



CODEN [USA]: IAJ PBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.3525932>Available online at: <http://www.iajps.com>

Research Article

**SAFETY AND EFFECTIVENESS OF METFORMIN IN OBESE
FEMALES SUFFERING FROM POLYCYSTIC OVARY
SYNDROME**¹Dr Irum Saeed, ²Dr Muhammad Nauman Bashir, ³Dr Fouzia Shaheen¹Allied / DHQ Hospital Faisalabad.**Article Received:** September 2019 **Accepted:** October 2019 **Published:** November 2019**Abstract:**

Objective: This research work aimed to assess the safety & effectiveness of the metformin in obese females suffering from POS (Polycystic Ovary Syndrome).

Methodology: We evaluated 44 obese females suffering from Polycystic Ovary Syndrome in this open label research work. We prescribed metformin five hundred milligram 3 times in a day for complete 6 months. Assessment of the main outcomes as the level of the fasting insulin, fasting glucose level of plasma, sensitivity of insulin, weight, body mass index, ratio of waist to hip and features of ultrasonography of obese females. The next outcomes were BP, menses cycles & hirsutism. Then we assessed the intervention safety in accordance with the self-reported side effects & performing renal as well as hepatic profiles. We evaluated every patient on monthly basis.

Results: Total 90.90% (n: 40) patients completed this research work. At the completion of 6 months, we found an important impact of the medicine on all the important features. Weight reduced from 85.70 ± 1.03 to 84.380 ± 1.020 , body mass index from 33.20 ± 0.320 to 32.80 ± 0.330 & ratio of waist to hip from 0.850 ± 0.003 to 0.830 ± 0.002 . Features of ultrasonography, BP also displayed important improvement. Menses cycles, hirsutism & metabolic features as level of serum insulin, glucose & HOMA index were also present with improvement. All the patients tolerated the medicine in a well manner. We observed no change in the urea of blood, level of ALT and levels of serum creatinine.

Conclusion: Metformin is very secure & effectual medicine for the therapy of the obese females suffering from polycystic ovary syndrome.

Keywords: Polycystic Ovary Syndrome, Creatinine, Ultrasonography, Hirsutism, Metabolic.

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Please cite this article in press Irum Saeed et al., Safety And Effectiveness Of Metformin In Obese Females Suffering From Polycystic Ovary Syndrome, Indo Am. J. P. Sci, 2019; 06(11).

INTRODUCTION:

Polycystic Ovary Syndrome is very common complication influencing 5.0% to 10.0% females in their age of fertility. Approximately 10.0% to 60.0% females with Polycystic Ovary Syndrome are present as obese. The high ratio of waist to hip is very frequent among females suffering from Polycystic Ovary Syndrome. Overall incidence of 6.0% to 8.0% is in population of American, but this occurrence rate can be high as 70.0% to 80.0% in females with oligomenorrhea & 60.0%-70.0% infertility of within-ovulatory. In one research work conducted in Pakistan, the rate of occurrence of the Polycystic Ovary Syndrome was 17.60% with great obesity rate (68.50%) & hyperinsulinemia (59.0%). Only fourteen percent females were present with normal body mass index whereas 29.70% females were present with BMI of up to 30.0 & 28.80% females were present with BMI of 30 to 35. The females with POS appeared with the abnormal tolerance to the glucose, DM and Met-S.

The long duration between the cycles of menses is the cause of high degree of resistance to insulin. Metformin activates the transporters of the glucose for the facilitation of the passage of glucose into the cells of muscle, thereby reducing the peripheral resistance to insulin & decreasing the levels of glucose in serum but no impact on the release of insulin and it does not the reason behind hypoglycemia.

METHODOLOGY:

This research work carried out in Pharmacology Department of the Allied / DHQ Hospital Faisalabad. A sum of total 44 obese patients suffering from Polycystic Ovary Syndrome were the participants of this research work. We took the consent from these patients. There were six overweight and thirty-eight obese patients in this research work. Females with eighteen to forty-two year of age with infertility, amenorrhea, obesity, hirsutism and features of ultrasonography of Polycystic Ovary Syndrome in accordance with the criteria of the Rotterdam were the part of this research work. Patients suffering from other serious complications were not the part of this

research work. Patients who did not follow the guidelines of the study were excluded from this current research work. This research work conducted from March to June of the year of 2019.

All the patients obtained five hundred milligrams three time in a day and they all followed up for complete 6 months. We also gave the advice to the patients to exercise & balanced diet. We followed up the patients on monthly basis. We recorded all the parameters at baseline and on monthly basis in addition with the side effects of the medicine. We defined the overweight with BMI of greater than 25.0 kg/m² & obesity as the BMI greater than 30.0 kg/m² in accordance with the criteria defined by WHO. BMI calculation carried out according to standard formula. We measure the ratio of waist to hip for all patients. Menstrual cycle contained oligo-menorrhea or amenorrhea lower than 2 cycles in one year. The evaluation of the hirsutism carried out with the utilization of the scores of Modified Ferriman Gallwey. We also assessed all the parameters related to insulin tolerance, glucose level & sensitivity of the insulin.

SPSS V. 11.5 was in use for the statistical analysis of the collected information. The presentation of the categorical data carried out in numbers. We also calculated the average & SDs for the quantitative information as weight, height, age, body mass index & ratio of waist to hip. The comparison of the different variables carried out with the utilization of the Chi-square test from first day to day 180. P value of less than .050 was the significant one.

RESULTS:

We enrolled the 44 overweight & obese patients in this research work. We excluded the patients who could not come for the follow up. The average age of the subjects was 24.40 ± 0.260 . All the patients tolerated the medicine very well. Total 12.50% (n: 5) patients suffered from nausea, 10.0% (n: 4) patients developed transient vomiting & 5.0% (n: 2) patients developed diarrhea but the symptoms improved with the passage of time (Table-1).

Table-I: Adverse Effects Observed After Metformin Therapy In Overweight And Obese Women With PCOS.

Days	Overweight & Obese Women with PCOS (n=44)					
	Nausea		Vomiting		Diarrhea	
	No	%	No	%	No	%
Day – 0	-	-	-	-	-	-
Day – 30	5.0	12.50	4.0	10.00	2.0	5.00
Day – 60	3.0	7.50	2.0	5.00	1.0	2.50
Day – 90	1.0	2.50	1.0	2.50	2.0	5.00
Day - 120	-	-	-	-	-	-
Day - 150	-	-	-	-	-	-
Day - 180	-	-	-	-	-	-

Most of the patients appeared with the amenorrhea (92.50%), followed by the infertility (90.0%). The average weight of the patients was 85.710 ± 1.04 kilogram & average height was 160.0 ± 0.360 centimeter & average body mass index was 33.20 ± 0.32 at the baseline & weight reduced to 84.38 ± 1.020 and average body mass index also reduced to 32.80 ± 0.330 . The average blood sugar in serum reduced from

103.780 ± 0.510 to 92.2 ± 0.4 & average level of insulin reduced to $23.17 \pm .38$ to $10.12 \pm .14$. We also saw the reduction in the HOMA index from 5.890 ± 0.120 to $2.280 \pm .04$.

Table-2 describes all the parameters with elaboration with the findings of ultrasonography for the whole course of treatment.

Table-II: Changes In Clinical Parameters After Metformin Therapy Obese Women With PCOS.

Clinical Parameters		Overweight & Obese Women with PCOS (n=44)	P value
		Mean \pm SD	
Weight (kg)	Day-0	85.710 ± 1.040	<0.0100
	Day-120	85.280 ± 1.020	
	Day-150	85.050 ± 1.030	
	Day-180	84.380 ± 1.020	
Waist Hip Ratio	Day-0	0.850 ± 0.003	<0.0100
	Day-120	0.840 ± 0.003	
	Day-150	0.840 ± 0.002	
	Day-180	0.830 ± 0.002	
BMI(kg/m ²)	Day 0	33.200 ± 0.320	<0.0500
	Day 180	32.800 ± 0.330	
Ultrasound - No. of follicles seen	Day-0	11.730 ± 0.630	<0.0100
	Day-180	2.880 ± 0.750	
Systolic Blood Pressure(mm Hg)	Day 0	130.500 ± 1.180	
	Day 180	121.500 ± 0.370	
Diastolic blood pressure(mm Hg)	Day 0	83.000 ± 0.750	<0.0100
	Day 180	80.000 ± 0.300	
Fasting Blood Sugar(mg/dl)	Day-0	103.780 ± 0.510	<0.0100
	Day-180	92.200 ± 0.400	
Fasting Serum Insulin level (mU/ml)	Day-0	23.180 ± 0.380	<0.0100
	Day-180	10.130 ± 0.140	
	Day-0	5.890 ± 0.120	<0.01
	Day-180	2.280 ± 0.040	

There was an improvement in the irregularity of the menstrual process which was available in 92.50% (n:

37) females, observed in 10% (n: 4) at the completion of the therapy as presented in Figure-1. The average

hirsutism was present 87.50% (n: 35) patients at baseline and 27.50% (n: 11) females at the end. The

average FGS was 13.30 ± 0.280 before treatment & 9.50 ± 0.15 after treatment as presented in Figure-2.

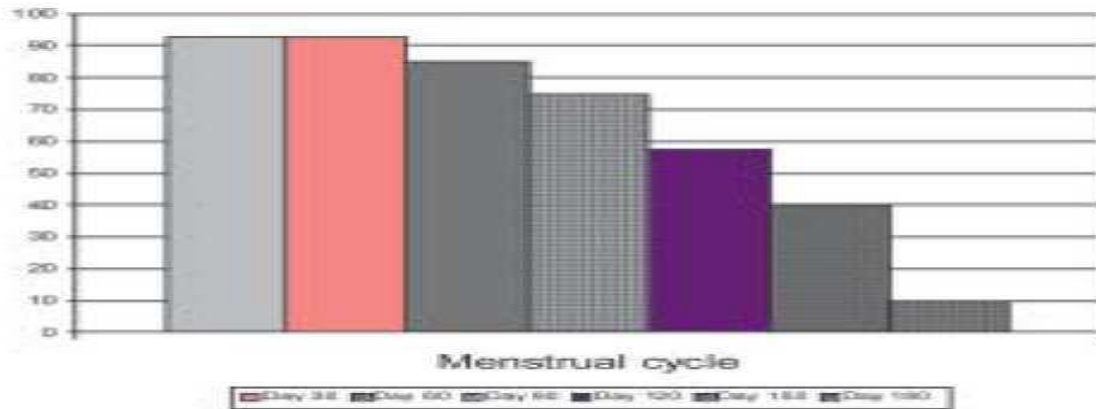


Figure 1

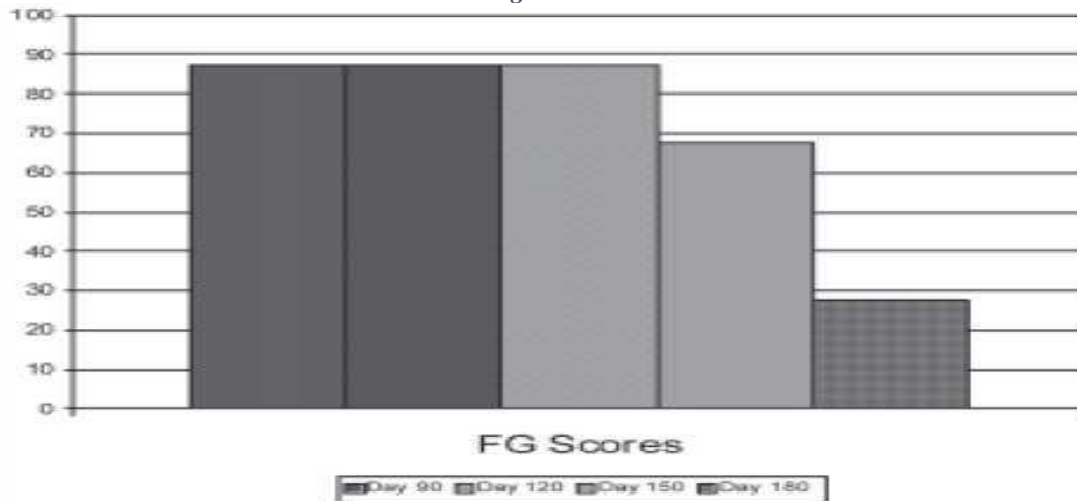


Figure 2

DISCUSSION:

POC is one of the important reason behind infertility of the females. A significant proportion of the females with Polycystic Ovary Syndrome are obese. The resistance to insulin is one of the main feature of the Polycystic Ovary Syndrome. High levels of insulin exert the anabolic impacts and modify the distribution of the fat. Metformin supports in the normalization of the insulin of plasma causing in decreased appetite. This recent research work approves the positive impact of metformin on the periods of menses and displays that the management of the medicine to females with obesity for the improvement hyper-androgenic signs like hirsutism. Metformin normalizes the level of insulin as displayed in this research work and causes in an important decrease in the body mass index. There is an important loss of weight between three & six months after the treatment of metformin. This current research work displayed that metformin lowers the weight as well as maintain

it. A research work showed that the treatment of the obese females suffering from Polycystic Ovary Syndrome with metformin leads to an important decrease in the body mass index in comparison with the treatment by placebo.

Aruna stated that 6months treatment of the metformin displayed important improvement in the body mass index, waist to hip ratio & menstrual anomaly and features of ultrasonography but there was no change in the insulin level of the serum. Santana stated that spontaneous menstruation was present in 81.0% patients out of which 67.0% patients were present with obesity. Obesity obviously increases the symptoms of the POS. In a research work of 6 months, metformin decreased weight, index of HOMA & FBG in the females with obesity with POS, well comparable with this research work. There is propensity among females with obesity to timely evidence of atherosclerosis. Metformin treatment was effectual in the decrease of

the resistance to insulin and hyper androgens in the females suffering from Polycystic Ovary Syndrome.

CONCLUSION:

The medicine of metformin is very secure & effectual for the therapy of the obese females suffering from the complication of Polycystic Ovary Syndrome. there are very minor side impacts which have very limited impacts on the purpose of the medicine. There was an important improvement in all the parameters.

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