Original Article

Compare the Mean Change in Homeostatic Model Assessment (HOMA) Index in Polycystic Ovarian Syndrome Patients Treated with Myoinositol Versus Metformin

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ABSTRACT

Objective: To compare the mean change in homeostatic model assessment (HOMA) index in polycystic ovarian syndrome patients treated with myoinositol versus metformin presenting in a tertiary care hospital.

Study Design: Randomized Controlled trial study.

Place and Duration of Study: This study was conducted at the Gynaecology unit IV, Fatima Memorial Hospital, Lahore for six months after approval of synopsis i.e. from 29th August 2018 to 29th January 2019.

Materials and Methods: Sample size of 150 cases (75 in each group) was included through Non-Probability consecutive sampling technique after the approval from hospital ethical committee. All the patients were followed up monthly for 6 months on OPD basis to check compliance and any side effects and HOMA after 6 months of treatment was calculated again for the patients.

Results: The mean age of the patients was noted 27.30 ± 7.82 years in the myoinositol group and 27.13 ± 7.43 years in the metformin group (P-value = 0.890). There were no significant intergroup differences found in the age groups. The mean body mass index was calculated to be (27.48 ± 2.61 vs 27.04 ± 2.43) in myoinositol and metformin groups respectively. HOMA-IR values decreased from 4.00 ± 0.69 to 2.36 ± 0.61 & 3.96 ± 0.69 to 3.50 ± 0.60 in group A & B respectively over a period of 6 months. Statistically significant difference was observed among both groups in terms of mean change in HOMA-IR.

Conclusion: The growing interest toward the clinical effects of myoinositol is witnessed by the recent analysis which demonstrated how this supplement is effective in decreasing HOMA-IR in patients with PCOS. Through the results of the current study we concluded that MI and metformin improves the metabolic profile of women with PCOS, when supplementation lasted at least 6 months.

Key Words: Polycystic ovary syndrome (PCOS), Myoinositol, Metformin, Homeostasis model assessment (HOMA) index

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INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a multifactorial endocrinopathy, influencing 5-10% of conceptive age ladies.

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The clinical show changes from eumenorrhea and a sonographic picture of polycystic ovaries however with unpretentious phenotypic irregularities or indications of hyperandrogenism, to cutting edge Stein and Leventhal condition and its related long haul sequelae. Additionally, most ladies with PCOS likewise exhibit metabolic disorder highlights, including insulin obstruction, stoutness and dyslipidaemia[1,2].

For quite a while, medicines for PCOS were centered around androgen concealment and enlistment of ovulation. All the more as of late it has been obviously exhibited that the powerful decrease of insulin obstruction reestablishes customary feminine cycles, ovulation and in this manner fruitfulness. Homeostatic model evaluation (HOMA) is one such record to decide the decrease in insulin opposition. Metformin is now being utilized as first line drug treatment for PCOS yet the job of myoinositol is likewise being concentrated on insulin obstruction[3]. Studies significantly affect

HOMA for the two medications. A new report distributed by Nehra J in 2017 directed on 30 patients in each gathering detailed that the pattern HOMA-IR was assessed to be 4.18 + 0.41 in myoinositol treated bunch and following a half year of treatment it was diminished essentially for example 2.88 + 0.27[4]. The mean decline was gotten to be (1.30 + 0.14; P= 0.000) also in the metformin treated bunch the standard HOMA-IR was shown to be 4.38 + 0.43 following a half year of treatment it was gotten to be 2.99 + 0.29 and the mean lessening was (1.39 + 0.14; p= 0.000). On examination between mean decline in myoinositol and metformin bunch genuinely immaterial outcomes was accomplished (P >0.05)[5].

On opposite, Angik et al. revealed that myoinositol fundamentally diminished HOMA-IRfrom 4.21 ± 3.63 to 3.39 ± 2.28 following a half year treatment(mean decline was viewed as 0.82 +1.35; p= 0.001) while metformin diminished HOMA-IR from 4.32 ± 4.61 to3.50 ± 2.34 (mean reduction was passed on to be 0.82 + 2.27; P=0.036) which was not detailed measurably critical. On looking at the two gatherings, the abatement in HOMA was critical with P worth of 0.004[6]. In any case, study led by Awalekar et al. detailed a measurably critical decrease in HOMA after treatment with metformin 25.85 + 16.27 versus 15.21+13.69(mean lessening was 10.63 + 2.58; P= 0.000) among 35 cases; while an increment of HOMA record from 23.74 + 25.00 to 23.8 + 44.62 was seen in myoinositol bunch (mean increment was 0.06 + 19.62; P=0.995)among 32 cases which was genuinely immaterial[7].

The reasoning of this study is to decide the mean change in HOMA file in myoinositol and metformin treated gatherings of patients with polycystic ovarian disorder. PCOS has been related with feminine and richness issues in an extensive extent of females and writing revealed the disputable outcomes on metformin and myoinositol as far as the critical decrease of HOMA file for example (Insulin obstruction) which is ended up being a vital connection in the age of the side effects of PCOS. In addition the examinations revealed above directed on lacking example size (for example < 50 cases in each gathering) and the turnover of PCOS patient is more in our nation so we will produce results on huge example size. This study will provide further evidence regarding the more effective line of treatment and management for patients suffering from PCOS thus decreasing the morbidity of the disease and improving the quality of life in these patients.

MATERIALS AND METHODS

Sample size of 150 cases (75 in each group) was included through Non-Probability consecutive sampling technique after the approval from hospital ethical committee.

Inclusion criteria: All female aged 15-40 years diagnosed as having PCOS (as per operational definition) presenting to Gynecology unit of teaching hospital.

Exclusion criteria:

- Patients with Deranged kidney function i.e. serum creatinine > 1.4 gm/dl serum urea level > 50 mg/dl.
- Patients with deranged liver function tests i.e. ALT >40 mg/dl or ALP > 310 U/L.
- Patients with Thyroid disorders determined on history and TSH levels < 0.3 or > 6.2 mIU/l.
- Patients with known hypersensitivity to myoinositol determined on history and medical record.

Data collection: After approval from hospital ethical committee, 150 patients with PCOS presenting to the gynecology department and fulfilling the inclusion criteria were approached and an informed consent was taken from before enrolling in the study. Information regarding their demographic data and baseline HOMA was noted in the proforma. All the patients were randomly divided into two groups by lottery method:

Group I (Myoinositol group): they had received tab myoinositol 2000 mg/ day.

Group II (Metformin group): they had received tab metformin 500 gm twice daily.

All the patients were followed up monthly for 6 months on OPD basis to check compliance and any side effects and HOMA after 6 months of treatment were calculated again for the patients as per operational definition by the researcher herself. Outcome variable in terms of mean change in HOMA-IR was documented (as per operational definition). All the information was recorded on a predesigned proforma attached and Confidentiality of the data was ensured.

Statistical analysis: Data was entered and analyzed using SPSS version 22.0. Numerical variable i.e. age, BMI, HOMA-IR at baseline and 6-months after treatment was summarized as mean and standard deviation. Mean change in HOMA-IR was calculated by subtracting post-treatment results from baseline in both groups.

RESULTS

There were total 150 PCOS patients (75 in each group) enrolled in this study for the treatment after taking an informed consent. The mean age of the patients in myoinositol group was 27.31 ± 7.82 (95% CI: 25.5-29.1) years with (range 15-40) and 27.13 $\pm$ 7.43 (95% CI: 25.4-28.8) in the metformin group with (range 15-40). Statistically insignificant difference was observed between both groups with P-value = 0.890. The body mass index among the patients of both groups was calculated to be (27.48 $\pm$ 2.61 vs 27.0 $\pm$ 2.43) (95% CI: 26.9-28.1 & CI: 26.5-27.6) kg/m^2 in myoinositol versus metformin group respectively with insignificant difference among both groups i.e. P-value =0.278. The baseline mean HOMA-IR was calculated to be 4.00 $\pm$ 0.69 in myoinositol group versus 3.96 $\pm$ 0.69 in the

metformin group. The 95% confidence interval for the difference was found to be (-1.82-0.26). At per baseline measurements insignificant difference was detected for the HOMA-IR among both groups with P-value = 0.718. In myoinositol group the measurement was noted to be less as compared to metformin group i.e. (2.36 ± 0.61 vs 3.50 ± 0.64; p= 0.000) with statistically significant difference in both groups.

Table No. 1: Descriptive Statistics of patients

Age	**N**	**Mean (years)**	**Std. Deviation**	**Range (years)**	**P-value**
Group -A (Myoinositol)	75	27.30	7.83	(15-40)	
Group-B (Metformin)	75	27.33	7.43	(15-40)	0.890
Mean BMI	**N**	**Mean (kg/m^2)**	**Std. Deviation**	**Range (kg/m^2)**	**P-value**
Group -A (Myoinositol)	75	27.49	2.61	(22-33)	
Group-B (Metformin)	75	27.04	2.43	(21-33)	0.278
HOMA-IR at Baseline	**N**	**Mean**	**Std. Deviation**	**Range**	**P-value**
Group -A (Myoinositol)	75	4.00	0.69	(3 - 5.84)	
Group-B (Metformin)	75	3.96	0.69	(2.15 - 5.56)	0.718
HOMA-IR values at six months of treatment	**N**	**Mean (kg/m^2)**	**Std. Deviation**	**Range (kg/m^2)**	**P-value**
Group -A (Myoinositol)	75	1.64	0.88	(-0.52 – 3.55)	
Group-B (Metformin)	75	0.46	0.89	(-1.24 – 3.00)	0.000

The outcome variable for this study was to compare the mean change in HOMA-IR in both groups which was established to be (1.64 ± 0.88 vs 0.46 ± 0.89) (95% CI of the difference: 0.90-1.47) in myoinositol vs metformin group respectively with strongly significant difference among both groups (P = 0.000).

Table No. 2: Paired Distribution according to (Myoinositol) Treatment

Myoinositol	**Mean**	**N**	**Std. Deviation**	**P-value**
Pre-treatment	4.0005	75	.69183	0.000
Post-treatment	2.3571	75	.61050	

Paired Distribution according to (Metformin) Treatment

Metformin	**Mean**	**N**	**Std. Deviation**	**P-value**
Pre-treatment	3.96	75	0.69	0.000
Post-treatment	3.50	75	0.60	

Table No. 3: Distribution according to Parity

Parity of the patients		**Treatment groups**		Total
		Myoinositol	**Metformin**	
.00	Count	28	22	50
	% within Parity	56.0%	44.0%	100.0%
1.00	Count	20	25	45
	% within	44.4%	55.6%	100.0%
2.00	Count	17	19	36
	% within Parity	47.2%	52.8%	100.0%
3.00	Count	7	6	13
	% within Parity	53.8%	46.2%	100.0%
4.00	Count	3	2	5
	% within	60.0%	40.0%	100.0%
5.00	Count	0	1	1
	% within	0.0%	100.0%	100.0%
Total	Count	75	75	150
	% within	50.0%	50.0%	100.0%

P-value = 0.752

When data was compared for both groups separately to check the mean difference in pre and post-treatment effect on HOMA-IR, we observed that in myoinositol group (95% CI of the difference was 1.44-1.84) and in metformin group (95% CI: 0.25-0.66) with statistically significant difference between both groups. Frequency was also calculated for parity among these patients in both groups and it was noticed that in myoinositol group mostly patients presented with PCOS were primigravida (56.0% vs 44.0%)) followed by parity 1 (44.4% vs 55.6%) , parity 2 (47.2% vs 52.8%), parity 3 (53.8% vs 46.2%), parity 4 (60.0% vs 40.0%) in metformin group respectively. On comparison it was perceived that there was no difference for parity among both treatment groups P-value = 0.752.

DISCUSSION

Insulin resistance (IR) is a typical problem, which can impede ladies ripeness and is described by phenotypic heterogeneity. For instance, polycystic ovary disorder (PCOS) is the most well-known endocrine illness influencing ladies fertility4 and IR is by all accounts one of the significant pathways at the foundation of feminine inconsistency, anovulation, and fruitlessness[8-10]. Today, metformin is thought of as one of the most widely recognized medicines for type 2 diabetes mellitus, because of its extraordinary adequacy in decreasing insulin levels. MET is additionally ordinarily utilized in pathologies described by insulin problems like IR and PCOS. By and by, its antagonistic impacts are very much portrayed in the writing, motivation behind why metformin use isn't generally suggested[11]. Present day examinations revealed a connected proof on myoinositol as an elective insulin-sharpening specialist for PCOS. Specifically, fascinating aftereffects of myoinositol have been found in a few examinations where this treatment had the

option to work on feminine modifications, hyperandrogenism and metabolic and hormonal changes[12]. Comparable to these discoveries, we wanted to investigate whether myoinositol could address an elective methodology in the administration of patients with HOMA-IR. In our review results the mean age of the patients was found to 27.3 (7.82) versus 27.1 (7.43) with unimportant contrast among the two gatherings which can be upheld by the outcomes distributed by Nehra J et al (23.8± .69 versus 23.26± 1.03; p=0.669) and on examination immaterial distinction was assessed between the two gatherings (8). One more review was finished on teen PCOS young ladies to really look at the viability of myoinositol where the typical age of the patients was 16.75 + 2.0 years, normal weight was 58.6 + 9.3 kg, and normal BMI was 22.3 + 3.08 kg/m2 and among them 4 patients (20%) had BMI > 25.5 kg/m2. Another review showed the age of 34 patients for the review were (26.4 ± 0.8 y). The mean BMI in our review was outlined to be 27.5 (2.61) versus 27.0 (2.43) which showed that greatest number of the patients gave PCOS were overweight and hefty in the two gatherings with no distinction. Insulin opposition is principal causative component for this multitude of outcomes and morbidity. Disappointment of the objective cells to answer typical or conventional degrees of insulin is viewed as insulin obstruction independent of the weight list (BMI)[13]. Hyperinsulinaemia because of insulin obstruction happens in roughly 80% of PCOS ladies focal corpulence and 30%-40% of lean PCOS ladies. Awalekar et al revealed the mean BMI at gauge and post-treatment with myoinositol and metformin to see the impact of these drug on body weight. The showed that in Metformin bunch n=32, prior to beginning treatment BMI mean was 25.40, following 3 months treatment with Myoinositol it diminished to 24.40 (p= 0.009) for example exceptionally critical genuinely[14-18]. The mean change in HOMA-IR in PCOS patients subsequent to seeking a half year treatment was the principal result for our review. HOMA list pretreatment was mean 25.85, decreased to 15.21(p=0.000). for example profoundly huge genuinely for the gathering metformin and HOMA file pretreatment was mean 23.74, diminished to 23.8 (p=0.995) [19].

HOMA-IR file values were under 2.5 in Gathering 1 and Gathering 2 toward the start of treatment. HOMA-IR file values showed diminishing propensities for the most part in the gatherings treated with MET (esteem toward the start of treatment: 2.95; esteem following a half year treatment: 2.41) and MET+MYO (esteem toward the start of treatment: 3.4; esteem following a half year treatment: 3.05), without measurable importance inside and among the gatherings toward the finish of a half year. In one more review done by Leo et al, 60 insulin safe PCOS patients were haphazardly doled out into three gatherings[20]. All gatherings were treated for a very long time with either myo-inositol (1500 mg BD) and monacolin k (3000 mg BD), inositol just (1500 mg BD) or metformin just (850 mg BD) in which metformin and myo-inositol were contrasted with notice their impacts on HOMA-IR record. The HOMA-IR list fundamentally diminished by 1.1 and 0.8 with inositol and metformin individually toward the finish of 24 weeks[21,22].

CONCLUSION

Our study results was illustrated that the findings on the primary outcome (mean change in HOMA-IR) are conclusive. Metformin and myoinositol can significantly improved insulin sensitivity in PCOS women. Myoinositol yielded significantly better results in in decreasing the insulin resistance in HOMA-IR among patient we studied, so it can be used as first line therapy in PCOS. Based on the our observations it can be said that, since the clinical features of PCOS are heterogeneous, they have to be investigated accordingly, for selection of appropriate treatment modality. Early identification of high risk cases and timely therapeutic intervention can halt this on-going process and prevent long term complications.

Author's Contribution:

Concept & Design of Study:	Mehvish Gul
Drafting:	Angbeen Ahmad, Arooj Butt
Data Analysis:	Sana Navid, Sidra Asif, Amna Aslam
Revisiting Critically:	Mehvish Gul, Angbeen Ahmad
Final Approval of version:	Mehvish Gul

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Leo VD, Musacchio MC, Cappelli V, Sabatino AD, Tosti C, et al. A combined treatment with myo-inositol and monacolin k improves the androgen and lipid profiles of insulin-resistant PCOS patients. J Metabolic Synd 2013; 2: 127.
2. Artini PG, Di Berardino OM, Papini F, Genazzani AD, Simi G, Ruggiero M, et al. Endocrine and clinical effects of myo-inositol administration in polycystic ovary syndrome. A randomized study. Gynaecol Endocrinol 2013;29(4):375-9.
3. Sanoee MF, Neghab N, Rabiee S, Amiri I. Metformin therapy decreases hyperandrogenism and ovarian volume in women with polycystic ovary syndrome. Iran J Med Sci 2011;36(2):90-5.
4. Cheang KI, Huszar JM, Best AM, Sharma S, Essah PA, John E. Long-term effect of metformin on metabolic parameters in the polycystic ovary

syndrome. NestlerDiabVasc Dis Res 2009;6(2):110-9.
5. Costantino D, Minozzi G, Minozzi E, Guaraldi C. Metabolic and hormonal effects of myo-inositol in women with polycystic ovary syndrome: a double-blind trial. Eur Rev Med Pharmacol Sci 2010;13:105-10.
6. Angik R, Jajoo SS, Hariharan C, Chimote A. A comparative study of metabolic and hormonal effects of myoinositol vs. metformin in women with polycystic ovary syndrome: a randomised controlled trial. Int J Reprod Contracept Obstet Gynecol 2015;4:189-94.
7. Awalekar J, Awalekar C, Jadhav VM, Chivate CG, Patwardhan MH. Effect of metformin & myoinositol & life style modification in patients of polycystic ovarian disease (PCOD). Int J of Biomedical Res 2015; 6(09): 698-704.
8. Nehra J, Kaushal J, Singhal SR, and Ghalaut VS. A Comparative Study of Myo Inositol versus Metformin on Biochemical Profile In Polycystic Ovarian Syndrome In Women. Int J Pharma Sci Res 2017;19:1664-1670.
9. Umland EM, Weinstein LC, Buchanan EM. Menstruation-related disorders. In: DiPiro JT, Talbert RL, Yee GC, et al, editors. Pharmacotherapy: A Pathophysiologic Approach. 8th ed. New York: McGraw-Hill; 2011.p.1393.
10. Lin LH, Baracat MC, Gustavo AR, et al. Androgen receptor gene polymorphism and polycystic ovary syndrome. Int J Gynaecol Obstet 2013;120:115–118.
11. Aubuchon M, Legro RS. Polycystic ovary syndrome: Current infertility management. Clin Obstet Gynecol 2011; 54(4):675–684.
12. American Congress of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 108: Polycystic Ovary Syndrome. Obstet Gynecol 2009;114(4):936–949.
13. McFarland C. Treating polycystic ovary syndrome and infertility. MCN Am J Matern Child Nurs 2012; 37(2):116–121.
14. Ndefo UA, Eaton A, Green MR. Polycystic ovary syndrome. PT 2013;38(6):336-338.
15. Sirmans SM, Pate KA. Epidemiology, diagnosis and management of polycystic ovary syndrome. Clin Epidemiol 2014;6:1-13.
16. Hayek SE, Bitar L, Handar LH, Mirna FG, Daoud G. Polycystic ovarian syndrome: An updated overview. Front Physiol 2016;7:124.
17. Azziz R, Adashi EY. Stein and Leventhal: 80 years on. Am J Obstet Gynecol 2016; 214:247-256.
18. Havelock J. Polycystic ovary syndrome. BCMJ 2018;6(4): 210-216.
19. Diamanti-Kandarakis E, Kandarakis H, Legro RS. The role of genes and environment in the etiology of PCOS. Endocrine 2006;30:19–26.
20. Shannon M, Wang Y. Polycystic ovary syndrome: A common but often unrecognized condition. J Midwifery Womens Health 2012;57:221–230.
21. Urbanek M. The genetics of polycystic ovary syndrome. Natl Clin Pract Endocrinol Metab 2007;3:103–111.
22. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metab 2004; 89:2745–2749.