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Mohamed Mohamed Ibrahim Farahat
Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

Ahmed Abdelkader El Tabakh
Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

Mahmoud Ahmed Abdelaziz Ibrahim
Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt,
modyaziz6@gmail.com

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ORIGINAL ARTICLE

Myo-inositol Effects on Induction of Ovulation in Women with Polycystic Ovary Syndrome

Mohamed M. I. Farahat, Ahmed A. El Tabakh, Mahmoud A. A. Ibrahim *

Department of Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

Abstract

Background: ***A long-term, multi-systemic metabolic-endocrine condition known as polycystic ovarian syndrome (PCOS) raises the risk of female neoplasms and has an impact on reproductive health.***

Aim and objectives: ***In order to assess the impact of Myo-inositol (MI) supplementation on ovulatory function and fertility in a woman with polycystic ovarian syndrome.***

Patients and methods: ***This prospective observational cohort investigation was conducted on 200 patients with PCOS at Al-Hussein University Hospital.***

Results: ***Hirsutism was found in 42.5%, acne was found in 50.5%, and alopecia was found in 14.5%. The median number of follicles was 2.32 ± 1.32, and the median largest follicle diameter was 15.9 ± 0.271 mm. There was a substantial decrease in serum androstenedione, total testosterone, and free testosterone post myo-inositol. Moreover, there is a substantial rise in serum progesterone post myo-inositol. Sixty-six 66% of the patients showed ovulation with a mean ovulation time of 14.74 ± 1.32. Moreover, 12% of the patients showed menstrual bleeding abnormality, and 78% of the patients showed restoration of spontaneous ovarian activity. While 51% of the patients were positive for pregnancy.***

Conclusion: ***For PCOS women, myo-inositol treatment is a safe, efficient method of ovulation induction and conception. They have resulted in considerable restoration of spontaneous ovarian activity and improvement in pregnancy rate.***

Keywords: Myo-inositol; Ovulation; Polycystic ovary syndrome

1. Introduction

A long-term, multisystemic metabolic-endocrine condition known as polycystic ovarian syndrome (PCOS) raises the risk of female neoplasms and has an impact on reproductive health. Anovulation and clinical or biochemical hyperandrogenism are the traditional characteristics of PCOS. Its estimated frequency in adult women varies greatly and may be as high as 11.2%, depending on the series used.[1]

It affects 5% to 10% of women who are of reproductive age and is the most prevalent cause of infertility.[2]

Two distinct mechanisms by which the associated hyperinsulinemia may cause PCOS women to create an excess of androgens are direct stimulation of the ovaries to make androgens and a decrease in blood levels of sex hormone binding globulin (SHBG).[3]

Inositol isoforms are a part of the vitamin B complex. Myo-inositol (MI) and D-chiro-inositol are two of the nine stereoisomers that are formed when inositol's six hydroxyl groups epimerize. While D-chiro-inositol, which is the byproduct of the epimerization of MI's C1 hydroxyl group, is relatively uncommon, MI is abundantly dispersed in nature.[4]

A measure of high-quality oocytes and elevated MI content in human follicular fluid is related to follicular maturity. Additionally, studies using mouse oocytes showed that adding MI to the culture media accelerated the meiotic development of germinal vesicles by improving intracellular Ca2þ oscillation.[5]

In order to get pregnant, many women with PCOS need to use assisted reproductive procedures. However, low egg quality is the primary cause of fertilization failure in over 60% of in vitro fertilization (IVF) cycles that end in pregnancy failure. As a result, the goal of assisted reproductive technologies nowadays is to produce oocytes of superior quality as opposed to large quantities of oocytes and embryos.[6,7]

This research aimed to assess the impact of Myo-inositol (MI) on ovulatory function and fertility in a woman with polycystic ovarian syndrome.

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* Corresponding author at: Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt.
E-mail address: modyaziz6@gmail.com (M. A. A. Ibrahim).

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2. Patients and methods

This prospective observational cohort investigation had 200 patients with PCOS at Al-Hussein University Hospital.

Sample size: The research that served as the basis for this one was conducted by Costantino et al.,[8] Epi Info STATCALC, which was utilized to determine the sample size based on the following assumptions: 80% power and a two-sided confidence level of 95%. & 5% inaccuracy in α. 186 was the final maximum sample size that could be obtained from the Epi-Info output.

As a result, 200 participants were included in the sample to account for potential dropout instances during follow-up.

x = Z(c/100)^2 r(100-r)

n = N x/((N-1)E2 + x)

E = Sqrt[(N - n)x/n(N-1)]

where Z(c/100) is the critical value for the confidence level c, N is the population size, and r is the proportion of replies that you are interested in.

CI 95%

Recommended sample size 200

Inclusion criteria: Women with age ranges from 20 to 35 years with BMI 20-30 kg/m2, women with PCOS diagnosed according to Rotterdam[9]. defined by raised free testosterone stages, which are defined as the upper quartile of free testosterone levels in PCOS women (>11 nmol/l), free of other medical diseases, no allergy to myo-inositol, a regular male partner, and CASA pass WHO criteria 2021. oligo- or amenorrhea, which is defined as six or fewer menstrual cycles over a year; hyperandrogenism, which includes hirsutism, acne, or alopecia; and typical ovarian features on an ultrasound scan.

Exclusion criteria: Hormonal testing ruled out other diseases that cause ovulatory failure, such as hypothyroidism, hyperprolactinemia, and androgen excess, like Cushing's syndrome or adrenal hyperplasia.

Methods:

All women were subjected to complete history taking, physical examinations, and general examinations; Examination included (abdominal and local clinical Examination: abdominal inspection, palpation, percussion (percuss the liver, the spleen, and the bladder and assess shifting dullness), auscultation and deep palpation of the abdomen, pelvic exam, vulvar Examination, vaginal Examination, and bimanual Examination) and investigational studies.

We began by reviewing a review of the exterior and then the vulva. We examined the vulvar anatomy's fundamental development, symmetry, hair distribution, lesions, discharge, growths, erythema, bruising, swelling, and pain of any anomalies.

We felt the labia to check for soreness or growth. To do this, the thumb was placed on the perineal region while the index finger was inserted into the vaginal entrance. Next, the fingers were run along each labia, feeling for soreness, cysts, abscesses, and nodules. The internal speculum examination came next.

Vulvar Examination: A fundamental developmental assessment, symmetry, hair quality and growth distribution, skin anomalies, swelling, ulcerations, growths such as tumors or external genital warts (EGW), rashes, lacerations, piercings, bruises, and discharge were all included in the Examination of the vulvar region.

Vaginal Examination: The hymenal ring was seen by carefully separating the labia minora. It was simpler to insert the speculum because light pressure on the bulbocavernosus muscle relaxes the vaginal walls, particularly posteriorly. A cystocele, urethrocele, cystourethrocele, or rectocele, along or apart from a vaginal wall defect or prolapse, might be assessed.

Bimanual ExThe aim of the bimanual Examination was to determine the uterus's dimensions and whether or not there were any examinations. The assessment included uterine movement and tenderness, and any adnexa discomfort should be documented. Many premenopausal women with typical habits have palpable ovaries.

Procedure: Myoinositol 2gm and folic acid 200mg (inofolic; Ibsa pharma) were given orally to PCOS women twice a day for the duration of the trial or until a positive pregnancy test resulted. The weekly plasma progesterone levels of less than 2.5 ng/ml were used to determine anovulation. Thus, we ascertain the most probable reason for the couple's subfertility at the conclusion of the diagnostic process. Patients were advised to document any menstrual bleeding throughout the six-month follow-up period. Additionally, weekly measurements of blood progesterone and testosterone levels, together with a transvaginal ultrasound scan to record the existence of luteal cysts or follicular development, were carried out during the first menstrual cycle to assess the restoration of spontaneous ovarian activity. The two-tailed t-test was used to compare the hormone concentrations before and after therapy statistically. Additionally, the detection of a baby's heartbeat on an ultrasound examination and a positive plasma b-human chorionic gonadotropin test verified any future pregnancies.

Folliculometry, serum-free and total testosterone, serum androstenedione, serum progesterone, and plasma B human Chorionic gonadotropin were used for follow-up.

Ethical Consideration: Informed permission was obtained for every patient and control group included in the study. Every safety measure was implemented to protect the patients' privacy. All

the findings should be used only for scientific purposes. Prior to beginning the study, approval was obtained from the Alazhar Faculty of Medicine's institutional review board (IRB).

3. Results

Table 1. Demographic information regarding the patients

	STUDIED PATIENTS (N=200)	
	Mean ± SD	Range
AGE (YEARS)	28.51 ± 2.69	23 - 34
BMI (KG/M²)	26.68 ± 2.1	20.6 - 29.9
RESIDENCE	N	%
RURAL	93	46.5%
URBAN	107	53.5%

Table 1 showed that mean age was 28.51 ± 2.69 years with mean BMI was 26.68 ± 2.1 kg/m2. Regarding residence, 46.5% of the patients were rural and 53.5% of the patients were urban.

Table 2. Clinical characteristics distribution among the studied patients.

	STUDIED PATIENTS (N=200)
OVARIAN VOLUME (CM³) MEAN ± SD	11.07 ± 1.34
LH (IU/L) MEAN ± SD	6.38 ± 1.64
FSH (IU/L) MEAN ± SD	4.74 ± 0.529
MENSTRUAL CYCLE REGULARITY	
REGULAR	76 (38%)
OLIGO/ANOVULATION	136 (68%)

Table 2 showed that mean ovarian volume was 11.07 ± 1.34 mm3 with mean LH was 6.38 ± 1.64 IU/L and mean FSH was 4.74 ± 0.529 IU/L. Moreover, 38% of the patients showed regular menstrual cycle and 68% of the patients presented with oligo/anovulation.

Table 3. Clinical presentation distribution among the studied patients.

	STUDIED PATIENTS (N=200)	
	N	%
HIRSUTISM	85	42.5%
ACNE	101	50.5%
ALOPECIA	29	14.5%

Table 3 showed that hirsutism was found in 42.5%, acne was found in 50.5% and alopecia was found in 14.5%.

Table 4. Follicle characteristics of the studied patients

	STUDIED PATIENTS (N=200)
NUMBER OF FOLLICLES MEAN ± SD	2.32 ± 1.32
LARGEST FOLLICLE DIAMETER MEAN ± SD	15.9 ± 2.71

Table 4 showed that mean number of follicles was 2.32 ± 1.32 and mean largest follicle diameter was 15.9 ± 0.271 mm.

Table 5. Laboratory data of the studied patients

	STUDIED PATIENTS (N=200)		P
	Pre	Post	
SERUM ANDROSTENEDIONE(NG/DL) MEAN ± SD	230.75 ± 20.1	203.45 ± 18.25	<0.001
SERUM PROGESTERONE MEAN ± SD(NG/ML)	1.9 ± 0.755	10.25 ± 2.38	<0.001
TOTAL TESTOSTERONE (NG/DL) MEAN ± SD	90.11 ± 8.47	47.17 ± 2.18	<0.001
FREE TESTOSTERONE (NG/DL) MEAN ± SD	0.943 ± 0.141	0.371 ± 0.059	<0.001

Table 5 showed that there was a substantial reduction in serum androstenedione, total testosterone, and free testosterone post myo-inositol. Moreover, there is a substantial increase in serum progesterone post myo-inositol.

Table 6. Outcome distribution among the studied patients

	STUDIED PATIENTS (N=200)
OVULATION	132 (66%)
OVULATION TIME MEAN ± SD	14.74 ± 1.32
MENSTRUAL BLEEDING ABNORMALITY	24 (12%)
RESTORATION OF SPONTANEOUS OVARIAN ACTIVITY	156 (78%)
PREGNANCY RATE	102 (51%)

Table 6 showed that 66% of the patients showed ovulation with mean ovulation time was 14.74 ± 1.32. Moreover, 12% of the patients showed menstrual bleeding abnormality and 78% of the patients showed restoration of spontaneous ovarian activity, while 51% of the patients were positive pregnancy.

4. Discussion

Regarding demographic information, the current study showed that the median age was 28.51 ± 2.69 years, with a mean BMI of 26.68 ± 2.1 kg/m2. Regarding residence, 46.5% of the patients were rural, and 53.5% of the patients were urban.

Polycystic ovary syndrome (PCOS) is the most prevalent endocrine disorder that impacts women of reproductive age, influencing an estimated 1 in 10 women prior to menopause. Comparable to the current study, Anu et al.,[10] revealed that the mean age of patients with PCOS who received Myo-inositol treatment was 26.70±6.78 years. Also, Kamenov et al.[11] revealed that the mean age of women with PCOS who received Myo-inositol treatment was 24.9 ± 5.1 years with a mean BMI of 24.0 ± 5.2 kg/m2.

Regarding clinical data, the current research showed that the mean ovarian volume was 11.07 ± 1.34 cm3, the mean LH was 6.38 ± 1.64 IU/L, and the mean FSH was 4.74 ± 0.529 IU/L.

Moreover, 38% of the patients showed a regular menstrual cycle, and 68% of the patients presented with oligo/anovulation.

In line with the current study, Anu et al.,[10] revealed that all patients have ovarian volumes greater than 10 ml. They also found a significant reduction in ovarian volume post-treatment with Myo-inositol (p-value—0.001).

Comparable to the current research, Rani et al.[12] showed that the median LH was 6.4±2.2 IU/L and median FSH was 5.2±1.4 IU/L among women with PCOS who received Myo-inositol treatment.

Regarding the Follicle characteristics of the studied patients, the mean number of follicles was 2.32 ± 1.32, and the median largest follicle diameter was 15.9 ± 0.271 mm.

Colazingari et al.,[13] showed that Myo-inositol lowers the risk of ovarian hyperstimulation by decreasing levels of estradiol on the day of ovulation trigger, decreasing the number of intermediate-sized follicles and increasing the number of large follicles (without enhancing the total number of oocytes retrieved). PCOS-afflicted women are more likely to get pregnant, have better oocyte maturation and quality, have higher cleavage rates, and create larger, higher-quality embryos.

Regarding clinical presentation, the current study showed that 42.5% had hirsutism, 50.5% had acne, and 14.5% had alopecia.

In concordance with the current study, Anu et al.,[10] showed that hirsutism was found in 45% and acne in 28%. However, Kamenov et al.[11] showed that hirsutism was found in 60%.

Regarding the change in laboratory data pre- and post-treatment, the current study showed that Following myoinositol, serum androstenedione, total testosterone, and free testosterone all significantly decreased. Additionally, serum progesterone significantly rose after myoinositol.

In concordance with the current study, a multicentric study by Hernandez et al.,[14] where 34 PCOS patients who were insulin-resistant after receiving myo-Ins and α-LA for six months reported considerable changes in their levels of androstenedione, HOMA-index, and insulinemia.

Also, the current study was supported by Rani et al.,[12] who evaluated the effects of metformin alone with metformin + Myo-inositol as a pre-treatment for ovulation induction in patients with insulin resistance and polycystic ovarian syndrome and revealed that adding myo-inositol to metformin resulted in a significant increase in serum progesterone level.

Regarding outcome, the current study revealed that 66% of the patients showed ovulation, with a mean ovulation time of 11.34 ± 2.46. Moreover, 12% of the patients showed menstrual bleeding abnormality, 78% of the patients showed restoration of spontaneous ovarian activity, and 51% of the patients were positive for pregnancy.

In line with the current study, Le Donne et al.[15] showed that the MI-treated group had a substantially greater ovulation frequency (25%) and a shorter latency to first ovulation (15%) than the placebo group.

Also, in harmony with the current study, an observational study by Regidor& Schindler[16] comprising 3602 infertile women with PCOS MI and folic acid therapy for an average of 10.2 weeks, led to 545 pregnancies (15.1% of all MI-medicated patients) and the restoration of ovulation in 70% of the women.

Limitations: The present investigation was limited by the small sample size, absence of a control group, single-center design, and short follow-up time. Further comparative research, including bigger sample sizes and longer follow-up times, is required to validate our findings and determine the risk variables associated with pregnancy failure.

4. Conclusion

For PCOS women, Myo-inositol treatment is a safe, efficient method of ovulation induction and conception. It resulted in considerable restoration of spontaneous ovarian activity and improvement in pregnancy rate.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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There are no conflicts of interest.

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