

## Role of Myo-Inositol in Treatment of Young Females Affected By Polycystic Ovarian Syndrome: Quasi Experimental Study

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### ABSTRACT

**Objective:** To determine the effects of Myo- inositol in young females with polycystic ovarian syndrome.

**Study Design and Setting:** This was a quasi-experimental study and was conducted in United Medical and Dental College and Creek General Hospital from January 2017 to January 2018.

**Methodology:** Total 100 patients were recruited based on the specific inclusion criteria of PCO diagnosed by symptoms (body mass index, menstrual irregularity, hirsutism, acne) biochemical markers (fasting insulin, random blood sugar) and ultrasound findings. Each subject in the study group was given sachet (Myo- inositol 2000mg and folic acid 400ug) once a day dissolved in glass of water for duration of 6 months. Improvement in symptoms, biochemical markers and ultrasound findings were reassessed after the completion of 6 months duration. The SPSS version 21 was used for data analysis. The paired T test was used to assess the effects of Myo-Inositol before treatment and after six months of treatment.

**Result:** The significant relation (0.001) was observed between the intervention and PCO and its related symptoms. An evident effect was noticed in each individual after the intervention was provided to them. The relatable symptoms such as irregularities in menses, hirsutism, weight and insulin resistance were reduced by significant ratio.

**Conclusion:** Myo – inositol has proven to be effective in reducing the PCO and its relatable symptoms in young females. Despite the limitations, enough evidence was collected that indicated a significant effect of the intervention.

**Key words:** Polycystic Ovarian Syndrome, young females, myo-inositol

### INTRODUCTION:

Polycystic ovary syndrome is a common hyperandrogenic disorder, resulting from escalating androgen hormone production. It is observed that 20 % of the reproductive age women suffer from this disorder.<sup>1</sup>

Guidelines from the Endocrine Society recommend using the Rotterdam criteria for diagnosis, which mandate the presence of two of the following three findings- hyperandrogenism, ovulatory dysfunction, and polycystic ovaries-plus the exclusion of other diagnoses that could result in hyperandrogenism or ovulatory dysfunction.<sup>2</sup>

The mechanisms leading to insulin resistance consist of a defect in insulin binding to its receptor or to changes in insulin signal transmission. However, the ovaries of these women maintain approximately a normal response to insulin. A partial elucidation of this mechanism is explained by the action of insulin on the ovary through the IGF-1 receptor. This binding occurs when insulin reaches high concentrations, as compensatory hyperinsulinemia. Moreover, the action of insulin on the ovary uses the inositol glycan system as a

signal mediator, a different mechanism from the system activated by phosphorylation of the receptor at tyrosine level in other tissues. An increase was observed in urinary clearance of inositol in some American and Greek women with PCOS. It reduces tissue availability of inositol. This mechanism could contribute to insulin resistance present in PCOS women.<sup>3</sup>

Due to the key role of insulin in the syndrome, insulin sensitizers such as metformin have been considered as possible therapeutic option in the management of these problems. Metformin has been used on patients with a hyperinsulinemic status for the improvement of ovarian dysfunction with consecutive anovulation, irregular menstrual cycles, and infertility problems.<sup>4</sup> Nevertheless, metformin, when used in the therapeutic dose range, was shown to have several side effects such as flatulence, diarrhea, and nausea, so that many patients are unable to use this treatment option in gynecology for a longer period of time.<sup>5</sup> Therefore, in parallel to the common use of metformin and other insulin sensitizer agents for the treatment of PCOS, in the recent years, other therapeutic alternatives have been investigated.<sup>6</sup>

Inositol is a member of vitamin B family; among nine forms of inositol, myo (MYO) and d-chiro-inositol (DCI) are the types, which have provided a beneficial result for treating the PCOS in current researches. The reason being that there is a defect in the secondary messenger of the women suffering from PCOs. Therefore, MYO-inositol in this situation acts as a secondary messenger to reduce the disturbance in the signalling pathway.<sup>7</sup>

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Based on the published results, both MI and DCI represent potential valid therapeutic approaches for the treatment of insulin resistance and its associated metabolic and reproductive disorders.. Furthermore, the combination MI/DCI seems also effective and might be even superior to either inositol species alone.<sup>8</sup> The use of 2×2000 mg Myo-inositol 2×200µg folic acid per day is a safe and promising tool in the effective improvement of symptoms and infertility for patients with polycystic ovary syndrome.<sup>9</sup>

The intervention of Myo - inositol have also shown effective result in other trials with an increase in HDL levels, resulting in weight loss. Myo inositol intervention resulted in lowering of insulin levels, triglycerides, testosterone, and blood pressure in women with PCOS.<sup>10</sup>

D-chiroinositol functions as an intracellular messenger in this process, which supports ovulation and improve fertility while Myo is responsible for increasing the insulin sensitivity.<sup>11</sup> Therefore; this study was aimed to evaluate the effects of myo- inositol in the treatment of young females affected by polycystic ovarian syndrome.

#### METHODOLOGY:

This was a quasi-experimental study design; to determine the effects of myo inositol in young females suffering from polycystic ovarian syndrome. This study was conducted in United Medical and Dental College and Creek General Hospital from January 2017 to January 2018. The inclusion criteria was women from aged 18 to 30 years and diagnosed with PCO on the basis of currently accepted criteria which include hyperandrogenism, anovulation and/ or polycystic ovaries as observed on ultrasonography.<sup>12</sup> PCOS is also accompanied by a number of metabolic disorders, such as insulin resistance, hyperinsulinemia, and obesity so women having BMI > 18kg/m<sup>2</sup> fasting insulin > 12mIU/L were also included in study. Other causes of hyperandrogenism (such as congenital adrenal hyperplasia or androgen-secretory tumours) and ovarian dysfunction (such as hyperprolactinaemia or thyroid gland impairment) were excluded.

Based on the inclusion criteria 100 subjects were enrolled in the study by non-randomization sampling technique. A single page leaflet was used to explain the study to the patients and the students in order to enrol them in the study. The subjects who were ready to participate in the study were given an informed consent to sign and fill a questionnaire. This study was executed by the approval obtained from Institutional Review Board. The women started with the intake of Myoinositol and folic acid at a dosage of 2000 mg Myoinositol and 400 µg folic acid/day and used it for 6 months. The primary outcome of the study was to determine the restoration of normal menstrual cycles, improvement in acne, reduction in hirsutism and weight loss. The data was collected through performa. The variables, which were assessed in the study include hirsutism, acne, ultrasound findings, BMI, random sugar level and fasting insulin levels.

The paired t Test was used to analyse the data before and after 6 months of treatment with Myoinositol and folic acid at a dosage of 2000 mg Myoinositol and 400 µg folic acid/day and used it for 6 months. After data collection, the results were analysed using SPSS version 21. The final results were displayed in the form of a bar chart and pie chart that displayed the difference between the variables evidently. P value > 0.05 was considered as statistically significant.

#### RESULT:

The data of 100 patients with PCO was evaluated. Table 1 shows BMI reduced to 25.59 in treated subjects from pre-treatment level of 27.03, lower level of random blood sugar were observed from pre-treatment value of 115.25 to 112.76 and fasting insulin levels reduced from 17.62 to 16.29 after the treatment.

Figure 1: According to the record menstrual cycle abnormalities improved significantly after the treatment. Oligomenorrhea reduced from 39% to 23 % in total number of subjects evaluated. 57% had regular cycles before starting treatment which increased to 73% after the treatment.

73% presented with hirsutism out of which 37 % showed significant reduction in hair growth. While only in 10% improvement in facial acne was observed.

Figure 2: In the studied subjects, 97% had ultrasound features of PCO. Out of these 57% patients had improvement while 43% subjects showed no change. It was also noticed that 81% subject had Myoinositol as 1<sup>st</sup> line treatment for PCO while 1% had already used oral contraceptive pills, 4% used anti androgenic hormonal therapy, 13 % used Glucophage in dose of 500mgTDS while 1% subjects used 250 mg Glucophage tds before this therapy. The evaluation of role of Myo inositol was not done in each group separately. All of these treatments were stopped before starting Myo inositol.

Regarding effect of diet control and exercise ,26% subjects had diet control along with treatment while 14% did exercise.

#### DISCUSSION:

As compared to a study conducted by Naz MSG et.al.<sup>13</sup> published in Sep 2019 the prevalence of polycystic ovarian syndrome in adolescents based on the Rotterdam criteria was 11.04% (95% CI: 6.84-16.09%)<sup>13</sup>. According to their result there is a variation in the prevalence of PCOS in adolescents based on different criteria. In our study the age group of 20 – 24 years occupied majority of the sample size.

Table 1 Paired t Test

|                 | Pre            | Post          | P-Value |
|-----------------|----------------|---------------|---------|
| BMI             | 27.03 ± 3.19   | 25.59 ± 2.66  | 0.000** |
| RBS             | 115.25 ± 16.09 | 112.76 ± 13.9 | 0.000** |
| Fasting Insulin | 17.62 ± 5.15   | 16.29 ± 4.07  | 0.000** |

Note: \* Significant at 0.05; \*\* significant at 0.01

Table 2: Proportion Testing

|                   |                      | Pre | Post | P-Value |
|-------------------|----------------------|-----|------|---------|
| Menstrual Cycle   | Regular              | 57% | 73%  | 0.02*   |
|                   | Polymenorrhea        | 2%  | 2%   | 1.00    |
|                   | Secondary Amenorrhea | 2%  | 2%   | 1.00    |
|                   | Oligomenorrhea       | 39% | 23%  | 0.01*   |
| Hirsutism         | Yes                  | 73% | 36%  | 0.00**  |
|                   | No                   | 27% | 27%  | 1.00    |
|                   | Improved             | 0%  | 37%  | 0.00**  |
| Facial Acne       | Yes                  | 94% | 84%  | 0.02*   |
|                   | No                   | 6%  | 6%   | 1.00    |
|                   | Improved             | 0%  | 10%  | 0.00**  |
| Ultrasound Pelvis | PCO                  | 97% | 43%  | 0.00**  |
|                   | Normal               | 3%  | 57%  | 0.00**  |

Note: \*Significant at 0.05; \*\*significant at 0.01

Figure 1: Menstrual Cycle

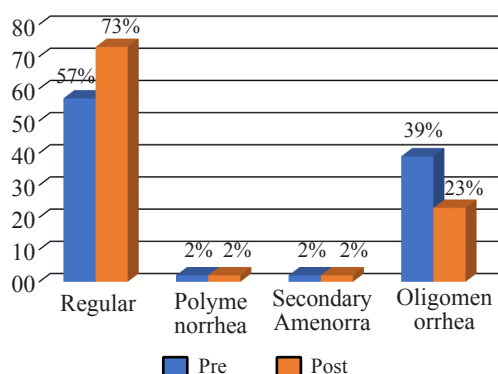
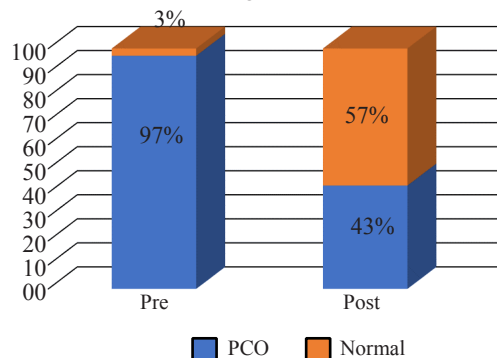


Figure 2: PCOs



This validated our study, which aimed to identify the effects of our treatment in young females.

The data collected showed a significant relation of the PCO with BMI as compared to a study done by Wang FF et al<sup>14</sup>, 42% of the PCOS had normal BMI, but clinical and hormonal profile was similar to PCOS patients with elevated BMI (overweight/obese). In our study the mean BMI was  $27.03 \pm 3.19$  which improved to  $25.59 \pm 2.66$ . Similarly significant

association was seen between the random blood sugar level and fasting insulin levels with PCO in young females.

Our results are comparable to the study conducted by Unfer V<sup>15</sup>, which showed Myo-inositol (MI) and D-chiro-inositol, two inositol stereoisomers, have been proven to be effective in PCOS treatment. However, in our study only MI has been shown to have beneficial effects on androgenic symptoms, whereas the administration of MI/D-chiro-inositol, in the physiological plasma ratio (i.e., 40:1) ensures better clinical results, such as the reduction of insulin resistance, androgens' blood levels, cardiovascular risk.

By Nordio M, Proietti E<sup>16</sup> the combined administration of MI and DCI in physiological plasma ratio (40:1) should be considered as the first line approach in PCOS overweight patients, being able to reduce the metabolic and clinical alteration of PCOS and, therefore, reduce the risk of metabolic syndrome, as compared to our study which showed significant weight loss by improving patient's BMI with myoinositol alone and folic acid without D-chiro.

Bevilacqua A, Bizzarri M<sup>17</sup> clinical data support the beneficial effects exerted by inositol by reducing glycaemia levels and hyperinsulinemia and buffering negative effects of sustained insulin stimulation upon the adipose tissue and the endocrine system. Due to these multiple effects, Myoinositols has become a reliable treatment option, as opposed to hormonal stimulation, for insulin-resistant PCOS patients. Viewing the frequency table of fasting insulin level, it can be observed that though majority of the insulin levels were  $17.62 \pm 5.15$ , indicates these young females are at risk of increase in insulin resistance.

Nas K, Tû L.<sup>18</sup> All the groups showed significant improvement ( $p < 0.05$ ) in prolactin and progesterone level after the treatment. Furthermore, the treated groups reported a significant improvement in the menstrual cycle disorders, while only life-style group showed an increase which was not statistically significant ( $p > 0.05$ ). After 6 months follow up, data was collected, to compare the results after the use of myo – inositol. The outcome displayed a significant effect (0.01) of myo-inositol in regulating the irregularities of the menses. Conclusion can be driven that females undergoing irregularities in menses can take this intervention.

Furthermore, the other symptoms hirsutism and acne, both showed different outcomes. Myo-inositol was successful in reducing the condition of hirsutism from 73% to 36.6 % while acne incidence reduced from 94.3 % to 84%. Therefore, it can be said that hirsutism is related to the hormonal imbalance while acne is associated with several factors; hence, does not portrair a definite relation with hormonal imbalance.<sup>19</sup>

Further after overviewing the entire result, it can be noted that Myo – inositol was not successful in treating entire sample of the young females, The reason for this can be deduced from the other studies that defect in the secondary

messenger is not the only reason for the disturbance in hormonal imbalance. Other reasons such as genetics or associated disorders can be responsible for irregular menses which eventually could lead to development of PCO; hence, this is supported by the results computed which displays a significant relation between the menstrual cycle and PCO<sup>20</sup>.

Advani K et al conducted a study to evaluate the efficacy and safety of the supplementation. They have suggested that combination therapy can be used for the comprehensive management of PCOS. Monotherapy of insulin sensitising agents, antioxidants and vitamins is beneficial in the treatment of PCOS. Combined use of insulin sensitising agents (myo-inositol, D-chiro-inositol and chromium picolinate), antioxidants (N-acetylcysteine and lycopene), and vitamins (vitamin D, biotin and folic acid) is safe and effective in obese and non-obese women with PCOS<sup>21</sup>.

As per a study by McBreaity LE,<sup>22</sup> diet control and exercise are considered as an additive factor, which supports the efficacy of the myo-inositol in playing an integral role as a secondary messenger in increasing the insulin sensitivity; thus, reduces any disruption in hormonal balance that can lead to obesity.<sup>22</sup> Hence, it can be stated that the role of the lifestyle balance is responsible in increasing the insulin sensitivity and lowering the BMI that maintains harmony in the body functions. The study holds some limitations, which leaves a gap in the literature to be further assessed. The blood sugar level taken was random rather than fasting, which would have given a more clear idea of high sugar level. The use of metformin, diet, exercise and other therapies was not evaluated as integrated treatment with Myo inositol. Myo-inositol used over last decade has been successful in treating insulin sensitivity. Use of Myo inositol in the PCO has displayed an evident result in our study conducted. The outcome displayed that Myo - inositol was successful in improving androgenic and metabolic effects of PCO syndrome. This improves compliance of the use resulting in better outcomes in the management of menstrual irregularities, hyperandrogenism, and metabolic parameters.

## CONCLUSION:

This concludes that Myoinositol is an effective alternative in the treatment of PCOS. It's a safe option in young females with no side effects in the standard dosage.

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