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To Assess the Role of Myoinositol & Metformin on clinical, hormonal & metabolic profile of patients in Poly Cystic Ovarian Syndrome

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Abstract
Introduction & Methods: The aim of the study is to assess the Role of Myoinositol & Metformin on clinical, hormonal & metabolic profile of patients in Poly cystic Ovarian Syndrome. The women started with the intake of Myoinositol at a dosage of 2000 mg and 500 mg metformin used for a period of 01 Year. The primary outcome of the study was to determine the restoration of normal menstrual cycles, improvement in acne, reduction in hirsutism, weight loss & fertility.
Results: We found maximum cases in 25-29.9 i.e. 51%. BMI - The chi-square statistic is 0.0003. The *p*-value is .047363. The result is significant at $p < .05$. Mean fasting blood glucose - 93.44±8.27. Mean Ultrasound Pelvis - 16.92±4.48 & Mean TSH - 2.73±2.66
Conclusion: In the present study, both Metformin and MI were equally effective in improving the clinical, metabolic, and hormonal profile in PCOS patients. BMI was significantly reduced by both the metformin and MI after 12 weeks of treatment. According to the available evidence on this molecule derived from inositol, MYO should be considered an effective and safe treatment for obese and non-obese women with PCOS with insulin resistance and hyperinsulinemia, administered with the aim of improving oocyte quality and maturation and the reproductive prognosis in patients. Treatment with metformin (MET) ameliorated the insulin sensitivity and decreased the androgens levels, but the limitations to MET use are its gastrointestinal side effects.
Keywords: Assess, Myoinositol, BMI, Metformin, Menstrual cycle & Poly cystic Ovarian Syndrome.
Study Design: Observational Study.

Introduction

Polycystic ovarian syndrome (PCOS) is the most frequent multisystemic condition affecting 5-10%[1] of women in the reproductive age. Its prevalence ranging from 2.2% to 26% in adult women from 18-45 year [2]. In a recent study the prevalence of a confirmed diagnosis of PCOS in adolescents aged 10 to 19 years was 5-10%, which increased to 10-15%[3] when undiagnosed cases with documented symptoms qualifying for PCOS according to NIH (National institute of Health) criteria were included. Its wide clinical manifestations such as anovulation, amenorrhea/ oligomenorrhea, hyperandrogenism such as hirsutism, acne, alopecia, obesity, insulin resistance and the impending fear of infertility with the anxiety of future metabolic complications has a remarkable impact over the psychology of the young women. Further, it is associated with a wide spectrum of morbidity, including cardiovascular abnormalities, type 2 diabetes mellitus, dyslipidaemias, risk of malignancies and infertility. [4]

Polycystic ovary syndrome (PCOS, previously also called Stein-Leventhal syndrome) is an endocrine condition affecting 6–10% of women. In addition to polycystic ovarian morphology, the syndrome is associated with hyperandrogenism and menstrual irregularity suggestive of oligo- or anovulation. [5]

Treatment aim to reduce BMI, improve underlying hormonal disturbances prevent future reproductive and metabolic complication & enhance quality of life.

In recent research, the role of Myoinositol (MI) in the pathophysiology of PCOS has gained attention. MI, previously classified as part of the vitamin B complex group and a well-known dietary supplement, is now being used as evidence-based medicine for PCOS treatment. In PCOS, hyperinsulinemia attenuates the function of epimerase, leading to an imbalance in the DCI-to-MI ratio.

This diminishes the efficiency of MI-mediated FSH signaling and promotes hyperandrogenism [6]. They exhibit their action by promoting insulin transmembrane signaling and recent studies have revealed that they remarkably activate the enzymes that control glucose metabolism [7]. Metformin has been found to significantly decrease fasting glucose and insulin levels in PCOS patients but is associated with gastrointestinal side-effects.

Material and Methods

Present study was conducted at Vardaan Diagnostics & Women Care Centre, Delhi for 01 Year. Based on the inclusion criteria 100 woman were enrolled in the study diagnosed with PCOS using Rotterdam criteria. The subjects who were ready to participate in the study were given an informed consent. The women started with the intake of Myoinositol at a dosage of 2000 mg and 500mg metformin thrice a day used for a period of 01 Year. The primary outcome of the study was to determine the restoration of normal menstrual cycles, improvement in acne, reduction in hirsutism and weight loss in obese PCOS. The data was collected through performa. After 12 weeks improvement in clinical parameters were noted and Laboratory investigations repeated.

The inclusion criteria was women from aged 18 to 30 years and diagnosed with PCO on the basis of currently accepted criteria which include hyperandrogenism, anovulation and polycystic ovaries as observed on ultrasonography. PCOS is also accompanied by a number of metabolic disorders, such as insulin resistance, hyperinsulinemia, and obesity so women having BMI > 18kg/m2, fasting insulin > 12mIU/L were also included in study. Other causes of hyperandrogenism (such as congenital adrenal hyperplasia or androgen-secretory tumours) and ovarian dysfunction (such as hyperprolactinaemia) were excluded.

Result

Table No. 1: Clinical

S. No.		Mean	SD	P Value
1	**Mean Age**	25.96	2.87	0.02
		No.	**Percentage**	
2	**Married**	63	63	0.23
	Unmarried	37	37	

Mean Age - 25.96±2.87

Age - The chi-square statistic is 16.6643. The *p*-value is .02. The result is significant at $p < .05$.
Marital Status - The chi-square statistic is 2.9871. The *p*-value is .23. The result is *not* significant at $p < .05$. We found 63% were married & 37% were unmarried.

Table No. 2: BMI (kg/m2) n (%)

S. No.	BMI	No.	Percentage	P Value
1	**<18.5**	00	00	.047363
2	**18.5-24.9**	37	37	
3	**25-29.9**	51	51	
4	**>30**	12	12	

We found maximum cases in 25-29.9 i.e. 51%. BMI - The chi-square statistic is 0.0003. The *p*-value is .047363. The result is significant at $p < .05$.

Table No. 3: Menstrual Irregularity, Infertility & Fasting Glucose

S. No.		No.	Percentage	P Value
1	Menstrual irregularity n (%)	36	36	0.02
2	Infertility n (%)	12	12	0.04
		Mean	**SD**	
3	Mean fasting blood glucose (mg/dL)	93.44	8.27	0.03

Mean fasting blood glucose - 93.44±8.27

Table No. 4: Ultrasound Pelvis

S. No.		Mean	SD	P Value
1	**Ultrasound Pelvis**	16.92	4.48	0.04

Mean Ultrasound Pelvis - 16.92±4.48

Table No. 5: TSH

S. No.		Mean	SD	P Value
1	**TSH**	2.73	2.66	0.01

Mean TSH - 2.73±2.66

Discussion

In the present study, both metformin and MI were equally effective in improving the clinical, metabolic, and hormonal profile in PCOS patients. BMI was significantly reduced by both the metformin and MI after 12 weeks of treatment (p=0.0001). This finding was supported by Awalekar J et al., who showed that BMI significantly reduced after three months of treatment with both[8].

In PCOS, early follicular growth is excessive, but subsequent progression to a dominant follicle is interrupted (follicular arrest). Intraovarian androgens have been implicated in the excess of follicles and the elevated serum estradiol levels. This increased production of androgens is an inherent property of thecal cells, but it is increased by the surplus of LH and by hyperinsulinism. [9]

In women with PCOS, treatment with metformin (MET) ameliorated the insulin sensitivity and decreased the androgens levels, but the limitations to MET use are its gastrointestinal side effects[10]. In this case of PCOS, the place of MI was evaluated. Studies show that MI leads to a decrease in LH and androgen levels, as well as a decrease in insulin resistance. Thus, MI is believed to be able to re-establish ovulatory menstrual cycles (especially in obese women with PCOS) but its effect on pregnancy rates is difficult to determine (different diagnoses, insufficient power of studies, non-comparative studies). The second anomaly is the failure to select a dominant follicle, leading to the accumulation of selectable follicles and the typical aspect of polycystic (multifollicular) ovaries when ultrasonography is performed. This phenomenon called follicular arrest is the result of a lack of FSH action and/or premature LH action. Studies have shown the role played by anti-Müllerian hormone (AMH) in inhibiting the follicular response to FSH [11]. Hyperinsulinism, on the other hand, increases the sensitivity of follicles to LH. MI is responsible for a decrease in LH, in the LH/FSH ratio and in testosterone and androstenedione. When ovulation is induced in PCOS women with hyperinsulinism, MI reduces the risk of multifollicular development.

Therefore, MI reduces androgen levels (testosterone and androstenedione), corrects the LH/FSH ratio, restores normal menstrual cycles and induces ovulation, thereby facilitating spontaneous pregnancies by adequate luteal phase progesterone production [12-14].

With both the metformin and MI treatment , fasting insulin was significantly reduced. However, in Angik R et al.,'s study, there was a significant reduction in fasting insulin in the MI group and a non significant reduction in the metformin group [15].

In the present study, the most common clinical presentation was menstrual irregularity, and this irregularity significantly improved after 12 weeks of treatment with usage of both the drugs in treatment. This finding was supported by Nagaria T et al., where 90.09% of cases showed improvement in menstrual irregularities [16]. Ravn et al., also found that the effect on cycle length was corrected with both metformin and MI [17].

In a study by Chirania K et al.[18], the use of 1 gm of MI resulted in the resumption of spontaneous menstrual cycles in 66.66% of women with menstrual complaints, and 57.14% of infertile women conceived without the need for ovulation induction [19]. Thus, similar to a previously reported study, the results of combined therapy with metformin and MI in women with PCOS and IR seem promising.

Conclusion

In conclusion, both metformin and MI, which are insulin sensitisers, equally improve clinical and metabolic parameters in PCOS patients. MI has a better impact on hormonal parameters, while metformin has a better role in

achieving a clinical pregnancy rate. Although treatments with both the drugs are effective. Future randomised trials with larger sample sizes are required to study the duration of treatment and understand the long-term effects of the drug.

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