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ORIGINAL ARTICLE

Comparison of the Effectiveness and Safety of Myo Inositol with Metformin for the Treatment of Polycystic Ovary Syndrome in Women

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ABSTRACT

Objective: This study was aimed to compare the efficacy and safety of Myo inositol versus Metformin in polycystic ovarian syndrome in women.

Study design: A retrospective randomized comparative study.

Place and Duration: In Gynaecology and Obstetrics Department of Combined Military Hospital, Peshawar for the period from June, 2020 to November, 2021.

Methods: The study was conducted on 100 patients that were randomly divided into two groups of 50 each: group A and group B. Group A was given the treatment: Tab Myoinositol 1gm twice daily and Group B was given: Tab Metformin 500mg thrice daily for six months. While treating women with Polycystic Ovary Syndrome, the efficacy assessment was done on observing menstrual irregularity, clinical (acne, hirsutism), infertility and changes in weight for 6 months. Safety assessment was also done. For statistical analysis, SPSS-20.0 was used.

Results: The mean age in group A was 24.6±3.22 years and mean BMI 25.7±4.24 kg/m^2 while in group B mean age was 23.12±7.40 years with mean BMI 26.1±4.31 kg/m^2. After a period of six months, we found that a significant improvement in all of the symptoms was present in both groups. On the other hand, when looking at the two groups' symptoms at three and six months, there was no discernible difference between them. In terms of its safety profile, myo-inositol came out on top when compared to metformin.

Conclusion: Both metformin and myo-inositol have been shown to be effective in treating PCOS. Insulin resistance, irregular menstruation, hyperandrogenism, and infertility are all helped by these medications. Treatments for PCOS were equally effective, relieving symptoms for patients, but a direct comparison showed no clear winner. In comparison to Metformin, myoinositol had a higher rate of patient acceptance.

Keywords: PCOS, Infertility, Metformin, Myoinositol, Insulin Resistance, Irregular menstruation

INTRODUCTION

The endocrinopathy polycystic ovarian syndrome (PCOS) affects 4-21% of women of reproductive age globally [1,2]. Ovulatory insufficiency, elevated testosterone levels, and polycystic ovarian appearance are all hallmarks of this condition. Many metabolic problems, including insulin resistance, hyperinsulinemia, and obesity, accompany these characteristics. The long-term effects of PCOS on health are well-documented [3, 4]; these include a higher risk of endometrial cancer, type 2 diabetes mellitus, and cardiovascular events. Among the benefits of the insulin sensitizer metformin (Met) for women with polycystic ovary syndrome (PCOS) is the reduction of hyperinsulinemia, hyperandrogenism, and abnormal metabolism; it also improves menstruation [5, 6]. Metformin may also have a preventative effect on long-term cardiovascular diseases. Persistent Met use, however, is associated with gastrointestinal unpleasant symptoms such as diarrhea and stomachache [6]. Care providers and patients now have access to a wider range of effective and safe oral insulin-sensitizing medications, including thiazolidinediones (TZDs), inositol, and berberine, for the treatment of PCOS-related endocrine, metabolic, and reproductive problems.

Rotterdam (2003) consensus on diagnosis: Oligo/Anovulation, Hyperandrogenism, polycystic ovaries, excluding other endocrine disorders.Due to abnormal Gonadotropin release, PCOS patients often have anovulation. As a result, the ratio of luteinizing hormone (LH) to follicle-stimulating hormone (FSH) rises to two to three times its normal level. About 60%-70% of PCOS women also have insulin resistance. [7,8]

Hyperandrogenism occurs when the ovarian theca cells create an abundance of androgens in response to the stimulation of luteinizing hormone (LH) by insulin. In addition to preventing the natural destruction of immature follicles by apoptosis, elevated androgens hinder the development of a single dominant follicle into a Graffian follicle. Under an ultrasound, polycystic ovaries will show up as a necklace-like pattern in the ovarian periphery. [9] Type 2 diabetes mellitus, obesity, dyslipidemia, atherosclerosis, and coronary artery disease are all components of metabolicsyndrome X, which describes a cluster of metabolic disorders. As a result, polycystic ovary syndrome is not a condition with temporary symptoms but rather a syndrome with permanent repercussions. In order to get pregnant after becoming married, some married women need to have their ovaries stimulated. Modifying one's way of life with things like exercise and a healthy diet constitutes the first line of defense. [10-13]

In humans, the vitamin B complex group member myo-inositol (MI) is synthesised spontaneously. Many foods naturally contain MI, which is one of nine forms of inositol. MI and d-chiro-inositol are two of the nine forms of inositol that exhibit insulin-sensitizing properties. Insufficient myo-inositol has been associated to polycystic ovary syndrome. Although we are able to produce MI from food sources, a lack of MI can reduce insulin sensitivity. Defects in the insulin-signaling pathways, which rely largely on inositol-containing compounds, are also thought to contribute to the development of PCOS in women (phosphoglycan mediators). Conditions like periconceptional periods in women with PCOS raise the physiological demands for MI. The synthesis of phosphatidyl inositol 3-kinase (PI 3-kinase), a crucial messenger to increase insulin sensitivity and decrease insulin resistance, relies on MI. Extra MI seems to temporarily restore normal insulin pathways and alleviate insulin resistance symptoms. [14,15] Hyperandrogenic and reproductive symptoms of polycystic ovary syndrome (PCOS) in women are ameliorated by insulin sensitizers such metformin and myo-inositol. Myo-inositol and metformin were both used to treat PCOS in women, hence their relative efficacy and safety was compared in this study.

MATERIAL AND METHODS

This study was conducted at gynaecology and obstetrics department of Combined Military Hospital, Peshawar for the period from June, 2020 to November, 2021 and comprised of 100

patients. Those who are pregnant or nursing, have active liver illness or renal impairment, have hyperprolactinemia, have Cushing's disease, have hypothyroidism or hyperthyroidism, have any neoplastic disease, or have hyperthyroidism. Patients with a diagnosis of type 1 or type 2 diabetes mellitus, a treatment history that includes the use of anti-diabetic medications or hormone replacement therapy during the last three months, Subjects who smoked cigarettes or drank alcohol excessively were also excluded, as were those who were unable to attend scheduled appointments.

Women of child-bearing age (17-48) who meet the AES (Androgen Excess Society)/2006 diagnostic criteria for polycystic ovary syndrome Ovarian volume >10 ml, presence of at least one ovary with 12 or more follicles (2-9 mm in diameter), and clinical or biochemical evidence of hyperandrogenism are all necessary, as is the willingness to provide written informed consent. Fifty patients from each of two groups were assigned at random to receive one of two treatments: In Group A, taking Myo-inositol 1 g twice daily via tablet form was recommended. Metformin 500 mg tabs, group B, three times each day for a total of six months. Consistent menstrual cycles and the absence or severity of hirsutism were measured as indicators of efficacy using the modified Ferriman Gallwey score, which assigns a value from 0 (no) to 4 (severe) across nine anatomical sites. For hirsutism, a score of 4 or less indicates mild cases, 4-7 indicate moderate cases, and 8 or more indicate severe cases. along with weight shifts over the course of a year. The risk level was also evaluated.

In the absence of a more explicit notation, data was reported as a Mean SEM. There were statistical comparisons made both within and between groups. Parametric data were analysed using ANOVA for repeated-measures within-group comparisons. To compare the two groups, we used the unpaired t-test for parametric data. The Chi-square test was used to compare the two groups based on categorical data such as the proportion of patients with normal menstrual cycles, the prevalence of acne, and the occurrence of adverse events. Probability value, or p-value

RESULTS

The mean age in group A was 24.6±3.22 years and had mean BMI 25.7±4.24 kg/m^2 while in group B mean age was 23.12±7.40 years with mean BMI 26.1±4.31 kg/m^2. Majority of the patients among both groups were married. 22 (44%) patients were literate in group A and in group B 25 (50%) patients were literate. 24 (48%) cases were from urban areas in group A and in group B 26 (52%) cases were from urban areas.(table 1)

Table-1: Demographics of the enrolled cases

Variables	Myoinositol Group	Metformin Group
Mean age (years)	24.6±3.22	23.12±7.40
Mean BMI (kg/m^2)	25.7±4.24	26.1±4.31
Marital Status		
Yes	35 (70%)	40 (80%)
No	15 (30%)	10 (20%)
Education Status		
Yes	22 (44%)	25 (50%)
No	23 (56%)	25 (50%)
Area of Living		
Urban	24 (48%)	26 (52%)
Rural	26 (52%)	24 (48%)

After a period of six months, we found that a significant improvement in all of the symptoms was present in both groups. On the other hand, when looking at the two groups' symptoms at three and six months, there was no discernible difference between them.(table 2)

Table-2: Favorable and unfavorable outcomes among both groups

After 12-weeks of Treatment	Group A	Group B
Normal ovaries on USG		
Yes	46 (92%)	47 (94%)
No	4 (8%)	3 (6%)
PCOM on USG		
Yes	5 (10%)	7 (15%)
No	45 (90%)	45 (90%)
Amenorrhea		
Yes	0 (0%)	0 (0%)
No	50 (100%)	50 (100%)
Oligomenorrhea		
Yes	9 (18%)	12 (24%)
No	41 (82%)	38 (76%)
Regular cycle		
Yes	42 (84%)	40 (80%)
No	8 (16%)	10 (20%)

In terms of its safety profile, myo-inositol came out on top when compared to metformin.(table 3)

Table-3: Post-treatment comparison of side effects

Adverse Effects	Group A	Group B
Nausea	1 (2%)	6 (12%)
Vomiting	3 (6%)	8 (16%)
Diarrhea	0 (0%)	3 (6%)
Abdominal Cramps	2 (4%)	8 (16%)
Headache	2 (4%)	5 (10%)
Weakness	3 (6%)	4 (8%)

DISCUSSION

Hyperandrogenism, chronic anovulation, and an irregular menstrual cycle are the hallmarks of polycystic ovary syndrome (PCOS), the most common cause of female infertility and one of the most prevalent endocrine illnesses affecting women. [16] It has been found that insulin receptor phosphorylation is disrupted in roughly 50% of PCOS patients (Dunaif et al. [17] Free androgen levels are increased because insulin promotes ovarian androgen release by boosting cytochrome P450C17 activity, which in turn disrupts normal follicular growth. The production of adrenal androgens in women with polycystic ovary syndrome (PCOS) is also amplified in vivo by this factor. [18]

Metformin, a well-known insulin sensitizer, lowers blood sugar levels by preventing the liver from producing glucose [19]. Numerous scientific research have shown its efficacy in treating PCOS symptoms such irregular periods, increased androgen production, and insulin resistance. Diarrhoea, nausea, and stomach pain are common adverse reactions [20].

Our results are consistent with these findings, since both therapy groups showed a statistically significant increase in menstrual cycle regularity. With both medicines, however, the improvement was even greater than in the aforementioned trial. Our study's positive findings with metformin may have resulted from the fact that we employed a greater dose (500 mg TDS) than the one used by Angik et al. (500 mg BD). Both our study and this one found that after 24 weeks of treatment with myo-inositol and metformin, there was a reduction in ovarian volume and antral follicle count, which is consistent with the findings of USG investigations. [21] Patients with insulin resistance and polycystic ovary syndrome (PCOS) were divided into three groups in a study by Leo et al. For 6 months, all patients were given either MI (1500 mg BD) and monacolin k (3000 mg BD) or inositol (1500 mg BD) or metformin (1500 mg BD) alone (850 mg BD). A decrease of 2.0 points in m FG score was observed after 6 months of treatment with both medicines, and the duration of menstrual periods was greatly reduced. [22]

After six months of treatment, the present study found that the myo-inositol group had improved by 84% in regularising their cycles and the metformin group had improved by 80%, which is comparable to earlier studies. [23] After a period of six months, we found that a significant improvement in all of the symptoms was present in both groups. On the other hand, when looking at the two groups' symptoms at three and six months, there was no discernible difference between them. In terms of its safety profile,

myo-inositol came out on top when compared to metformin. These were in-line with the previous study.[24]

REFERENCES

1 Azziz R, Carmina E, Chen Z, Dunaif A, Laven JS, Legro RS, Lizneva D, Natterson-Horowtiz B, Teede HJ, Yildiz BO. Polycystic ovary syndrome. Nat Rev Dis Primers. 2016;267(2):2056–676.

2 Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. Fertil Steril. 2016;106(1):6–15.

3 Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, Piltonen T, Norman RJ, International PCOS Network. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertil Steril. 2018;110(3):364–79

4 Aversa A, La Vignera S, Rago R, Gambineri A, Nappi RE, Calogero AE, Ferlin A. Fundamental concepts and novel aspects of polycystic ovarian syndrome: expert consensus resolutions. Front Endocrinol (Lausanne). 2020;11:516.

5 McCartney CR, Marshall JC. CLINICAL PRACTICE. Polycystic Ovary Syndrome. N Engl J Med. 2016;375(1):54–64.

6 Renato P. Metformin in women with PCOS, Pros. Endocrine. 2015;48(2):422–6.

7 Hoffman, Schorge, Schaffer, Halvorson, Bradshaw, Cunningham. Williams Gynecology, 2 nd edition, chapter 17: pages 460-1.

8 Fritz MA & Speroff L, Clinical Gynecologic Endocrinology, and infertility, 8th edition, chap 12:503-6.

9 Ciampelli M, Fulghesu Am, Cuccinelli F, Pavone V, Ronsisvalle E, Guido M, Caruso A, Lanzone A. Impact of insulin and body mass index on metabolic and endocrine variables in polycystic ovary syndrome. Metabolism. 1999;48(2):167-72.

10 Hoffman, Schorge, Schaffer, Halvorson, Bradshaw, Cunningham. Williams Gynecology, 2nd edition, chapter 17: pages 460-62.

11 Hemraj. B. Chandalia .RSSDI Textbook of Diabetes mellitus, 3rd edition, chap 16:216-8

12 Gilvaz S, Kumari BP. Postgraduate Gynaecology. chap 9. 2011:145-9.

13 Alvin C. Powers. Harrison's principles of internal medicine, 19th edition, volume 2, chap 417: 2405- 06.

14 Antoni J. Medical management of metabolic dysfunction in PCOS. J Steroids. 2012; 77(4): 306-11

15 Govindarajan C, Pitchaipillai R, Shanmugasundaram B, Thangam S, Arokiasamy J, Pillai MS. Myoinositol: a review of its use in patients with polycystic ovary syndrome. World J Pharm Pharmaceut Sci. 2015; 4(6): 137-55.

16 Knochenhauer ES, Key TJ, Kahsar-Miller M, Waggoner W, Boots LR, Azziz R. Prevalence of the polycystic ovary syndrome in unselected black and white women of the southeastern United States: a prospective study. J Clin Endocrinol Metab 1998; 83: 3078– 3082.

17 Dunaif A, Xia J, Book CB, Schenker E, Tang Z. Excessive insulin receptor serine phosphorylation in cultured fibroblasts and in skeletal muscle. A potential mechanism for insulin resistance in the polycystic ovary syndrome. J Clin Invest. 1995; 96: 801–10.

18 Brettenhaler N, De Geyter C, Huber PR, Keller U. Effect of insulin sensitizer pioglitazone on IR, hyperandrogenism and ovulatory dysfunction in women with PCOS. J Clin Endocrinol Metab. 2004; 89(8): 3835–40.

19 Diamanti-Kandarakis E, Christakou CD, Kandaraki E, Economou FN. Metformin: an old medication of new fashion: evolving new molecular mechanisms and clinical implications in polycystic ovary syndrome. Eur J Endocrinol. 2010;162(2):193–212.

20 Rena G, Hardie DG, Pearson ER. The mechanisms of action of metformin. Diabetologia. 2017;60(9):1577–85

21 Angik R, Jajoo SS, Hariharan C, Chimote A. A comparative study of metabolic and hormonal effects of myo inositol versus metformin in women with Polycystic ovary syndrome: a randomized controlled trial. Int J ReprodContraceptObstet Gynecol. 2015 Feb; 4(1): 189-94.

22 Leo VD, Musacchio MC, Cappelli V, Sabatino AD, Tosti C, et al. A Combined Treatment with Myo-Inositol and Monacolin K Improve the Androgen and Lipid Profiles of Insulin-Resistant PCOS Patients. J Metabolic Synd. 2013; 2(2): 100127.

23 Shivani D, Sravanthi P, Jyothi NG. Comparative study on efficacy of myo inositol over metformin in Polycystic ovary syndrome patients. Int J Reprod Contracept Obstet Gynecol 2021;10:1899-905.

24 Zhao H, Xing C, Zhang J, He B. Comparative efficacy of oral insulin sensitizers metformin, thiazolidinediones, inositol, and berberine in improving endocrine and metabolic profiles in women with PCOS: a network meta-analysis. Reprod Health. 2021 Aug 18;18(1):171.