptives have been the backbone of management for PCOS, but metformin is the best option as it helps women with oligo or amenorrhea because they are ovulating and wanting to be pregnant and is safe even during pregnancy¹³⁻¹⁴. Second, metformin modifies metabolic irregularities, including hyperinsulinemia also in controls and PCOS females. We required to see if our people would respond in the similar way¹⁵. This showed a reduction in levels of serum fasting insulin after metformin treatment in our study group. Various analysis has also revealed a decrease in levels of insulin after a glucose load, which we did not do due to economic restrictions¹⁶⁻¹⁷. After six months, 84% of the females are ovulating; Additional studies have also found an advanced incidence of ovulation through given treatment than without taking treatment. Weight loss alone is probable to have many valuable effects on the endocrine, metabolic and clinical characteristics of females with Polycystic ovary syndrome¹⁸⁻¹⁹. In addition, insulin-sensitive metformin therapy has been shown to reduce leptin levels in obese females with PCOS. Although the waist / hip ratio reduced with metformin in several analysis, no significant change in body weight was observed in this studied populace, signifying that clinical and metabolic abnormalities were independently corrected. We understand that the most scientific body mass index (BMI) should be done by us; though, some other studies also showed no alteration in body weight with metformin therapy²⁰⁻²¹. The response to weight may differ in various inhabitants, and the BMI should be done over a larger sample to draw conclusions. Metformin treatment was well endured by most of our patients, which is constant with other studies²²⁻²³.

CONCLUSION

Metformin treatment in females with Polycystic ovary syndrome decreased hyperinsulinemia, primarily corrected menstrual irregularities, and resulted in a higher ovulation index independent of changes in body weight.

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The mean body weight reduced from 73.2 kg to 72 kg ($p = 0.097$), which was not statistically significant (Table 2).

Table 2: Statistical analysis of alteration in body weight with therapy of metformin

		Mean	95% CI for mean	Standard Deviation	Median	Average Absolute Deviation from Median	Result of paired t-test
Body weight treatment	before	75.2	70.01-80.02	11.8	72.6	-9.74	t = 1.70 Degrees of freedom = 22 p=0.097
Body weight treatment	after	74.1	69.32-77.34	12.2	74	9.61	
Difference		1.1	-0.69-2.62	1.78	0.06	1.38	

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