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Original Article

Myoinositol plus D-chiroinositol combination versus metformin on hirsutism in patients with polycystic ovarian syndrome

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ABSTRACT

Polycystic ovary syndrome is most commonly associated with hirsutism. Weight loss or pharmacologic interventions that lower insulin levels reduce androgen levels and improve menstrual cycle patterns in many of these women hence the study was planned specifically to evaluate the efficacy of metformin versus myoinositol plus d-chiroinositol combination therapy in hirsute PCOS patients. Newly diagnosed PCOS patients from the department of Obstetrics and Gynaecology, GMC Amritsar, were enrolled and randomly divided into 2 groups of 25 each. Group 1 were given metformin 500 mg twice daily and group 2 were given myoinositol plus d-chiroinositol combination therapy 1000 mg twice daily for 9 months. Follow up was done at 3, 6, 9 months. At each visit, serum testosterone levels and Modified Ferriman-Gallwey score were evaluated. Informed consent was taken from all the patients. The percentage change from baseline in serum free testosterone levels (22.46±6.47) and mean Modified Ferriman Gallwey score (33.85±3.92) showed statistically significant decrease in group 2 (p value<0.05). It was observed that both treatments improved hirsutism but the results were statistically significant in myoinositol and d-chiroinositol group.

***Keywords*:** PCOS, Metformin, Myoinositol and D-chiroinositol, Modified Ferriman Gallwey Score

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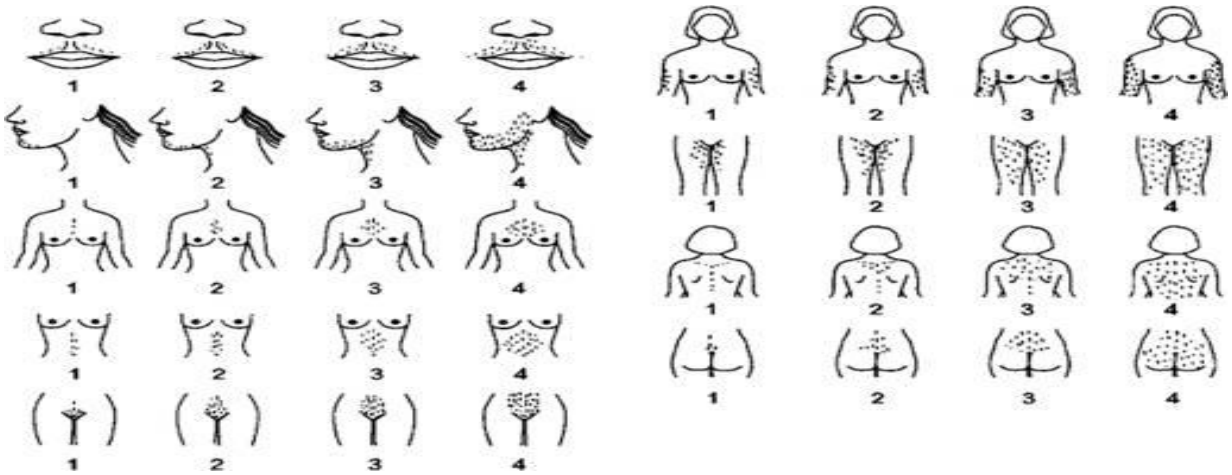
INTRODUCTION

Polycystic Ovarian Syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age characterized by hyperandrogenism and hyperinsulinemia. PCOS is the most common cause of hirsutism responsible for around 72 to 82 percent of all cases. [1] Hirsutism is defined as excessive terminal hair growth in androgen-dependent areas of the body in women, which grow in a typical male distribution pattern. Hirsutism was assessed using the Modified Ferriman Gallwey score. It is the most common visual method of scoring the hair growth in nine androgen-dependent areas in women is based on a modification of the method originally described by Ferriman and Gallwey in 1961. [2] This scoring system evaluates nine body parts (upper lip, chin, chest, upper back, lower back, upper abdomen, lower abdomen, arm, and thigh), with scores ranging from zero (no excessive terminal hair growth visible) to four (extensive hair growth visible) for each body part. A score of ≥ 8 indicates hirsutism.



Modified Ferriman Gallwey scoring system [3]

Metformin improves ovulation induction and increases insulin sensitivity in women with PCOS.[4] Glucose transport and utilization take place under the regulation of myoinositol whereas glycogen synthesis is mainly controlled through d-chiroinositol.[5] In the ovary, myoinositol regulates glucose uptake and follicle-stimulating hormone signaling while d-chiroinositol modulates insulin-induced androgen synthesis.[6] This study was aimed to observe the effect of metformin versus myoinositol plus d-chiroinositol combination therapy on hirsutism in Cowwomen.

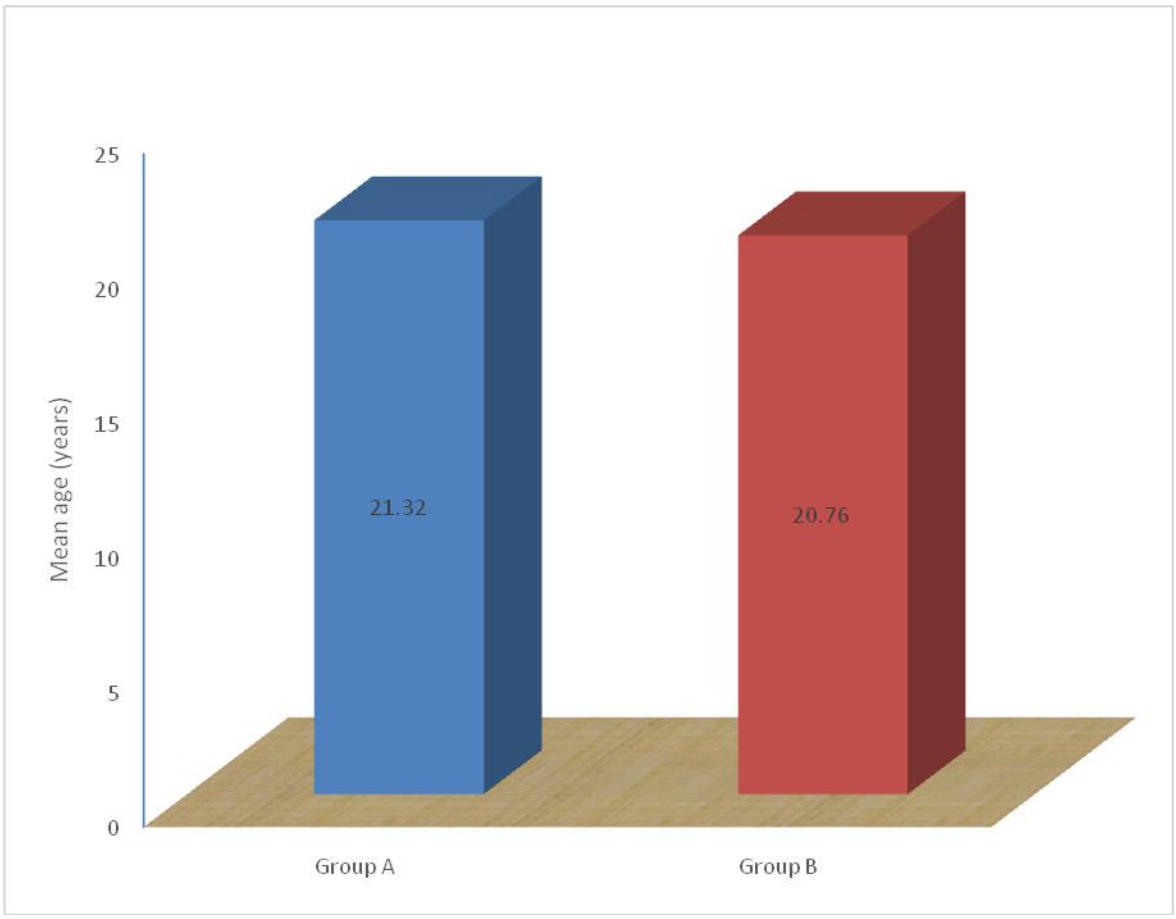
METHODS

Newly diagnosed PCOS patients from the department of Obstetrics and Gynaecology, GMC Amritsar, were enrolled and randomly divided into 2 groups of 25 each. Group 1 were given metformin 500 mg twice daily and group 2 were given myoinositol plus d-chiroinositol combination therapy 1000 mg twice daily for 9 months. Follow up was done at 3, 6, 9 months. At each visit, serum testosterone levels and Modified Ferriman-Gallwey score were evaluated. Informed consent was taken from all the patients. The diagnosis of the syndrome was made according to the Rotterdam's criteria in which at least two out of three criteria (hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology) are needed to diagnose the disorder. [7] Patients with history of hypertension & Diabetes Mellitus, women who received previous treatment with other drugs within last 6 months and pregnant females were excluded from the study.

Statistical Analysis: Analysis was based on data obtained from patients who have completed nine months of study phase. Data generated from the study was tabulated with respect to all parameters at specific intervals. The results were expressed as mean ± SD of each variable. Comparison between the two groups was done by unpaired T-test. All the statistical analysis was done using SPSS software. Significance was expressed as p value of <0.05 for each parameter.

RESULTS AND DISCUSSION

The present study found that the mean free testosterone at the start of the study was 5.17±1.69 and 3.46±1.39 which decreased to 4.68±1.57 and 2.73±1.23 at 9 months in group 1 and 2 respectively with percentage change from baseline as 9.31±11.99 and 22.46±6.47. Statistically significant decrease in group 2 (p value< 0.05) was observed which was consistent with the study conducted by Troisi et al., Ozay et al. and Regidor et al.[8,9,10] Tiwari. N et al. also observed similar trends in testosterone levels at 6 months with metformin. [11]



Graph 1: Age distribution in Group 1 & Group 2

Graph 1. Shows comparison of age in both the groups.

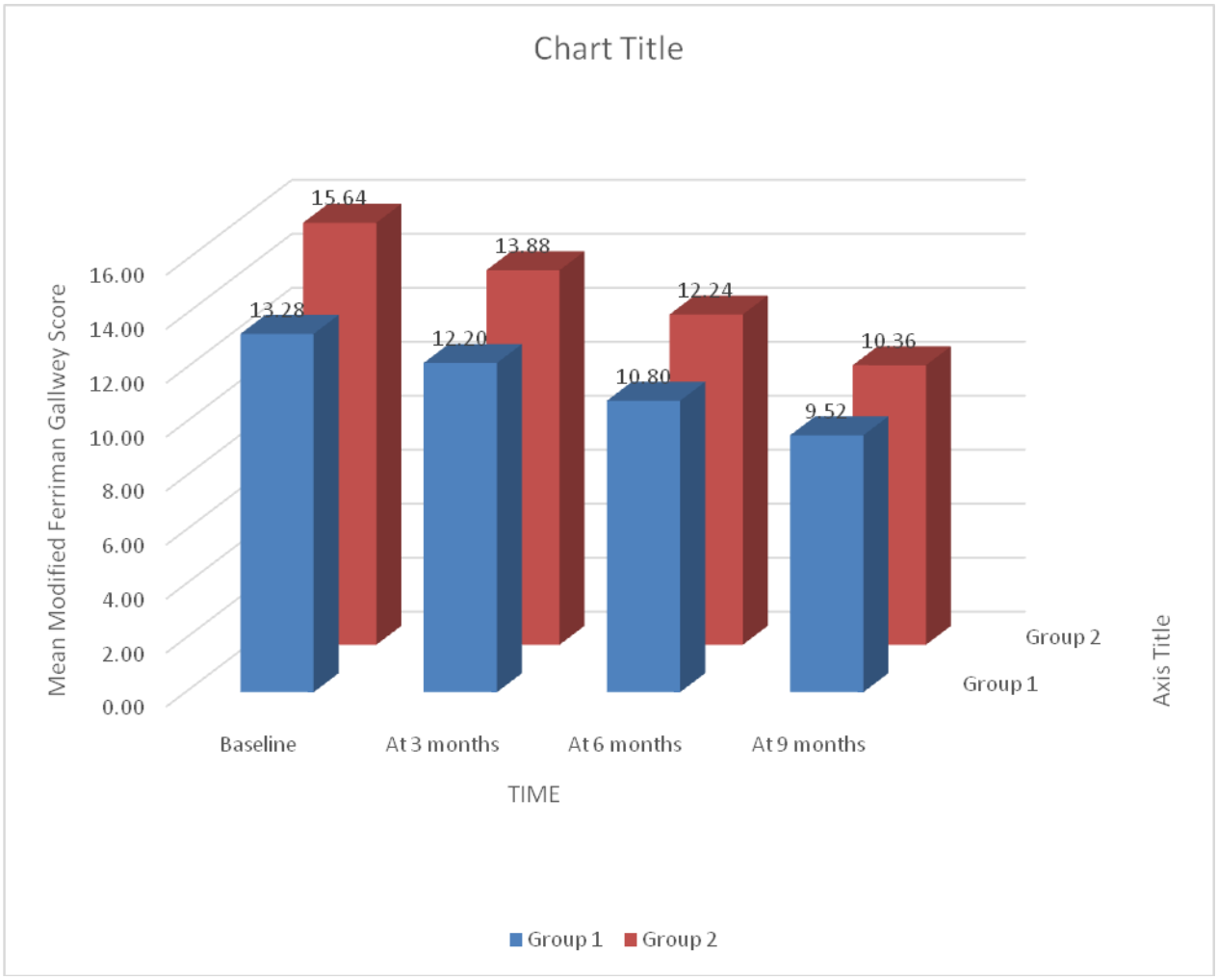
The age group was not statistically significant among the two groups.

Time	Group 1		Group 2		P value
	Mean	SD	Mean	SD	
Baseline	5.17	1.69	3.46	1.39	0.000
At 3 months	5.07	1.68	3.29	1.36	0.000
At 6 months	4.91	1.62	3.08	1.30	0.000
At 9 months	4.68	1.57	2.73	1.23	0.000
%age change at 3 months	1.98	4.57	5.19	2.82	0.004
%age change at 6 months	4.68	10.71	11.50	4.93	0.006
%age change at 9 months	9.31	11.99	22.46	6.47	0.000
p>0.05; Not significant; *p<0.05; Significant; **p<0.001; Highly significant					

Table 1: Serum free testosterone levels in pg/ml in patients in Group 1 & Group 2

Table 1 shows that the percentage change of serum free testosterone from baseline among the group 1 and 2 show statistically significant decrease in group 2 (p value<0.001).

The mean Modified Ferriman Gallwey score on day 1 was 13.28 ± 2.52 and 15.64 ± 1.44 in group 1 and 2 respectively. The levels showed marked decrease in values measured as 9.52 ± 1.92 and 10.36 ± 1.25 after final follow up at 9 months. The percentage change at 9 months from baseline was 28.10 ± 6.75 and 33.85 ± 3.92 in the two study groups showing statistically significant fall in patients on myoinositol and d-chiroinositol (p value< 0.05). Our results were in consistence with the study conducted by Thalamati where myoinositol and d-chiroinositol combination therapy caused significant reduction in Modified Ferriman Gallwey score than metformin. [12] In a study on treatment of hirsutism in PCOS by Harborne et al., metformin showed significant reduction in hirsutism score. [13] The results of the present study are, quite invariably, in agreement with the findings of several parallel researches.



Graph 2: Modified Ferriman Gallwey Score in pg/ml in patients in Group 1 & Group 2

Graph 2 shows that the percentage change of Modified Ferriman Gallwey Score from baseline among the group 1 and 2 show statistically significant decrease in group 2 (p value<0.05).

Treatment in both the groups was found to be safe. Most patients receiving metformin complained of dyspepsia and few complained of nausea, loss of appetite and diarrhea during the treatment. In contrast, no gastrointestinal side effects were reported in the myoinositol group and d-chiroinositol group, except for one who reported of diarrhea, confirming the high tolerability of myoinositol plus d-chiroinositol combination.

CONCLUSION

Metformin and myoinositol plus d-chiroinositol combination resulted in decreased hair growth in hirsute PCOS women with more significant results seen with combination group. Since the present study was carried out for a short duration and on a small number of patients, more studies are required to establish the effects of myoinositol + d-chiroinositol combination therapy for effective treatment of PCOS. Myo-inositol effectively controlled hyperandrogenism and hirsutism in the hirsute PCOS women, producing significant reductions in the hirsutism score and serum androgen concentrations.

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