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Original Research Article

The effects of combined therapy of myo-inositol and D-chiro inositol in reduction of the individual components of metabolic syndrome in overweight PCOS patients compared to myo-inositol supplementation alone: a prospective randomised controlled trial

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ABSTRACT

Background: Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorder affecting five to ten percent women of reproductive age group. Variability of signs and symptoms along with metabolic syndrome as one of the long term complications make it worthy of early diagnosis and treatment. Medical management of PCOS is aimed at the treatment of metabolic derangements, anovulation, hirsutism, and menstrual irregularities.
Methods: 140 patients, using inclusion and exclusion criteria, were selected and randomly divided into two groups (seventy in each) and age, BMI, waist hip ratio, blood pressure (systolic, diastolic), serum fasting insulin, fasting blood sugar, total cholesterol, HDL, LDL, triglycerides were measured. Study group were given {Myo-inositol (550 mg) + D-chiro-inositol (13.8 mg)} (MI+DCI) twice daily and the control group were given Myo-inositol (1 gm) (MI) twice daily for six months. Same variables were measured at the end of three and six months and compared with repeated measurement ANOVA using SPSS (version 20).
Results: Comparison between these two groups before study was non-contributory. Combined drug therapy has provided statistically significant decrease in BMI, W:H ratio, Diastolic BP, Fasting blood sugar at the end of both 3rd and 6th month but in case of LDL it was at the end of 3 months. Combined drug therapy also increased the HDL level significantly in both the occasions.
Conclusions: Combined medical therapy by (MI+DCI) is very much helpful in reducing the metabolic complications of PCOS without any major side effects.

Keywords: Anovulation, D-chiro-inositol, Hirsutism, Myo-inositol, PCOS

INTRODUCTION

As the name suggests PCOS is a syndrome characterized by variable gynaecological and systemic signs and symptoms in association with cystic changes in ovary.

The signs and symptoms and their prevalence in PCOS are variable to a large extent and in one study (1) it was found to be as following: infertility 40%, hyperandrogenism 70%, amenorrhoea 50%, obesity 60-80%, abnormal uterine bleeding 30% and abnormal menstruation 20%.[1] A severe form of PCOS

characterized by hyper-androgenism, insulin resistance and acanthosis nigricans is commonly referred as a popular acronym HAIR-AN Syndrome.[2] It is the the most common cause of female infertility which is caused by a combination of hyperandrogenism, chronic anovulation and irregular menstrual cycle.[3-5] Several patients affected by PCOS are also affected by insulin resistance (±) signs of diabetes hyperinsulinemia.[6-8] PCOS-induced insulin resistance determines a higher risk for the development of type 2 diabetes75, hypertension and dyslipidemia, all elements of the metabolic syndrome.[2,9]

Diagnosis of PCOS

Rotterdam Criteria May 2003 for the diagnosis of PCOS Any two of the following three features Oligo- or anovulation, clinical and/or biochemical signs of hyperandrogenism, polycystic ovaries.[2]

Modified definition of the WHO criteria for Metabolic Syndrome[10]

- Hyperinsulinemia (the upper fourth of the fasting insulin level among nondiabetic subjects) or hyperglycemia (fasting glucose ≥110 mg/dl),
- In addition to at least two of the following: a) waist girth ≥94 cm, b) dyslipidemia (triglycerides ≥150 mg/dl or HDL cholesterol <40 mg/dl), c) BP ≥140/90 mmHg or taking BP medication.

Inositol (myo-inositol, D-chiro-inositol etc), a six-carbon polyol which has been characterized as an insulin sensitizer; in-deed, inositolphosphoglycan (IPG) mediators play a key-role in multiple cellular processes that control glucose metabolism and inositol is integral to properly functioning insulin receptors. Thus, a defect in tissue availability or altered metabolism of inositol, as in PCOS women, is a key factor in insulin resistance.[11] Different studies have proved the efficacy of myo-inositol in controlling the metabolic components of PCOS. Here we have compared the effects of (D-chiro-inositol + myo-inositol) combined therapy vs myoinositol therapy alone in controlling the components of metabolic syndrome.

Aims and objective of present study were to compare the effects between (myo-inositol+D-chiro-inositol) and myo-inositol monotherapy in controlling individual components of metabolic syndrome and to evaluate the complications and side effects of the two drugs.

METHODS

Double blinded (subject/patient and outcome assessor) Randomized controlled trial with parallel group design. Considering at least one overweight PCOS women attending OPD clinic per day and giving consent to participate in the study,the study period would be till we complete our required number of sample size (upto a maximum period of 18 months-March2015 to September 2016). All overweight (BMI>27) PCOS women attending the OPD of Obstetrics and Gynaecology at VIMS, Kolkata. A total of number of 140 patients will be included in the study (70 patients in each group).

Inclusion criteria

For each group:

- Overweight (BMI>27) women satisfying Rotterdam criteria for diagnosis of PCOS.
- No other known causes of infertility
- No known metabolic disorder.

Exclusion criteria

- Women less than 18 years or more than 41 years old
- Patients on hormonal medication
- Known diabetic/hypertensive patient
- Known alcoholic or smoker.

Patients selected using inclusion and exclusion criteria will be randomized using computer generated randomization sequence into two groups (70 in each group). Pre-intervention tests are done for all the parameters and compared. One group has received myo-inositol (1 gm BD) and another group has received [myo-inositol (550mg) and D-chiro-inositol (13.8mg)] (1 tab BD) for 3 months. All the parameters are tested again and compared to test the significance. The same drug therapy to continue for the same group of patients for next 3 months. And at the end of 6 months all the parameters are measured and compared using appropriate statistical test. The protocol and both the patient information sheet and the consent form were submitted to the Institutional Ethics Committee of VIMS, Kolkata.

Statistical analysis

All the data collected are compiled in Microsoft excel sheet and have been analyzed using statistical software Statistical Package for the Social Sciences (SPSS Version 20) as per nature of the data with appropriate statistical tests. Analysis will be two tailed and $p<0.05$ has been considered as statistically significant.

RESULTS

Continuous variables like Age, BMI, Waist Hip Ratio, Systolic Blood Pressure, Diastolic Blood Pressure, Serum Fasting Insulin, Fasting Blood Sugar, Total Cholesterol, HDL, LDL, Triglycerides as Mean ± Standard Deviation and compared across the two groups using unpaired ‘t’ test and it shows that there is no statistically significant difference between these two groups in the beginning of the study. After three months and six months of intervention all the parameters are studied and repeated measurement ANOVA (Analysis of Variances) is applied to test the significance.

Table 1a: Demographic and other study parameters of study participants.

		Groups			
		Myoinositol (n =70)	**Combined myoinositol and D-chiroinositol (n=70)**	**Total**	**Sig.**
BMI1(BMI at the starting)	Mean	29.710	30.029	29.869	0.524
	Std. Deviation	3.0692	2.8206	2.9413	
BMI2 (BMI at 3 months)	Mean	29.580	28.306	28.943	0.040
	Std. Deviation	3.2879	2.7750	3.0980	
BMI3 (BMI at 6 months)	Mean	29.483	27.487	28.485	0.000
	Std. Deviation	3.3528	2.6614	3.1779	
WH1 (waist hip ratio at te starting)	Mean	.8827	0.8836	.8831	0.797
	Std. Deviation	.02092	0.01834	.01960	
WH2 (waist hip ratio at 3 monts)	Mean	.8799	0.8636	.8717	0.049
	Std. Deviation	.02210	0.01737	.02142	
WH3 (waist hip ratio at 6 months)	Mean	.8796	0.8454	.8625	0.000
	Std. Deviation	.02039	0.02250	.02741	
SBP1 (systolic blood pressure at the starting)	Mean	120.64	125.54	123.09	0.055
	Std. Deviation	15.715	9.029	13.004	
SBP2 (systolic blood pressure at 3 months)	Mean	123.00	123.23	123.11	0.200
	Std. Deviation	16.003	8.391	12.731	
SBP3 (systolic blood pressure at 6 months)	Mean	119.46	118.51	118.99	0.265
	Std. Deviation	11.607	8.897	10.314	
DBP1 (diastolic blood pressure at the starting)	Mean	78.41	81.06	79.74	0.059
	Std. Deviation	6.717	4.919	6.014	
DBP2 (diastolic blood pressure at 3 months)	Mean	78.83	77.09	77.96	0.015
	Std. Deviation	6.806	4.989	6.009	
DBP3 (diastolic blood pressure at 6 months)	Mean	78.57	72.86	75.71	0.024
	Std. Deviation	6.613	5.023	6.515	
SFU1 (serum fasting insulin at the starting)	Mean	18.40	18.46	18.43	0.866
	Std. Deviation	1.929	2.076	1.997	
SFU2 (serum fasting insulin at 3 months)	Mean	17.79	17.87	17.83	0.690
	Std. Deviation	2.049	1.941	1.989	
SFU3 (serum fasting insulin at 6 months)	Mean	17.74	17.81	17.78	0.721
	Std. Deviation	1.674	1.883	1.775	
FBS1 (fasting Blood Sugar at the starting)	Mean	96.70	96.60	96.65	0.945
	Std. Deviation	8.037	9.158	8.585	
FBS2 (fasting Blood Sugar at 3 months)	Mean	96.97	93.41	95.19	0.021
	Std. Deviation	8.460	8.674	8.721	
FBS3 (fasting Blood Sugar at 6 months)	Mean	96.79	90.93	93.86	0.027
	Std. Deviation	8.477	8.650	9.025	
TC1 (Total cholesterol at the starting)	Mean	187.20	184.57	185.89	0.488
	Std. Deviation	25.005	19.348	22.315	
TC2 (Total cholesterol at 3 months)	Mean	185.96	183.46	184.71	0.430
	Std. Deviation	24.789	19.216	22.134	
TC3 (Total cholesterol at 6 months)	Mean	185.60	182.71	184.16	0.475
	Std. Deviation	24.677	19.139	22.050	
HDL1 (serum HDL at the starting)	Mean	49.30	49.59	49.44	0.806
	Std. Deviation	7.020	6.745	6.861	
HDL2 (serum HDL at 3 months)	Mean	50.363	53.046	51.704	0.012
	Std. Deviation	7.2907	6.5240	7.0233	
HDL3 (serum HDL at 6 months)	Mean	52.290	57.017	54.654	0.029
	Std. Deviation	7.3304	6.7335	7.4032	
LDL1 (serum LDL at the starting)	Mean	125.460	130.766	128.113	0.058
	Std. Deviation	15.8881	15.5403	15.8833	
LDL2 (serum LDL at 3 months)	Mean	125.704	125.784	125.744	0.013
	Std. Deviation	15.8989	15.1120	15.4546	

Table 1b: Demographic and other study parameters of study participants.

		Groups			
		Myoinositol (n =70)	**Combined myoinositol and D-chiroinositol (n=70)**	**Total**	**Sig.**
LDL3 (serum LDL at 6 months)	Mean	125.539	135.871	130.705	0.329
	Std. Deviation	15.9789	119.1797	84.8790	
TG1 (serum triglycerides at the starting)	Mean	165.46	171.07	168.26	0.112
	Std. Deviation	20.989	20.596	20.909	
TG2 (serum triglycerides at 3 months)	Mean	168.34	174.14	171.24	0.150
	Std. Deviation	21.138	20.652	21.023	
TG3 (serum triglycerides at 6 months)	Mean	165.31	171.27	168.29	0.102
	Std. Deviation	20.910	20.635	20.913	

An alpha level of 5% has been taken, i.e. if any 'p' value was less than 0.05, it has been considered as significant. The power of our study was 90%. Coming to the analysis, age and other parameters are studied as baseline evaluation (pre-intervention) and statistical tests applied to test the presence of any significance. It was found that there was no statistically significant difference between these two groups.

At the end of three months and six months the measurements were again studied and it was found that those datas were normally distributed and no statistically significant difference present between these two groups. At the end of 3 months BMI, WH Ratio, Diastollic BP, FBS, LDL were found to be reduced significantly and HDL was increased significantly in combined therapy group than myo-inositol only group. Other values of other parameters were unrewarding.

At the end of 6 months in the combined therapy group all of the above-mentioned parameters except LDL in which statistically significant changes noted were again found to carry statistically significant difference from the myo-inositol group.

DISCUSSION

Carlomagno G et al and Heimark D et al in two separate studies from two independent laboratories have reported a significant reduction of (Myo-inositol/D-chiro-inositol) ratio in D-chiro-inositol from 100:1 in healthy women to 0.2:1 in PCOS patients.[12,13] Those studies suggest marked MI depletion and an increased DCI reduction indicating the need of their supplementation in PCOS patients.

A trial was conducted by Nordio M and Proietti E on fifty patients where the metabolic effect and pre-determined parameters were assessed between two groups; one group treated with combined (Myo-inositol and D-chiroinositol) and the second group was given myo-inositol only.[14] The study showed that combined therapy is effective in reducing diastolic blood pressure and serum sex hormones significantly. It also showed that plasma glucose and insulin sensitivity index measurements were more controlled at the end of 3 months with combined therapy than myo-inositol only.

A study conducted by Mnozzi M et al on Cardio-vascular risk factor of PCOS patients by giving [Myo-inositol (550 mg) + D-chiro-inositol (13.8 mg)] (MI+DCI) twice daily for six months.[15] Statistical analysis shows statistically significant reduction in serum fasting insulin, fasting blood sugar, LDL and statistically significant increase in HDL level.

In present study, at the end of 3 months BMI, WH Ratio, Diastollic BP, FBS, LDL were found to be reduced significantly and HDL was increased significantly in combined therapy group than myo-inositol only group. At the end of 6 months in the combined therapy group all of the above-mentioned parameters except LDL have shown statistically significant changes.

CONCLUSION

Considering the wide range of presenting signs and symptoms of PCOS, early diagnosis and treatment, not only to control gynaecological problems but also to prevent and treat metabolic complications, is necessary. Combined (Myo-inositol+D-chiro-inositol) therapy proved to be more efficacious than Myo-inositol only in reducing individual components of metabolic syndrome. Dietary habits and physical exercise of individual may play some role which has not been confounded.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Genazzani AD, Battaglia C, Malavasi B, Strucchi C, Tortolani F, Gamba O. Metformin administration modulates and restores luteinizing hormone

spontaneous episodic secretion and ovarian function in nonobese patients with polycystic ovary syndrome. Fertil Steril. 2004;81(1):114-9.
2. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81(1):19-25.
3. Azziz RJ. Controversy in clinical endocrinology: diagnosis of polycystic ovarian syndrome: the Rotterdam criteria are premature. Clin Endocrinol Metab. 2006;91(3):781-5.
4. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. Positions statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an Androgen Excess Society guideline. J Clin Endocrinol Metab. 2006;91(11):4237-45.
5. 5. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril. 2009;91(2):456-88.
6. Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults: Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 2001;285:2486-97.
7. Vause TD, Cheung AP, Sierra S, Claman P, Graham J, Guillemin JA et al. Ovulation induction in polycystic ovary syndrome. J Obstet Gynaecol Can. 2010;32(5):495-502.
8. Lisi F, Carfagna P, Oliva MM, Rago R, Lisi R, Poverini R et al. Pretreatment with myo-inositol in non-polycystic ovary syndrome patients undergoing multiple follicular stimulation for IVF: a pilot study. Reprod Biol Endocrinol. 2012;10:52.
9. Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R et al. Diagnosis and Treatment of Polycystic Ovary Syndrome: An Endocrine Society Clinical Practice Guideline. J Clini Endocrinol Metab. 2013;98(12):2013-2350.
10. Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR) (Letter). Diabet Med. 1999;16:442-3.
11. Iuorno MJ, Jakubowicz DJ, Baillargeon JP, Dillon P, Gunn RD, Allan G et al. Effects of D-chiroinositol in lean women with the polycystic ovary syndrome. Endocr Pract. 2002;8:417-23.
12. Heimark D, McAllister J, Larner J. Decreased Myo-inositol to chiro-inositol(m/c) ratios and increased m/c epimerase activity in PCOS theca cells demonstrate increased insulin sensitivity compared to controls. Endocr J. 2014;61(2):111-7.
13. Unfer V, Carlomagno G, Papaleo E, Vailati S, Candiani M, Baillargeon JP. Hyperinsulinaemia alters myo-inositol to d-chiro-inositol ratio in the follicular fluid of PCOS patients. Reprod Sci. 2014;21(7):854-58.
14. Minozzi M, Nordio M, Pajalich R.. The combined therapy myo-inositol plus d-chiro-inositol, in a physiological ratio, reduces the cardio-vascular risk by improving the lipid profile in PCOS patients. Eur Rev Med Pharmacol Sci. 2013;17:537-40.
15. Nordio M, Proietti E. The Combined therapy myo-inositol and d-chiro-inositol reduces the risk of metabolic disease in PCOS overweight patients compared to myo-inositol alone. Eur Rev Med Pharmacol Sci. 2012;16:575-81.

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