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Original Article

Comparison of Therapeutic Effects in terms of Menstrual Irregularities between Statins and Metformin in Unmarried Patients with Polycystic Ovarian Syndrome

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ABSTRACT

Objective: To compare therapeutic effects in terms of menstrual irregularities between Statins and Metformin in unmarried patients with polycystic ovarian syndrome.

Study Design: Quasi-experimental study.

***Place and Duration of Study*:** Department of Obstetrics and Gynecology, Combined Military Hospital, Zhob Pakistan, from Sep 2021 to Feb 2022.

Methodology: A study sample of 60 unmarried women aged 18-35 years diagnosed with PCOS having menstrual irregularity was collected and randomly allocated into two treatment groups. Women in Group-A were given simvastatin, while Group-B received Metformin. The outcome variable was an improvement in menstrual irregularity, assessed after three months of treatment in terms of the spontaneous normal menstrual cycle (28-35 days).

Results: The mean age of the patients was 27.43±4.72 years, while the mean duration of the disease was 23.63±5.99 months. The mean BMI of these women was 26.78±3.47 Kg/m2, and 20 (33.3%) women were obese. The frequency of improvement in menstrual irregularity was significantly higher in women receiving Simvastatin as compared to Metformin [24 (80.0%) vs. 10 (33.3%); p-value<0.001)].

Conclusion: In the present study, simvastatin was found more efficacious in the treatment of women with polycystic ovarian syndrome than Metformin in terms of normalization of menstrual irregularities regardless of patient's age, duration of disease and BMI, which advocates the preferred use of statins in the management of future gynaecological practice.

Keywords: Menstrual irregularity, Metformin, Polycystic ovarian syndrome, Statins.

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INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a heterogeneous disorder that is defined by a combination of signs and symptoms of androgen excess (hirsutism and/or hyperandrogenaemia) and ovarian dysfunction associated with metabolic dysfunction (dyslipidemia).[1,2] This syndrome may be the most frequent endocrine and metabolic illness in women of reproductive age.[3] Metformin and, more recently, statins have been proven to help with the endocrine and metabolic symptoms of PCOS.[4] Statins are lipid-lowering drugs that can help with dyslipidemia associated with PCOS and other metabolic and endocrine issues, such as improving metabolic symptoms and menstrual irregularity.[5] Statins are beneficial in lowering serum testosterone levels in women with PCOS, which improves symptoms.[6]

In some studies, Metformin and statins have been shown to lower inflammatory markers in PCOS patients, but the data is conflicting.[7] In addition to improving lipid profiles, statins reduce several other cardiovascular risk factors in women with PCOS.[8]

The rationale of our study is to compare therapeutic Effects in Terms of Menstrual Irregularities between Statins and Metformin in Unmarried Patients with Polycystic Ovarian Syndrome. There are currently no formalised recommendations or guidelines for statin therapy in PCOS women lacking dyslipidemia. However, the American Congress of Obstetricians and Gynecologists suggests a statin for treating atherosclerotic alterations.[1] Statins are well-known for their ability to lower LDL cholesterol. Statins also reduce menstrual irregularity and clinical symptoms of androgen excess.[9,10]

In Pakistan, and especially in our setups, we have never taken statins as a treatment option for PCOS. Considering these beneficial effects (anti-androgenic properties), our study aims to compare statins with the

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most commonly prescribed Metformin, so better management could be adopted in future.

METHODOLOGY

The quasi experimental study was conducted at the Obstetrics & Gynaecology Department, Combined Military Hospital, Zhob Pakistan, from September 2021 to February 2022 after permission of the Hospital Ethical Committee obtained (certificate number 350/ Estb/21). WHO sample size calculator was used to calculate a sample size, keeping expected frequency of improvement in menstrual irregularity as 71% and 33%, respectively, with statins and Metformin.[11]

Inclusion Criteria: All unmarried females aged 18-35 years, (diagnosed cases) with PCOS had a duration of disease >12 months, were included in the study.

Exclusion Criteria: History of any endocrine disorders or Pelvic (ovarian) tumours, pregnant females, patients already taking statins or Metformin were excluded.

Non-probability consecutive sampling was used to collect the sample. Written informed consent was obtained from all participants. Statins of 20mg once the daily dosage was used in the study. Metformin: 500mg thrice daily dosage was used in the study. Patients were labelled as having PCOS if they had the following factors:-1) Oligo-ovulation (clinically diagnosed by menstrual irregularity <28 or >35), signs of androgen excess (clinical: hirsutism, acne, weight gain etc., 2) biochemical raised testosterone levels), 3) Polycystic ovarian morphology on ultrasonography (multiple cysts in one or both ovaries).[12]

Patients suspected of PCOS were screened by ultrasonography, clinical examination and history taking. Confirmed cases were explained in the study, and informed consent was taken. Relevant information regarding bio-data, phone numbers, addresses and contraindications was taken. Patients were divided into two groups. Patients of Group-A were given simvastatin, while Group-B received Metformin. Randomization of the patient was done by the lottery method. All the patients were provided with a questionnaire and were asked to fill it out. The outcome was studied after three months. A period chart was provided to the patients (calendar) so that they had ease in remembering the dates of a cycle and brought the ticked calendar so we had written proof to see the effect of the drug. The effect of both drugs was studied after three months.

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics. The *p*-value of ≤0.05 was set as the cut-off value for significance.

RESULTS

A total of 60 patients were included in the study, and the outcome in terms of frequency in improving menstrual irregularity was assessed. The patients' ages ranged from 18-35 years old, with a mean of 27.43± 4.72, while the disease lasted anywhere from 12-36 months, with a mean of 23.63±5.99 months. These women's BMIs varied from 21.3-34.5 kg/m^2, with a mean of 26.7-83.47 kg/m^2, and 20(33.3%) of these women were obese. As demonstrated in Table-I, both study groups were equivalent in terms of mean age (*p*-value=0.957), mean disease duration (*p*-value=0.966), mean BMI (*p*-value=0.852), and the distribution of different subgroups depending on the patient age (*p*-value =0.791), duration of symptoms (*p*-value=0.795), and BMI (*p*-value=0.861). Improvement in menstrual irregularity occurred in 34(56.7%) women with PCOS.

Table-I:Baseline Characteristics of Study Groups (n=60)

Characteristics	Group-A n=30	Group-B n=30	*p*-value
Age(years)			
18-26 years	19(63.3%)	18(60.0%)	0.791
27-35 years	11(36.7%)	12(40.0%)	
Duration of Disease(months)			
12-24 months	14(46.7%)	13(43.3%)	0.795
25-36 months	16(53.3%)	17(56.7%)	
BMI(Kg/m^2)			
20-25 Kg/m^2	9(30.0%)	10(33.3%)	0.861
25-30 Kg/m^2	10(33.3%)	11(36.7%)	
30-35 Kg/m^2	11(36.7%)	9(30.0%)	

As demonstrated in Table-II, the frequency of improvement in monthly irregularity was substantially higher in women getting simvastatin compared to Metformin (80% vs. 33.3%; *p*-value 0.001).

Table-II: Comparison of Improvement in Menstrual Irregularity in Women with PCOS in Study Groups (n=60)

Improvement	Study Groups		*p*-value
	Group-A (n=30)	Group-B (n=30)	
Yes	24	10	<0.001
	(80.0%)	(33.3%)	
No	6	20	
	(20.0%)	(66.7%)	

A similar significant difference was noted between the groups across various subgroups of patients based on age, BMI and duration of disease as shown in Table-III.

Table-III: Comparison of Improvement In Menstrual Irregularity associated with different variables in Study Groups (n=60)

Subgroups	Improvement in Menstrual Irregularity		*p*-value
	Group-A (n=30)	Group-B (n=30)	
Age (years)			
18-26	15/19 (78.9%)	6/18 (33.3%)	0.005
27-35	9/11 (81.8%)	4/12 (33.3%)	0.019
Duration of Disease (month)			
12-24	11/14 (78.6%)	4/13 (30.8%)	0.013
25-36	13/16 (81.3%)	6/17 (35.3%)	0.008
BMI (kg/m²)			
20-25	7/9 (77.8%)	3/10 (30.0%)	0.037
25-30	8/10 (80.0%)	4/11 (36.4%)	0.044
30-35	9/11 (81.8%)	3/9 (33.3%)	0.028

DISCUSSION

This study aimed to examine the prevalence of recovery in menstrual irregularity in females with PCOS who took simvastatin versus Metformin. Metformin has been a drug of choice in managing such women due to its effect on insulin resistance and obesity.[12] A recent study claimed that statins were superior to this conventional practice of Metformin in such women in terms of improved normalization of menstrual irregularity.[13] However, the known information could have been more extensive, and no locally published material necessitated the current investigation.

The average age of the patients in this study was 27.4±4.7 years. Artani *et al*. and Wahab *et al*. found a similar mean age of 27.2±4.8 years and 27±5.2 years among women with PCOS at Jinnah Postgraduate Medical Centre in Karachi and Lady Reading Hospital in Peshawar, respectively.[13,14] While Akram *et al*. found a comparable mean age of 26.7±4.8 years among such women who presented at Mayo Hospital in Lahore,[15] Usmani *et al*. found it to be 28.2 years at Karsaz Hospital in Karachi.[16] Chaudhari *et al*. and Kumar *et al*. made similar observations, reporting an average age of 27.7±7.6 years and 28.6±6.3 years, respectively, among Indian women.[17,18]

We discovered that these women had a mean BMI of 26.78±3.47 Kg/m² and that 20(33.3%) were obese. Akram *et al.* (26.2±4.5 Kg/m²),[15] and Qazi *et al.* (27.6± 5.7 Kg/m²) showed similar mean BMI among women with PCOS in the local population,[19] and Gupta *et al.* (26.5±5.1 Kg/m²) in India.[20] Raja *et al*. found a comparable prevalence of obesity in Indian women, with 32%.[21]

Simvastatin was found to be more effective than Metformin in the treatment of women with polycystic ovarian syndrome in terms of normalising menstrual irregularities, regardless of the patient's age, duration of disease, or BMI, implying that statins should be used in the management of such women in future gynaecological practise.

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LIMITATIONS OF STUDY

We did not evaluate other outcome measures, including endocrinological and biochemical parameters, as well as clinical aspects like hirsutism, which could have further emphasized the function of statins in the care of women with PCOS. Furthermore, we did not investigate the effect of a combination of statin and metformin medication in this trial, which could have aided in the effective management of this kind of patient. Future research should include a study like this.

CONCLUSION

In this study, simvastatin was found to be more effective than Metformin in the treatment of women with polycystic ovarian syndrome in terms of normalising monthly irregularities, regardless of the patient's age, length of disease, or BMI, suggesting that statins should be used in the management of such women in the future.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

SN & NM: Data acquisition, data analysis, drafting the manuscript, approval of the final version to be published.

AW & SN: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

SA & SAB: Critical review, concept, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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