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ORIGINAL ARTICLE

Role of Myo-inositol and D-Chiro-Inositol in Improvement of Endocrine and Clinical Parameters in Teenage Girls affected by PCOS: A Prospective Cohort Study

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ABSTRACT

Aim: To evaluate the effectiveness of Myo-inositol and D-chiro-Inositol combination therapy in improvement of Endocrine and clinical parameters in teenage girls affected by PCOS.

Methods: This Prospective Cohort study was conducted in the Department of Gynaecology & Obstetrics, Avicenna Medical College and hospital after approval from Institutional ethical committee from January 2021 to June 2021. We have enrolled 106 teenage girls from 13 to 19 years with PCOS. Baseline clinical, ultrasound and biochemical parameters were noted and assigned them into two treatment groups (A & B) randomly. Group A was given MI plus DCI and Group B was given placebo for 6 months. Differences were analyzed in pretreatment and post treatment ultrasound findings and Clinical variable of BMI, Acne, hirsutism and menstrual irregularities. Biochemical parameters including LH:FSH ratio, 17-beta Estradiol and fasting glucose were also evaluated in both groups. Statistical Analysis was done using SPSS version 21.

Results: A statistically significant improvement was observed in clinical & Laboratory parameters in treatment group showing reduced LH:FSH ratio, fasting glucose and increased Estradiol levels along with decreased BMI, Acne and hair growth and improved ultrasound parameters in same group as compared to placebo group.

Conclusion: The current study showed promising results of combined therapy with MI plus DCI for treatment and improvement of clinical and lab parameters in teenage girls affected with PCOs as compared to placebo.

Keywords: PCOS, Myo-inositol, D-chiro-inositol, Hirsutism, Acne.

INTRODUCTION

Polycystic ovary syndrome is an endocrine disease of very high prevalence in females with the onset in a large no of cases as early as with the onset of puberty; verily it is yet considered the most common endocrine disorder in females. Hence being no exception; Pakistan has even a higher prevalence of around 52% then western countries where it is up to 25%[1]. Despite of high prevalence in developing as well as developed countries it is yet considered a debatable disease in terms of treatment[2]. PCOS is a lifelong disease of multigenic, multifactorial origin affecting reproductive, metabolic, physical & psychological health of women. It has colossal impact on health related quality of life due to varied short term and long term complications including endometrial carcinoma, Diabetes mellitus and depressive disorders[3].

Rotterdam criteria is used to diagnose the disease since 2003 (Fig. 1). Although pathogenesis (Fig 2) of this disease is still not very clear, the genetics, lifestyle and endocrine factors contribute to initiate a cascade of events that culminate in disease manifestations with insulin resistance playing key role.[4]It is therefore, metformin being insulin sensitizer has been widely used for quite a long time for improvement in metabolic disturbances, ovarian function and reduction in hyperandrogenism symptomatology. But despite of its use within therapeutic range; metformin use has been associated with certain side effects including nausea, diarrhea, flatulence weight loss, bloating and metallic taste, necessitating more research leading to discovery of new better therapeutic options with lesser side effects[5].

Inositol is a polyalcohol phytoglycon with nine stereoisomers in existence and among them 2 stereoisomers are myo-inositol (MI) and D chiro-inositol (DCI) acting as insulin sensitizers in human body[6]. These two stereoisomers function in distinct ways due to discrete ratio in varied organs according to specific biological needs. DCI has a role in glycogen synthesis. MI is most abundant inositol in human body and plays a pivotal role in human reproduction, metabolism, oocyte quality, maturation as well as ovulation[7].

The role of MI/DCI therapy has been well proven for treatment of subfertility and altered physiological ratio has been postulated as a trigger in pathogenesis of PCOs. Hence we ponder giving MI/DCI in physiological ratio of plasma 40:1 can possibly ameliorate PCOs symptoms and improve laboratory parameters in teenage girls with lesser side effect profile and be a better first line therapeutic option for PCOs in future as compared to existing options of metformin, pioglitazone, OCPs, statins and non-pharmacological therapies[8].

The objective of the study was to evaluate the effectiveness of Myo-inositol and D-chiro-Inositol combination therapy in improvement of Endocrine and clinical parameters in teenage girls affected by PCOS.

Fig: 1.

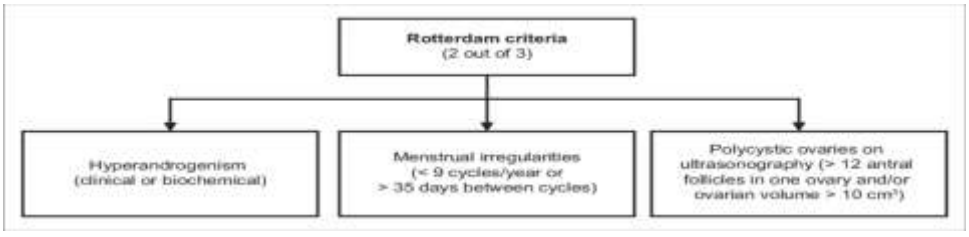

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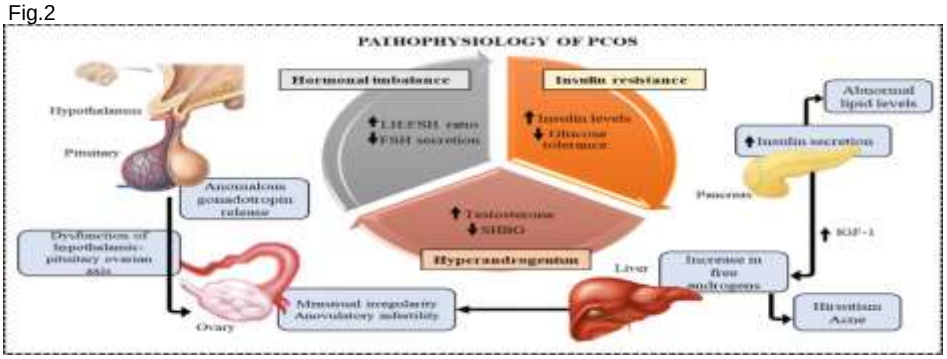
Fig.2



METHODOLOGY

The study, Role of Myo-inositol and D -chiro-inositol in improvement of Endocrine and clinical parameters in teenage girls affected by PCOs was conducted in the department of Obs & Gynae Avicenna Hospital, Lahore for a period of six months, from January 2021 - June 2021. 106 eligible teen age girls, 13--19 years of age with PCOs were enrolled in the study after taking informed consent. A prospective cohort study was carried out. The participants were randomly assigned to two groups A and B. Patients in group A and group B did not differ significantly. The demographic characteristics of both groups age, height, weight and BMI were recorded. Patients with endocrine and metabolic disorders , Type I diabetes and thyroid disease were excluded.

In Group A 53 women received MI plus DCI combined treatment at the ratio of 40:1 (the physiologic ratio of two isomers in the body) in soft gel capsule containing 550 mg of MI, 13.8 mg of DCI and 200µg folic acid twice a day. Group B with 53 women received the same amount of folic acid (200µg) as placebo twice a day. All the participants in both groups were evaluated for clinical parameters of obesity, menstural irregularity hiruitism and acne. The biochemical markers; LH: FSH ratio, 17 beta-estradiol and fasting glucose (mg/dl) were assessed in the pre and post treatment period. Pelvic ultrasonography for the findings of polycystic ovary was carried out in all the participants. Statistical Analysis was done using SPSS version 21.

RESULTS

One hundred and six young patients affected by PCOs were randomly distributed in two groups A and B (53 in each group). They were treated with MI plus DCI at the ratio of 40:1 and placebo respectively for 6 months. Demographic characteristics of the participants (Table 1). Clinical parameters, endocrine profile and fasting blood glucose levels were evaluated at base line and after the six months therapy. Only 19 out of 46 obese girls still had increased BMI and thus 58.7% showed marked improvement regarding weight reduction. Menstrual irregularity like oligoamenorrhoea, hypomenorrhoea and secondary amenorrhoea was also significantly improved in 56.8% girls post treatment with MI plus DCI as only 16 girls out of 37 still had menstrual irregularity. Similarly combined therapy of MI plus DCI significantly rebalanced the endocrine and metabolic profile of free testosterone and LH levels as was evident clinically when we found a profound reduction in socially distressing conditions of Hirsuitism and acne. (54.1% and 63.4% respectively of the participants). Only 17 and 11 girls still manifested the hirusitism and acne post treatment (Table 2). Thus p. value was significant in the treatment group .Table 3 also depicts significant positive modifications in the sonographic findings of ovarian morphology in post therapy period for a quite large number of cases 60% and 59.2% (Picture of PCOD still persisted in 6/15 and 7/23 patients only). On the other hand in the placebo cohort only 18.18% and 16% manifested the change (life style modifications and exercise being a contributor as well). In the majority (9 out of 11 and 21 out of 25) no positive outcome was recorded Table 3.

When the biochemical parameters were compared at the base line and in the post therapy period, levels of serum LH were markedly reduced (p< 0.005) thus improving the LH/FSH ratio significantly. 17 beta estradiol (pg/ml) was raised significantly with a p value of 0.01. In the palcebo group p-value for these endocrinological bio markets remained non significant. There were no relevant changes in the fasting blood glucose levels in both the groups Table 4. Only the combined therapy of MI plus DSI significantly rebalanced the endocrine and metabolic profiles of these patients, ameliorating their insulin resistance and the ovulatory function as successfully recorded by ultrasound findings also in the treatment group.

Table 1: Characteristics of Patients in both groups

	Group A (n= 53)	Group B (n=53)
Age (years)	15 ± 3.0	15 ± 3.8
Height (cm)	160 ± 6.7	163 ± 6.9
Weight (kg)	68 ± 10.5	65 ± 10
BMI (kg/m$^{2)}$	28 ± 4.8	28 ± 4.0

Fig. 3

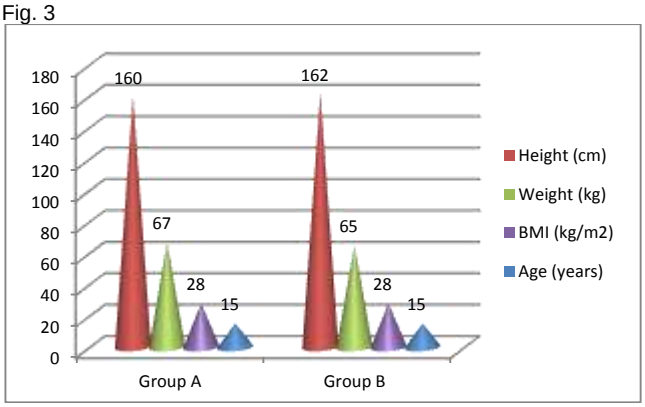


Table 2: Clinical Parameters

	Treatment Group (A)					Placebo Group (B)				
	Base Line	Post-Therapy	Post-therapy Improved	Improved Cases%	P-value	Base Line	Post-Therapy	Post-therapy Improved	Improved Cases%	P-value
Obesity	46	19	27	58.7	< 0.05	42	39	3	7.2	n s
Menstrual Irregularity	37	16	21	56.8	< 0.05	33	28	5	15.2	n s
Hirsuitism	37	17	20	54.1	< 0.05	35	31	4	11.5	n s
Acne	30	11	19	63.4	< 0.05	32	27	5	15.7	n s

Fig. 4:

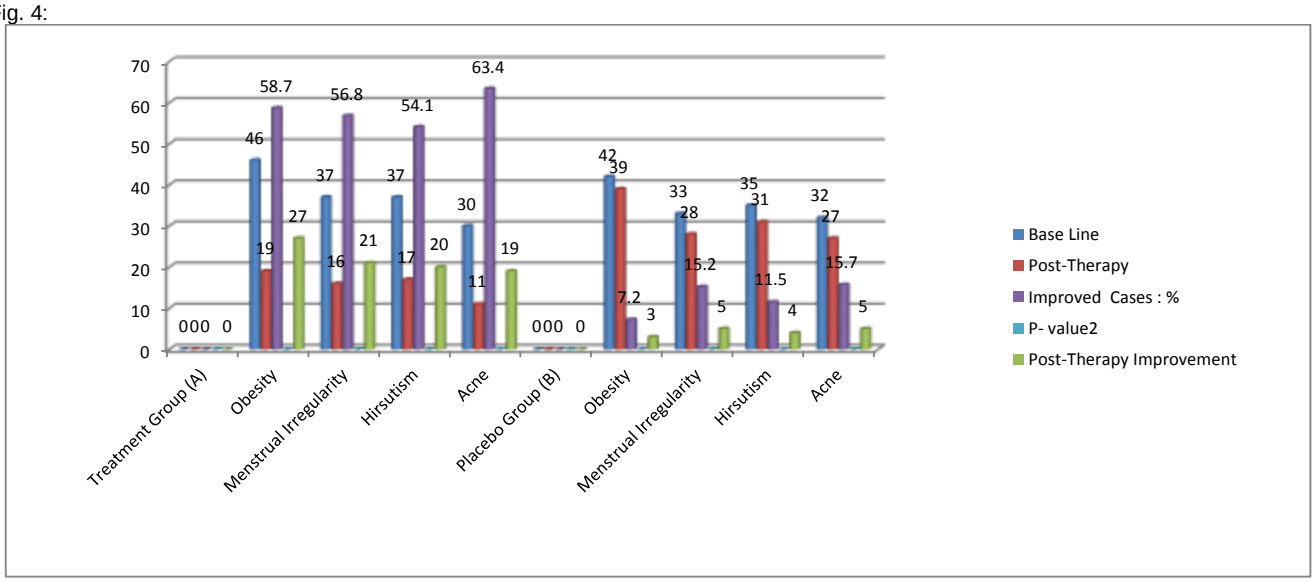


Table 3: Pelvic Ultrasound findings in both Groups

	Treatment Group (A) n=53				Placebo Group (B) n=53			
	Base Line	Post-Therapy	Post-Therapy Improved	Improved Cases%	Base Line	Post-Therapy	Post-Therapy Improved	Improved Cases : %
Normal	19	19			17	17		0
Unilateral polycystic Ovary	15	6	9	60	11	9	2	18.18
Bilateral Polycystic Ovary	23	7	16	59.2	25	21	4	16

Table 4: Biochemical Parameters

	Treatment Group (A)			Placebo Group (B)		
	Pre-treatment	Post-treatment	P- value	Pre-treatment	Post-treatment	P-value
LH(mIU/ml)	13.5 ± 6.0	9.2 ± 3.04	< 0.05	10.27 ± 6.2	10.25 ± 6.30	ns
FSH(mIU/ml)	4.66 ± 1.75	4.20 ± 1.54	ns	4.67 ± 1.11	4.47 ± 0.63	ns
17-beta Estradiol(pg/ml)	48.06 ± 10.30	100.42 ± 12.66	< 0.01	45.37 ± 19.45	43.0 ± 22.2	ns
Fasting Glucose(mg/dl)	87.0 ± 4.66	84.0 ± 7.12	ns	85.2 ± 6.1	84.13 ± 7.3	ns

DISCUSSION

Inositols had been researched since last many years for treatment of a large array of diseases including diabetes, dyslipidemia and metabolic syndrome. Many scientists have made efforts to discover the role of MI alone or in combination of DCI in metabolic and reproductive dysfunction in cases of polycystic ovarian syndrome as disturbed physiological ratio of MI/DCI might be a culprit in pathogenesis of syndrome[9]. Many studies have identified the notable role of MI/DCI in subfertility. They have also looked for its effectiveness in teenage girls with symptoms of metabolic & reproductive dysfunction or hyperandrogenism symptoms of PCOs as compared to conventional insulin sensitizers and other drugs due to their side effects leading to decreased patient compliance.

Our study deduced that combined therapy with MI/DCI for treatment of PCOs in teenage girls has a strong influence on mitigating clinical, biochemical as well as ultrasound features of syndrome by enhancing insulin sensitization and reducing circulating androgens due to altered steriodogenesis at ovarian level. Existing evidence proclaimed that among conventional treatments OCPs has a role in menstrual irregularities but there is also an array of side effects associated with them[10]. A comprehensive review[11] and a meta-analysis[12] of available literature has strengthened present study results and signified strong role of inositol in teenage PCOs treatment. Similar results were also shown in a meta-analysis by Kamenov Z et al[13]. When compared with metformin[14] or glucomanon[15] our investigational product showed similar efficacy in clinical as well as biochemical characteristics, nonetheless metformin was found a little more effective in improving endocrine parameters but also caused various side effects while MI/DCI combination has been the safest alternate without any side effects. Many other investigators have looked for and identified promising role of MI/DCI combination therapy not only in improving all three parameters of the syndrome in teenage girls[16] or women of higher age group with metabolic & reproductive dysfunction[17] but also showed Improvement in troublesome prima facie features of hyperandrogenism such as hirsutism and acne by targeting pathogenesis of the disease[18]. This enhances patient's compliance with a long term usage.

CONCLUSION

The present study concludes that MI and DCI combination therapy has a statistically significant role in treatment of polycystic ovarian syndrome by improving all three parameters (clinical, biochemical and ultrasound) as compared to placebo with a better side effect profile than available treatment options. Rendering this nutraceutical, a safe and effective first line or adjuvant therapy in management of PCOs reducing its short term and long term sequelae. Nonetheless large population based trials are required to recommend the drug for large scale usage.

Author's contribution: RBK: Study design, Data collection, **MS:** Data analysis and interpretation, critical analysis, **SA:** Literature review.

Conflict of interest: Nil

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