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COMPARISON OF MYO-INOSITOL WITH METFORMIN IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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Abstract

Background: Polycystic Ovarian Syndrome (PCOS) is a hormonal metabolic syndrome that is increasingly affecting women in the current generation. Emerging as a significant health concern, PCOS can disrupt various aspects of women's bodily functions, leading to issues such as menstrual irregularities, pregnancy concerns, acne, and hirsutism, among others. Treatment options for PCOS include Metformin and the more recently introduced Myo-inositol. This article aims to compare the efficacy of both drugs, primarily focusing on menstrual cycle regularity and secondarily on pregnancy rates, symptom improvement, hormonal level enhancement, and adverse effects.

Methodology: A systemic search of articles from PubMed, ResearchGate, and Google Scholar was conducted, resulting in a comprehensive selection of studies published from 2016 onwards. This literature review provides a synthesized overview of existing research to compare the effectiveness of Metformin and Myo-inositol in managing PCOS.

Results: The study reveals that Metformin exhibits a slightly higher improvement rate in menstrual cycle regularity. Conversely, Myo-inositol demonstrates a modestly higher rate of symptomatic improvement, encompassing factors such as cyst morphology, hirsutism, mean weight reduction, and enhancement of hormone levels, coupled with gradual menstrual regularity. Importantly, Myo-inositol shows a comparatively lower incidence of adverse effects.

Conclusion: In conclusion, while Metformin displays a slight advantage in improving menstrual cycle regularity, Myo-inositol proves to be more effective in overall symptom management and hormonal improvement with a decreased likelihood of adverse effects. This study provides evidence-based insights to assist physicians in making informed decisions tailored to the needs of patients, considering their symptoms, the nature of PCOS, and individual physiological responses to drugs.

INTRODUCTION

PCOS, known as polycystic ovarian syndrome, is a condition affecting more women nowadays, marked by hormonal and metabolic irregularities. Its impact on women's daily rhythms is concerning, and its causes are still largely unknown. PCOS affects multiple bodily organs, including the adrenal glands, and disrupts the balance of hormones like estrogen, testosterone, and others from the pituitary gland. The syndrome can be identified through three primary presentations: clinical, metabolic, and endocrine. [1,2]

From a clinical standpoint, individuals may present with irregular periods, pimples, hirsutism, hair loss (alopecia), lack of ovulation, difficulties conceiving, and increased chances of miscarriage. Metabolically, they might display insulin resistance, obesity, abnormalities in lipid levels, and a heightened risk of impaired glucose tolerance, potentially leading to the onset of type 2 diabetes. Regarding endocrine aspects, PCOS may result in elevated androgen levels, luteinizing hormone, and prolactin. While obesity often correlates with PCOS, it's worth noting that this condition can also affect women who are not overweight. Additionally, those with PCOS may grapple with feelings of depression and anxiety. [1,2,3,4]

Recommendations for managing PCOS often include lifestyle changes, particularly focusing on weight loss. In treatment, insulin-sensitizing medications like Metformin (MET) are commonly employed. Metformin is recognized for its positive effects on insulin resistance and regulation of menstrual cycles. It is frequently prescribed to aid in ovulation induction and promote pregnancy. However, its effectiveness may vary, especially for lean individuals compared to those who are overweight or obese, and its side effects may impact overall well-being. Given the complex nature of PCOS and the unclear mechanisms involved, finding a definitive treatment to restore a symptom-free, normal lifestyle remains a challenge. [1]

In recent times, Myo-inositol (MI), a naturally synthesized carbocyclic sugar in the body, has garnered attention for its potential in enhancing the quality of life among women with PCOS. A deficiency in MI can disrupt ovarian function, but supplementation has demonstrated efficacy in alleviating symptoms and promoting ovarian well-being. Naturally occurring in citrus fruits and legumes, MI serves as an insulin sensitizer and has been shown to positively influence insulin resistance in women diagnosed with PCOS. As a dietary supplement, MI is known for its minimal incidence of side effects and is generally well-tolerated, facilitating a gradual and sustained improvement in health outcomes.[2]

The primary objective of this study is to conduct a comparative analysis between the established treatment option metformin and a newly established drug myoinositol which is a naturally occurring substance found in the human body. The comparison will revolve around assessing the efficacy of these two drugs in alleviating symptoms and evaluating their tolerance among women affected with PCOS.

PCOS is a complex medical condition for which there is no pathological explanation. There are several hormonal and metabolic imbalances that are noticed in PCOS which lead to its hypothetical root cause. The morphological characteristic of the disease indicates formation of tiny cysts on the ovaries which in reality are immature ovarian follicles. The main reason as to why these follicles remain immature and cause menstrual irregularities is cause of the androgen imbalance within women and high levels of testosterone. These changes can either inflict other metabolic changes such as insulin imbalance or vice versa. PCOS is also considered to be hereditary. Though hereditary places a role in the condition, it not necessary for every woman to develop PCOS as they grow.

PCOS commonly occurs in obese females. Obesity at any age can be hazardous to health, therefore can mess up the hormone and metabolite profile in women leading to them suffering from PCOS. Though the disease was first commonly noted in obese women and was considered as a “fat women problem”, the condition is not restricted to them alone. Several lean women also suffer from PCOS and remain undiagnosed for a long period of time. This becomes an issue of worry in lean women as delayed diagnosis can lead to damage to ovarian tissue and other complications. (11)

Missed cycles, inflamed ovaries, lower back ache, hirsutism, acne, weight gain, hair loss, infertility, skin tags, skin hyperpigmentation and fatigue and the major symptoms seen in women suffering from PCOS. All these symptoms might not be present all together in women but can have variation and if PCOS remains undiagnosed, the unhealthy and tiring lifestyle can lead to women developing mental health conditions such as anxiety and depression due to PCOS. Therefore, diagnosis of PCOS is very important. It requires the women to be aware of the condition and to look out for discomfort or change in skin, hair and body. Ultrasound for ovarian morphology and blood tests for hormonal and metabolic changes are done to check for PCOS. (9)

The treatment for PCOS varies depending on the symptoms the patient is experiencing and whether the doctor can prescribe MET to the patients. Changes in everyday lifestyle such as exercise and dietary changes are mandatory for maintaining and managing ovarian health and treating the respective symptoms. Recently MI has gained a lot of attention and importance in the treatment of PCOS.

PCOS encompasses various diagnostic criteria, including irregular menstrual cycles, hyperandrogenism, and the presence of polycystic ovaries. It is categorized into two phenotypes: overweight/obese and lean, with the latter being less common. Despite this differentiation, clinical manifestations in both lean and overweight women with PCOS often mirror each other. Similar rates of acanthosis nigricans, menstrual irregularities, hirsutism, and endometrial hyperplasia are observed in both groups, particularly among those struggling with infertility. [8,9,10]

Women diagnosed with polycystic ovary syndrome (PCOS) often experience substantial social and financial pressures, which can exacerbate mental health challenges, including anxiety and depression. According to a recent study, the prevalence rates of anxiety and depression among women with PCOS stand at 38.6% and 25.7%, respectively. Additionally, neurotransmitter imbalances are implicated in PCOS-related depression. Notably, inhibitory neurotransmitters like serotonin, dopamine, gamma-aminobutyric acid (GABA), and acetylcholine are typically reduced in PCOS, whereas levels of glutamate, which stimulates gonadotropin-releasing hormone (GnRH) and luteinizing hormone (LH), are elevated. These neurochemical changes may contribute to the underlying mechanisms of depression observed in women with PCOS.[9]

The complexity of PCOS and the lack of clarity of its causes make it challenging to identify a definitive and universally effective treatment. The most common drug used for PCOS is MET showing positive impact on insulin resistance as well as menstrual cycle. However, it is important to note that while MET can bring about these positive changes, it may not necessarily enhance the quality of life. Whereas MI might just be the perfect alternative to the condition. With bare minimum amount of side effects and improvement in PCOS, the supplement has been shown to improve quality of life.

Metformin which primarily was introduced as a insulin sensitizer has been in use for type 2 diabetes for along time and has been further explored over the year. Some studies suggest that metformin in non-obese women has proven to be beneficial in term of ovulation and regulating the menstrual cycle over other drugs such as oral contraceptive drugs. However, metformin comes with its own adverse effects and has been known to cause discomfort. It has also been recorded that metformin has different effects in obese and non-obese women. Whilst in obese women MET is given to help them with their weight loss and insulin regulation. This does not mean that, in obese women MET will not help regulate ovulation but that it might take time to help in ovulation regulation. (12)

MI on the other hand has proven to have lesser side effects and help all women regulate their menstrual cycles and prevent anovulation. In a clinical trial involving teenagers, it was noted that the group of girls that were given MI had outcomes and the study was suggestive of MI playing an important role in PCOS.(13)

Another randomized clinical trial conducted a study in which 116 infertile women were involved and randomly distributed into two groups and give MET + MI and only MI. The results were recorded after three months and after 6 months and it was noticed that MI had better outcomes than the combined therapy. It was also highlighted that the adverse effects amongst the two groups were higher in the group receiving MET than compared to the group only receiving MI. (14)

Even though these studies showed significant results in comparison and as the individual drug, MI needs to further be explored as an insulin sensitizer and need to be further studied in terms of PCOS.

METHODOLOGY

The investigation involved an analysis of two randomized controlled trials (RCTs), alongside one systematic review, one prospective randomized comparative study, and one retrospective randomized comparative study. Individuals diagnosed with polycystic ovary syndrome (PCOS) were identified based on the Androgen Excess Society (AES) 2006 criteria and the Rotterdam criteria. Subsequently, they were randomly allocated to various treatment groups to assess the effectiveness of metformin and myo-inositol. The duration of these trials ranged from 4 to 6 months.

ELIGIBILITY CRITERIA

The analysis of studies within this research underscores the safety and efficacy of myo- inositol (MI) in comparison to metformin (MET) among women diagnosed with PCOS, without age restrictions. The intervention focused on MI as a sole treatment, irrespective of treatment duration or dosage, and was juxtaposed with MET administered similarly.

The primary endpoint assessed was the enhancement of ovarian function, gauged by the rate of menstrual cycle normalization (reflecting the number of women with regular.

menstrual cycles in each study group). Secondary endpoints included pregnancy rates, body mass index (BMI), markers of carbohydrate metabolism (fasting glucose, fasting insulin, oral glucose tolerance test—OGTT, Homeostatic Model Assessment insulin resistance—HOMA-IR index), clinical and laboratory indicators of hyperandrogenism (hirsutism, testosterone, androstenedione, dehydroepiandrosterone-sulfate—DHEAS, SHBG), and the occurrence of treatment-related adverse effects.

EXCLUSION CRITERIA

Excluded from the study were case studies, clinical trials, cross-sectional studies, and animal studies. Studies that compared more than just myo-inositol and metformin, as well as those focusing on pregnancy outcomes, were not included.

SEARCH STRATEGIES

A comprehensive search strategy was employed, utilizing databases such as PubMed, ResearchGate, and Google Scholar. Additionally, the reference lists of pertinent articles were scrutinized to ensure thorough data collection. The search encompassed records from 2016 to the present, focusing on keywords like "MI for PCOS treatment," "MET for PCOS treatment," and "MI vs MET for PCOS treatment."

RESULTS

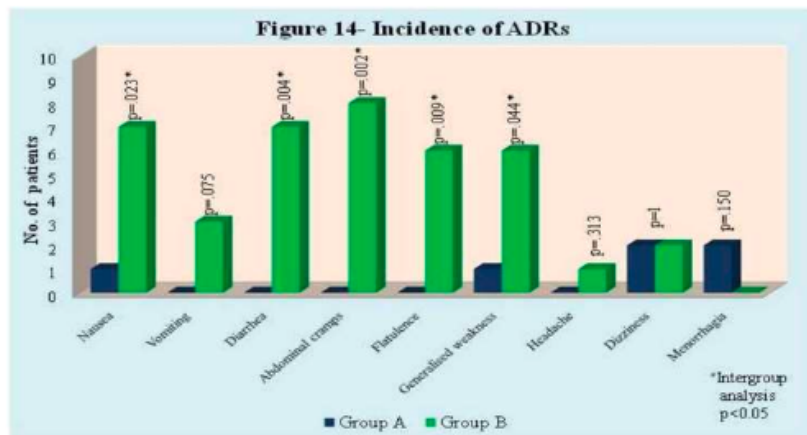


Figure 1

With regard to different treatment modalities of PCOS, it is necessary to note that not every treatment given for a metabolic condition can always provide an easy lifestyle. Keeping in mind the adverse effects and the potential mental health problems PCOS can give rise to, it is necessary to learn more about every treatment option.

The clinical trials demonstrated that both drugs improved menstrual cycles: 87% with MI and 90% with MET. Improvement in polycystic ovarian morphology (PCOM) was observed in 83% of MI cases and 80% of MET cases. The modified Ferriman-Gallwey (mFG) score for assessing hirsutism was 0.83 for MI and 0.93 for MET. Mean weight reduction was 2.76 kg with MI and 2.72 kg with MET. BMI improvement was 1.14 for MI and 1.13 for MET. Acne improvement was noted in 31% of MI cases and 32% of MET cases. MI also reduced free testosterone and androstenedione levels and increased SHBG (sex hormone-binding globulin) levels. Both treatment methods had similar effects on the glycemic profile, triglycerides, VLDL-cholesterol levels, and total testosterone.[3,5,6,7]

Additionally, MI exhibited superior effectiveness in alleviating symptoms of depression and anxiety when compared to MET. Adverse reactions, such as nausea, vomiting, diarrhea, abdominal cramps, flatulence, weakness, headache, dizziness, heavy menstrual bleeding, megaloblastic anemia, and lactic acidosis, were monitored on a monthly basis. The MET group experienced a higher incidence of adverse effects in comparison to the MI group. Figure 1 illustrates the frequency of side effects between Group A (receiving myo-inositol) and Group B (receiving metformin).[6,3]

The figure shown below indicates the number of side effects that are usually seen in patients, and it is recorded in two groups. Group A taking MI and group B taking MET. This is a pictorial representation on how Met even though helpful in reducing the symptoms of PCOS and helping women regulate their menstrual cycle and get back on track with others symptoms, cannot fully feel comfortable as the rate of adverse effects is higher in MET than MI. (3)

DISCUSSION

The study's results suggest that both Metformin (MET) and Myo-inositol (MI) demonstrate positive impacts on various aspects of Polycystic Ovarian Syndrome (PCOS) management. These include improvements in menstrual cycle regularity, reduction in polycystic ovarian morphology (PCOM), and the management of hirsutism, weight, BMI, and acne. Both treatments also show similar effects on glycemic profiles, triglycerides, VLDL-cholesterol, and total testosterone levels. However, MI stands out due to its advantage of causing fewer adverse effects, making it a more tolerable option for women with PCOS. Furthermore, MI exhibits potential in addressing the mental health aspects of PCOS, particularly in improving depression and anxiety, thereby enhancing overall quality of life.

Given the complexity of PCOS and the variability in individual treatment responses, the choice between MET and MI should be made on a case-by-case basis, considering factors such as the patient's specific symptoms, tolerance to side effects, and personal preferences. Future research should focus on investigating the long-term effects of MI as an insulin sensitizer and its broader role in managing PCOS. Nevertheless, MI emerges as a promising first-line treatment option for women with PCOS, offering comparable benefits to MET with minimal adverse effects, ultimately improving the quality of life for those affected by this condition.

CONCLUSION

In summary, polycystic ovarian syndrome (PCOS) is a multifaceted condition with diverse clinical and metabolic ramifications for women. This investigation sought to compare the efficacy and tolerability of two widely utilized PCOS treatments: Metformin (MET) and Myo- inositol (MI).

The findings from this comprehensive analysis reveal that both MET and MI yield favorable outcomes in enhancing menstrual cycle regularity, mitigating polycystic ovarian morphology (PCOM), and addressing concerns like hirsutism, weight management, BMI, and acne.

Moreover, both treatments exhibit similar effects on glycemic profiles, triglycerides, VLDL-cholesterol, and total testosterone levels. However, MI distinguishes itself by boasting fewer adverse effects, rendering it a more tolerable choice for women grappling with PCOS. Notably, MI exhibits promise in ameliorating the depression and anxiety often associated with PCOS, underscoring its potential to address the mental health facets of this condition. Furthermore, it enhances the overall Quality of Life (QoL).

Given the intricacies of PCOS and the individual variabilities in treatment response, the selection between MET and MI should be tailored to each patient, accounting for their specific symptoms, side effect tolerance, and personal preferences. While further investigation is warranted to unveil the long-term implications of MI as an insulin sensitizer and elucidate its role in PCOS management, MI emerges as a compelling alternative or adjunct therapy for women contending with PCOS. It not only promises significant benefits but also offers a superior overall treatment experience with fewer adverse effects.

Considering that MI demonstrates the capacity to produce equivalent results to MET with minimal adverse effects, it warrants strong consideration as the primary treatment choice for women grappling with PCOS.

DECLARATION

Ethical Statement

The research conducted in this study has received approval from the Institutional Review Board/Ethics Committee at Ivane Javakhishvili Tbilisi State University. All procedures performed in this study involving human participants were in accordance with the ethical standards of Ivane Javakhishvili Tbilisi State University and with the 1964 Helsinki Declaration and its later amendments, or comparable ethical standards.

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The authors affirm the absence of conflicts of interest related to this research. No financial or non financial competing interests exist.

Conflicts of Interest

The authors maintain that there are no conflicts of interest related to this research. Neither financial nor non-financial competing interests are present.

Data Availability

The data supporting the findings of this study are comprehensively presented within the article and its supplementary materials. For any additional data, interested parties may request access, and such requests will be considered.

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