

## Efficacy of Metformin to Achieve Menstrual Regularity in PCO Patients

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### ABSTRACT

**Aim:** To assess the effectiveness of metformin to achieve menstrual regularity in patients with polycystic ovary syndrome.

**Study design:** Descriptive case series.

**Setting:** This study was conducted in outpatient department of Lady Willingdon Hospital Lahore.

**Duration:** Six months from 01-02-2012 to 31-07-2012.

**Methods:** A total of 85 patients of polycystic ovary syndrome were selected for this study. An informed consent was obtained from them for investigating in detail and using their data for research. Demographic history including name, age and address etc. were obtained from all the patients. Metformin was given in dose of 500mg three times a day. Patients were evaluated after three months for achievement of menstrual regularity.

**Results:** The mean age of the patients was 27.4±5.7 years. There were 76(89.4%) patients had oligomenorrhea and 9(10.6%) patients had amenorrhea. In the distribution of patients by efficacy of treatment i.e. regular menstrual cycle achieved after treatment, there were 68(80%) patients in which the treatment was effective and 17(20%) patients in which the treatment was not effective.

**Conclusion:** It is concluded from this study that metformin is effective in patients of polycystic ovary syndrome. It corrects menstrual irregularity in majority of the women with polycystic ovary syndrome.

**Keywords:** Polycystic ovary syndrome, metformin, efficacy, oligomenorrhea, amenorrhea.

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### INTRODUCTION

Polycystic ovary syndrome is characterized by anovulation, infertility and hyperandrogenism<sup>1</sup>. It affects 5-10% of women with childbearing age<sup>2</sup>. The most common presenting feature of polycystic ovary syndrome is fertility deprivation followed by menstrual irregularities, hirsutism and weight gain<sup>3</sup>.

The majority of women with this syndrome have some form of insulin resistance, and compensatory hyperinsulinemia also play a role in androgen excess and anovulation.<sup>2</sup> Chronic anovulation most often manifests as oligomenorrhea (fewer than nine menses per year) or amenorrhea. Chronic anovulation is associated with an increased risk of endometrial hyperplasia and carcinoma<sup>4</sup>. Hyperinsulinemia is an established risk factor for non insulin dependent diabetes mellitus, hypertension, dyslipidemia and cardiovascular disease, collectively known as metabolic syndrome<sup>5</sup>. For some women, infertility is the principal issue. When fertility is not a concern an estrogen progestin contraceptive, has been the mainstay of long term therapy. This approach is effective in ameliorating the effects of androgen excess and restoring regular menses, thereby preventing endometrial hyperplasia<sup>2</sup>.

However, given the metabolic derangements associated with the polycystic ovary syndrome, it is appropriate to plan long term therapy that addresses not only management of the consequences of androgen excess and anovulation but also the new goal of ameliorating insulin resistance and reducing the risk of type 2 diabetes and cardiovascular disease. The use of oral contraceptives aggravates insulin resistance and worsens glucose tolerance in women with the polycystic ovary syndrome.<sup>2</sup> The use of estrogen-progestin contraceptives is associated with a twofold increase in the relative risk of cardiovascular arterial events in the general female population<sup>2</sup>.

Metformin improves insulin sensitivity and retard or prevent progression to type 2 diabetes in patients with impaired glucose tolerance. The use of metformin as a protective measure against the adverse cardiovascular effect of insulin resistance, thus addressing the traditional goals of long term treatment<sup>2</sup>. In one study showing three months treatment with metformin, 83.3% women achieved regular menstrual cycle<sup>6</sup>.

The approach to the management of the polycystic ovary syndrome depends on therapeutic objectives. For some women, infertility is the principal issue. Although metformin is being used to improve fertility, but my concern is to regulate the menstrual cycle with this drug as other drugs used to regulate

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menstrual cycles further impair metabolic derangement.

## MATERIAL & METHODS

This descriptive case series study was conducted in the Outpatient Department of Lady Willington Hospital, Lahore from 01-02-2012 to 31-07-2012. Calculated sample size with 8% margin of error, 95% confidence level taking expected percentage of menstrual regularity with metformin therapy i.e. 83.3% is 85 cases. Sampling technique was non-probability purposive sampling. The study included Patients of polycystic ovary syndrome, aged 16-35yrs with irregular menstrual cycles (oligomenorrhoea/amenorrhoea). Exclusion criteria included women with history of abnormal menstrual disorder with galactorrhoea, women with abnormal thyroid function tests on laboratory measures, history of diabetes mellitus and women with renal impairment (serum creatinine level >1.4mg per deciliter). 85 patients with polycystic ovary syndrome, fulfilling inclusion criteria were included in the study. An informed consent was obtained from them for investigating in detail and using their data for research. Demographic history including name, age and address etc. were obtained from all the patients. Women with history of menstrual disorder with galactorrhoea or abnormal thyroid stimulating hormones were excluded from the study. Women who were known diabetic and history of renal impairment were also excluded.

Metformin was given in dose of 500mg three times a day. Patients were evaluated after three months for achievement of menstrual regularity. All the information was collected on a specially designed proforma. The collected information was entered into SPSS version 11 and analyzed accordingly. Mean and standard deviation was calculated for age. Frequency and percentage was used to present qualitative variables of study menstrual regular cycle achieved (Yes, No). Data was stratified for oligomenorrhoea and amenorrhoea.

## RESULTS

A total of 85 patients of polycystic ovary syndrome fulfilled the inclusion criteria were selected from outpatient department, Lady Willington Hospital Lahore.

The mean age of the patients was 27.4±5.7 years. There were 20(23.5%) patients in the age range of 16-20 years, 30(35.3%) patients in the age range of 21-25 years, 23(27%) patients in the age range of 26-30 years and 12(14.2%) patients in the age range of 31-35 years (Table 1).

In the distribution of patients by menstrual cycles before treatment, there were 76(89.4%) patients had oligomenorrhoea and 9(10.6%) patients had amenorrhoea (Table 2).

In the distribution of patients by efficacy of treatment i.e., regular menstrual cycle achieved after treatment, there were 68(80%) patients in which the treatment was effective and 17(20%) patients in which the treatment was not effective (Table 3).

In the comparison of efficacy of treatment and oligomenorrhoea, there were 64(75.3%) patients who achieved menstrual cycle after treatment out of 76 (89.4%) patients of oligomenorrhoea (Table 4).

In the comparison of efficacy of treatment and amenorrhoea, there were 4(4.7%) patients who achieved menstrual cycle after treatment out of 9 (10.6%) patients of amenorrhoea (Table 5).

Table 1 Distribution of patients by age (n=85)

Age (Years)	No.	%age
16-20	20	23.5
21-25	30	35.3
26-30	23	27.0
31-35	12	14.2

Mean±SD=27.4±5.7

Table 2: Distribution of patients by menstrual cycles before treatment (n=85)

Menstrual cycle	Yes	No
Oligomenorrhoea	76(89.4%)	9(10.6%)
Amenorrhoea	9(10.6%)	76(89.4%)
Total	85(100%)	85(100%)

Table 3: Distribution of patients by efficacy of treatment (n=85)

Efficacy	No.	%age
Yes	68	80
No	17	20

Table 4: Comparison of efficacy with oligomenorrhoea (n=85)

	Oligomenorrhoea	Efficacy
Yes	64(75.3%)	12(14.1%)
No	4(4.7%)	5(5.9%)
Total	68(80%)	17(20%)

Table 5: Comparison of efficacy with amenorrhoea (n=85)

	Oligomenorrhoea	Efficacy
Yes	4(4.7%)	5(5.9%)
No	64(75.3%)	12(14.1%)
Total	68(80%)	17(20%)

## DISCUSSION

Our study demonstrates the efficacy of metformin therapy in achieving menstrual cyclicity in the majority of women in our population within three months treatment. The same has been reported in

some western studies previously<sup>7</sup>. Oral contraceptives and anti androgens have been the mainstay of treatment of PCOS, but as these women with oligomenorrhea / amenorrhea are anovulating and want to conceive, metformin is a better option as it helps women to become pregnant and is safe even during pregnancy<sup>8,9</sup>. Secondly metformin corrects the metabolic abnormalities e.g., hyperinsulinemia as well<sup>10</sup> in both PCOS and controls.<sup>11</sup> We wanted to observe whether our population also responds in the same manner. Some studies have shown a reduction in post-glucose load insulin levels as well<sup>12</sup>, which was not performed by us due to financial constraints. Half of the women achieved ovulation at the end of three months, other studies have also resulted in higher frequency of ovulation during treatment than before treatment. The majority of women with this syndrome have some form of insulin resistance, and compensatory hyperinsulinemia also play a role in androgen excess and anovulation<sup>2</sup>. Chronic anovulation most often manifests as oligomenorrhea (fewer than nine menses per year) or amenorrhea. Chronic anovulation is associated with an increased risk of endometrial hyperplasia and carcinoma<sup>4</sup>.

Hyperinsulinemia is an established risk factor for non insulin dependent diabetes mellitus, hypertension, dyslipidemia and cardiovascular disease, collectively known as metabolic syndrome<sup>5</sup>.

For some women, infertility is the principal issue. When fertility is not a concern an estrogen progestin contraceptive, has been the mainstay of long term therapy. This approach is effective in ameliorating the effects of androgen excess and restoring regular menses, thereby preventing endometrial hyperplasia<sup>2</sup>.

However, given the metabolic derangements associated with the polycystic ovary syndrome, it is appropriate to plan long term therapy that addresses not only management of the consequences of androgen excess and anovulation but also the new goal of ameliorating insulin resistance and reducing the risk of type 2 diabetes and cardiovascular disease. The use of oral contraceptives aggravates insulin resistance and worsens glucose tolerance in women with the polycystic ovary syndrome.<sup>2</sup> The use of estrogen-progestin contraceptives is associated with a twofold increase in the relative risk of cardiovascular arterial events in the general female population<sup>2</sup>.

Metformin improves insulin sensitivity and retard or prevent progression to type 2 diabetes in patients with impaired glucose tolerance. The use of metformin as a protective measure against the adverse cardiovascular effect of insulin resistance

and insulin ovulation and menstrual cyclicity, thus addressing the traditional goals of long term treatment<sup>2</sup>.

In our study the mean age of the patients was 27.4±5.7 years. As compared with the study of Tariq et al<sup>3</sup> the mean age of the patients was 26.6 years, which is comparable with our study. In another study conducted by Meyer et al<sup>13</sup> the mean age of the patients was 31 years, which is also comparable with our study.

In our study before treatment, there were 89.4% patients had oligomenorrhea and 10.6% patients had amenorrhea. As compared with the study of Tariq et al<sup>3</sup> before treatment 76% patients had oligomenorrhea and 5% patients had amenorrhea, which is comparable with our study.

In our study 80% patients achieved regular menstrual cycle after treatment of metformin therapy. As compared with the study of Tariq et al<sup>3</sup> the efficacy of metformin in polycystic ovarian syndrome was found in 80% patients which is comparable with our study.

In another study conducted Zafar<sup>14</sup> who observed the role of metformin in correcting oligomenorrhea / amenorrhea and anovulation within six month in hyperinsulinemic women with PCOS and found that metformin therapy was effective in 86% patients, which is also comparable with our study.

In one study showing three months treatment with metformin, 83.3% women achieved regular menstrual cycle<sup>6</sup>. While in our study after three months treatment with metformin, 80% women achieved regular menstrual cycle, which is comparable with the above study.

Siddiq et al<sup>15</sup> assessed the efficacy of metformin therapy in polycystic ovarian disease induced infertility and menstrual disturbances and found that metformin therapy is effective in 73% women. Metformin therapy is effective in the treatment of oligomenorrhoea and PCO induced infertility, result being more pronounced in those cases who showed weight reduction and decrease in serum insulin levels.

On the above discussion, it is suggested that metformin therapy is effective in patients of polycystic ovary syndrome as it corrects menstrual irregularity in majority of the patients.

## CONCLUSION

It is concluded from this study, that metformin therapy is effective in patients of polycystic ovary syndrome as it corrects menstrual irregularity in majority of the patients.

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