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Role metformin versus metformin in addition with lifestyle modifications in polycystic ovarian syndrome

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Abstract---Metformin alone is beneficial in management of patients of PCOS but the effect of combined therapy i.e. metformin along with lifestyle modification is clearly superior to the results of therapy alone. Hence, it can be concluded that a combination of lifestyle modifications with metformin therapy would be an appropriate therapy for managing PCOS patients.

Keywords---metformin, lifestyle modifications, polycystic ovarian syndrome.

Introduction

Polycystic ovary disease is the commonest endocrine disorders affecting women in reproductive age.[1] PCOS is a multifactorial disorder and associated with biochemical as well as metabolic disturbances. It is characterized by features of hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphological features.[2] The presentation includes some or all of the following manifestations i.e. menstrual irregularities (in the form of oligomenorrhea or even amenorrhea), infertility, acne, hirsutism, male pattern of hair growth, hair loss, weight gain and obesity, sometimes also emotional disturbances.

Worldwide prevalence of PCOS is 6%- 20% in females of reproductive age group.[3,4] Although, the exact prevalence of PCOS in India is not known, but its prevalence using Rotterdam criteria has been reported to range from 6% to 22.5%

in South India and Maharashtra.[5-7] With the above background, the present study was thus conducted at a tertiary care centre to find out the role of lifestyle modifications in patients of PCOS. We have taken into account, clinical examination, biochemical tests and USG to study the effectiveness during the study period.

Materials and Methods

The present study was conducted as a prospective observational study. Duration of study was 18 months (2019-2020). All the females diagnosed as a case of PCOS using Rotterdam's criteria (2003)[8] were included in the study. According to this criteria, presence of any two of the following was considered as PCOS.

1. Oligo or anovulation
2. Clinical and/or biochemical signs of hyperandrogenism
3. Polycystic ovaries (with the exclusion of related disorders) detected on ultrasound i.e. presence of 12 or more follicles in each ovary (with one ovary sufficient for diagnosis), measuring 2-9 mm in diameter or increase ovarian volume >10 ml.

Sample size was calculated according to a study by Ganie MA et al (2019),[9] prevalence of PCOS was 4%. Based on this study, sample size was calculated to be 100. All the females with PCOS fulfilling the inclusion criteria were enrolled. All the females were randomly allocated into 2 groups comprising of 50 subjects each using computer generated random number table.

- Group A – females of this group received only metformin therapy.
- Group B– females were managed using both lifestyle modifications as well as metformin therapy.

Patients were subjected to the following interventions:

1. Lifestyle modification:
 - a. Dietary intervention
 - b. Exercise
2. Metformin therapy:

Follow up

Females of all the groups were followed up at 1 month interval upto 6 months.

Statistical analysis

Data was analyzed using IBM SPSS software version 20. Categorical data was expressed as frequency and proportions whereas numerical variables were expressed as mean and standard deviation. P value less than 0.05 was considered statistically significant.

Results

Majority of patients belonged to 21-25 years of age. The present study observed no statistically significant difference in age composition of patients between three groups ($p > 0.05$). USG was done at baseline and 6 months in present study. At baseline, USG showed findings suggestive of PCOD in 28 and 33 cases of group A

and group B respectively. The observed difference was statistically insignificant at baseline ($p>0.05$). However, at 6 months, USG revealed bulky ovaries in 3 cases of group A whereas 5 cases in group B had bulky ovaries and PCOD each. Peripheral follicles were observed in 2 and 4 cases of group A and group B respectively. The observed difference in USG findings between three groups at final follow up was statistically insignificant ($p>0.05$).

In present study, mean FSH level at baseline in patients of group A and group B were 6.72 ± 1.71 , 6.57 ± 1.1 respectively which showed no significant improvement during various follow up within as well as between the group ($p>0.05$). Mean LH level at baseline in patients of group A was 6.79 ± 1.09 , which changed to 6.52 ± 1.66 and 7.01 ± 1.88 at 3 months and 6 months. Similarly mean LH levels reduced from 6.52 ± 1.1 at baseline to 6.3 ± 1.5 at 6 months in group B. Though mean LH levels reduced in each group over the period of 6 months as compared to baseline, but the difference was statistically insignificant ($p>0.05$).

In present study, we observed no significant difference in mean LH levels between three groups at baseline ($p>0.05$). However, at each follow up, mean LH level decreased in each groups but the observed difference in mean LH levels at 3 months and 6 months between the groups was statistically insignificant ($p>0.05$). Mean testosterone level at baseline in patients of group A was 57.2 ± 21.01 , which reduced to 56.52 ± 12.66 and 51.01 ± 41.88 at 3 months and 6 months. Similarly mean testosterone level reduced from 57.4 ± 21.9 at baseline to 52.3 ± 43.5 at 6 months in group B. Though mean testosterone level reduced in each group over the period of 6 months as compared to baseline, but the difference was statistically insignificant ($p>0.05$). We observed no statistically significant difference in mean testosterone levels between patients of different groups at baseline, 3 months as well as at 6 months ($p>0.05$).

Table 1- Distribution according to age

Age	Group A	Group B
<20	6	8
20 to 35	30	27
>25	14	15
Total	50	50

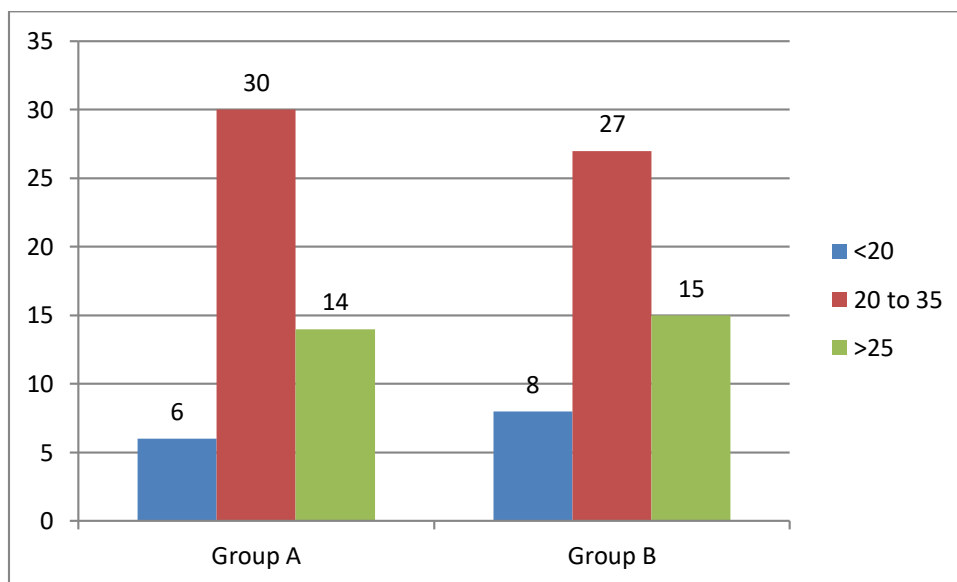


Table 2- Comparison of USG at each follow up between groups

USG	Group A	Group B
Baseline		
PCOD	28	33
WNL	19	16
6 months		
Bulky ovary	3	5
PCOD	0	5
Peripheral follicles	2	4
WNL	45	36

Table 3- Comparison of FSH levels at each follow up

	Group A	Group B
Baseline	6.72±1.71	6.57±1.1
3 months	6.84±1.64	6.26±1.4
6 months	6.81±1.88	6.3±1.5

Table 4- Comparison of LH levels at each follow up

	Group A	Group B
Baseline	6.79±1.09	6.52±1.1
3 months	6.52±1.66	7.12±1.4
6 months	7.01±1.88	6.3±1.5

Table 5- Comparison of testosterone levels at each follow up

	Group A	Group B
Baseline	57.2±21.01	57.4±21.9
3 months	56.52±12.66	53.12±14.4
6 months	51.01±41.88	52.3±43.5

Discussions

Polycystic ovary disease presents with varied clinical features such as menstrual irregularities (in the form of oligomenorrhea or even amenorrhea), infertility, acne, hirsutism, male pattern of hair growth, hair loss, weight gain and obesity, sometimes emotional disturbances. Though, the etiology of PCOS is poorly understood, it is thought to be multifactorial. Overall, the prevalence as well as severity of PCOS has been reported to be high in obese individuals.[10]

Though weight loss through lifestyle modification may help in decreasing androgen levels and is first line of management of such patients but its efficacy is limited. The present study entitled “Role metformin versus metformin in addition with lifestyle modifications in polycystic ovarian syndrome” was conducted with the aim to study and compare the effectiveness of lifestyle modifications, metformin therapy and combination of both on a total of 100 patients with PCOS. PCOS is commonly a disorder of women of reproductive age group. However, aging is significantly associated with increased risk of metabolic disturbances and insulin resistance.[11] In present study, majority of them belonged to 21-25 years of age. Similarity was found in a study by Fux Otta C et al (2010)[12]. In a meta-analysis conducted by Haqq L et al (2014)[13] the mean age of patients with PCOS ranged between 21 to 32 years.

In PCOS, compensatory hyperinsulinemia along with insulin resistance attribute to increased secretion of ovarian androgen. All these factors lead to increased testosterone levels.[14,15] In present study, though mean testosterone and LH level improved in each group over the period of 6 months as compared to baseline, but the difference was statistically insignificant ($p>0.05$). Also, we documented no significant difference in reduction in these hormones between three groups at each follow up ($p>0.05$). Similarly, we documented no significant difference between the groups at various follow ups within as well as between the group ($p>0.05$).

Guan Y et al (2020) observed significant improvement in metabolic indicators, including testosterone, follicle-stimulating hormone, luteinizing hormone following metformin. But they documented no significant improvement in sex hormone-binding globulin and androstenedione levels.[16] Haqq L et al (2014) in their review documented significant improvements in follicle-stimulating hormone (FSH) levels, total testosterone levels following lifestyle intervention.[13] Fux Otta C et al (2010) observed significant reduction in testosterone levels following metformin therapy as compared to lifestyle modification. The findings of present study were contrasting to findings of reference study in context of individual hormones. We observed no significant change in these hormonal levels between

the groups. This could be due to short term follow up of the study participants. Long term follow up might have resulted in actual finding.

USG was done in all the cases at baseline and at 6 month follow up. Though the PCOD changes reduced at final follow up as compared to baseline in all the groups, bulky ovaries were still present in few cases. We observed no significant difference in USG findings between three groups at baseline as well as at final follow up ($p>0.05$). Similar USG findings were noted by Ladson G et al (2011) between metformin and placebo group in patients with PCOS.[17]

Conclusion

Metformin alone is beneficial in management of patients of PCOS but the effect of combined therapy i.e. metformin along with lifestyle modification is clearly superior to the results of therapy alone. Hence, it can be concluded that a combination of lifestyle modifications with metformin therapy would be an appropriate therapy for managing PCOS patients.

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