Effect of Myoinositol (MI) In Patients of Polycystic Ovarian Disease (PCOD)

Authors

Dr Jayshree Awalekar¹, Dr Chidanand Awalekar², Dr M. H. Patwardhan³

¹M.D, Professor, Dept of Medicine, Bharati Vidyapeeth Deemed University Medical College & Hospital, Sangli
Email: jaysri2065@gmail.com, Mobile: 09422045082 Fax No. : 0233-2601201

²M.D, Professor & Head Of Dept, Medicine, Bharati Vidyapeeth Deemed University Medical College & Hospital, Sangli
Email: awalekar11cd7@gmail.com, Fax No. : 0233-2601201, Mobile: 09422045081

³M.D.D.M. (Endocrinology), Patwardhan Endocronology Clinic & Research Centre, Miraj
Email: rajapatwardhan@yahoo.co.in, Mobile: 09860615285 Fax No. : 0233-2601201

Abstract

Polycystic ovarian disease (PCOD) is a common endocrine disorder. Majority of young females are affected. Insulin resistance along with dysfunction of hypothalamo pituitary adrenal axis is a key etiological factor in development of all manifestations of PCOD. They present with irregular menses, infertility, obesity, hirsutism, acanthosis Nigricans etc. MI(MI),an insulin sensitizer is widely accepted treatment modality. Data suggests variable r responses to MI. So we aimed to study efficacy of MI in PCOS. Here 32 cases are recruited those diagnosed by using Rotterdam’s criteria .BMI, menstrual irregularity, infertility, hirsutism, acanthosis Nigricans, acne were common presenting features. Hormonal & biochemical profile was studied S.LH (Luteinizing Hormone), FSH (Follicle stimulating hormone), Serum. Prolactin levels, Serum Insulin levels were studied. Weight loss, menstrual regularity, LH/FSH Ratio, HOMA Index was studied initially & compared all parameters after 3 months of treatment. In our study BMI mean was 26.71, after MI treatment it became 25.6. Differences of all parameters before & after MI suggests, there is significant reduction in BMI & LH/FSH ratio. Other parameters are not affected by MI. It suggests MI has been effective in reducing BMI & LH/ FSH ratio significantly. But there was no change in HOMA index. So MI can be good supportive treatment option in PCOD.

The present study gives us idea about efficacy of MI treatment in PCOD cases & will be useful in patient treatment schedules.

Keywords- PCOD (Polycystic ovarian Disease), Hyperinsulinemia, Myoinositol (MI), Body Mass Index (BMI), LH/FSH-Luteinizing hormone & Follicle stimulating hormone ratio, HOMA index-Homeostatic model assessment.

Introduction

Nowadays Poly Cystic Ovarian Disease (PCOD) is commonest endocrine disorder in young females. It is characterised by insulin resistance & is strongly implicated in its aetiology. "Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan". In 2003 a consensus workshop sponsored by ESHRE/ASRM in Rotterdam indicated PCOS to be present if any 2 out of 3 criteria are met, it also includes many women without androgen excess too. Rotterdam’s criteria are widely accepted.
1) Oligoovulation and/or anovulation.
2) Excess androgen activity.
3) Polycystic ovaries (by ultrasound).
4) Other entities are excluded that would cause these.\(^{(5,7)}\)

PCOS patients present with menstrual irregularities like amenorrhea, oligomenorrhoea about half of them have infertility because of anovulation caused by hormonal dysfunction & insulin resistance. Hirsutism, acne, obesity, miscarriages, hypertension, Ischaemic Heart Disease, diabetes, sleep apnoea etc \(^{(2,3,8)}\).

The population studies revealed first, that overt and occult PCOD accounted for 90% of patients with oligomenorrhoea and 37% with amenorrhea, or 73% with oligo or amenorrhea. Oligo or amenorrhea accounted for 21% of couples with infertility and the annual incidence was 247 patients per million of the general population. The annual incidence of infertility due to PCOD per million was 41 with overt PCOD and 139 with occult PCOD (total 180). Of those, 140 appeared to respond well to clomiphene (78%) but 40 (22%) failed, requiring alternative therapy \(^{(4,5)}\).

Insulin resistance & obesity is observed in majority of PCOD patients. Elevated insulin levels cause abnormal functioning of hypothalamic-pituitary-ovarian axis that lead to PCOS. Women with PCOS experience an increased frequency of hypothalamic GnRH pulses, which in turn results in an increase in the LH/FSH ratio \(^{(4,5,8)}\).

Insulin resistance is main causative factor for all these consequences & morbidity. Failure of the target cells to respond to normal or ordinary levels of insulin is regarded as insulin resistance irrespective of the body mass index (BMI). Hyperinsulinaemia due to insulin resistance occurs in approximately 80% of PCOS women with central obesity & 30%–40% of lean PCOS women. Measurement of the fasting insulin concentration \(^{(10)}\) is an easy marker of insulin resistance. S. Insulin levels of 20 or higher indicates that insulin resistance is present. Hyperinsulinemia is the main causative factor in PCOS women both obese & lean \(^{(4,5)}\) & cause hyperandrogenism. Insulin directly promotes ovarian steroidogenesis, and inhibits liver release of the sex hormone binding globulin (SHBG) and production of insulin-like growth factor binding protein 1 (IGFBP-1). Increased concentrations of IGF-1 additionally promote ovarian release of androgens \(^{(1,4,7)}\).

**Insulin Resistance**

We have used HOMA index as a marker of insulin resistance, based on measurements of fasting glucose and insulin levels, is the homeostatic mode assessment (HOMA-IR). Resistance to insulin is diagnosed at HOMA-IR levels ≥3.8 \(^{(1,4)}\).

Insulin resistance can manifest as follows:

1. Insulin resistance/Type II diabetes \(^{(1,4,9,11)}\).
2. Weight gain \(^{(1,3)}\).
3. High blood pressure, in obese and/or during pregnancy. \(^{(1,5,7)}\).
4. Cardiovascular disease-two fold increased risk of arterial disease in PCOS patients as compared to women without PCOS \(^{(7,11)}\).
5. Strokes \(^{(2,5)}\).
6. Miscarriage \(^{(6,7)}\).
7. Sleep apnoea, in obese \(^{(7,11)}\).
8. Non-alcoholic fatty liver disease, in obese \(^{(11)}\).
9. Acanthosis nigricans (patches of darkened skin under the arms, in the groin area, on the back of the neck) \(^{(1,6,11)}\).

Adipose tissue enzyme, aromatase, converts androstenedione to estrone and testosterone to estradiol. The excess of adipose tissue in obese led excess androgen formation, which are responsible for hirsutism and virilization Excess estrogens inhibits FSH via negative feedback \(^{(15)}\). It is been treated with various treatment modalities successfully.

MI (MYO) and D-chiro- inositol (DCI); both stereoisomers were used, as insulin sensitizer drugs, in the treatment of PCOS treatments \(^{(1,4,11)}\).

Inositol belongs to the vitamin B complex. Epimerization of the six hydroxyl groups of inositol leads to the formation of up to nine stereoisomers, including Human adults consume...
approximately 1 g of inositol (mainly MI) per day in different biochemical forms (4,7,11). Inositol phosphoglycans (IPGs) activate enzymes that control glucose metabolism (6,11). Defect in the IPGs, second messenger can cause impaired insulin metabolism (1,11). In PCOS women, a defect in tissue availability or altered metabolism of IPGs (inositol) mediators may contribute to insulin resistance (10,11). Circulating free MYO is taken up by most tissues by a membrane-associated sodium-dependent inositol co-transporter; inositol uptake is inhibited by glucose (4,7). In particular, it was shown that MYO had 10 times more affinity for the transporter compared to DCI (11).

PCOS is associated with selective increase in urinary clearance of D-chiro-inositol (DCI) & impaired DCI inositol phosphoglycan release in response to insulin. That means defect in tissue availability or utilization of DCI in PCOs that may contribute to insulin resistance.

DCI increases the action of insulin in patients of PCOS, thereby improving ovulatory function & decreasing serum androgen concentration, blood pressure & plasma triglyceride concentration. Women with PCOS have Insulin Resistance with hyperinsulinemia because of deficiency of DCI containing phosphoglycan that mediates action of insulin (3,4).

Elevated concentrations of MYO in human follicular fluid play a role in follicular maturity and provide a marker of good-quality oocytes (4,6). Previous studies have demonstrated that MI is capable of restoring spontaneous ovarian activity, and consequently fertility, in most patients with PCOS (6).

Criteria of Inclusion- All diagnosed cases by using to Rotterdam criteria.

Criteria of Exclusion-
1. Cushing’s syndrome
2. Thyroid disorders
3. Pituitary tumours
4. Diabetes Mellitus
A. Written consent is taken before starting examination.

- History & Clinical examination is done.
Following points were considered for comparison.
1. Height in metre, weight in Kg & Body Mass Index (BMI) is calculated.
2. Menstrual irregularities are noted as amenorrhea, oligomennorrhoea & irregular cycles.
3. Infertility.
4. Hirsutism, unwanted hair growth, acanthosis Nigricans - The features of excess androgen levels is noted.

B. Following investigations were done-
1) LH (Luteinizing Hormone).
2) FSH (Follicle stimulating hormone).
3) Serum. Prolactin levels-
4) Serum Insulin levels-
C. Following parameters were studied for comparison
1. BMI reduction-
2. LH/FSH Ratio-
3. HOMA Index-homeostatic model assessment (HOMA) -method used to quantify IR & beta-cell function. It also predicts cardiometabolic risk. Calculated by using formula HOMA-IR = [Glucose] x [Insulin] / 405 (Glucose in mg/dl).

Study Procedure
We have included 32 patients of PCOD in this group. Tab MI 2 gm BID along with Tab. Folic acid 5mg OD is advised to these patients. All parameters of comparison given above repeated after 3 months.
RESULTS & DISCUSSION-

MI Effect Before(pre) & After(post) Treatment-

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error</th>
<th>T</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pre BMI</td>
<td>25.40</td>
<td>6.53</td>
<td>1.15</td>
<td>2.77</td>
<td>0.009</td>
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<tr>
<td>post BMI</td>
<td>24.40</td>
<td>5.91</td>
<td>1.04</td>
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<td>pre HOMA index</td>
<td>23.74</td>
<td>25.00</td>
<td>4.42</td>
<td>0.006</td>
<td>0.995</td>
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<td>post HOMA index</td>
<td>23.8</td>
<td>44.62</td>
<td>7.88</td>
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<tr>
<td>Pre LH/ FSH</td>
<td>2.32</td>
<td>0.29</td>
<td>0.05</td>
<td>3.78</td>
<td>0.001</td>
</tr>
<tr>
<td>Post LH/FSH</td>
<td>2.10</td>
<td>0.43</td>
<td>0.077</td>
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<tr>
<td>Pre prolactin</td>
<td>19.73</td>
<td>12.75</td>
<td>2.25</td>
<td>-0.817</td>
<td>0.420</td>
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<tr>
<td>Post prolactin</td>
<td>21.69</td>
<td>10.40</td>
<td>1.84</td>
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</tr>
</tbody>
</table>

1) BMI before treatment with MI mean was 25.4, reduced to 24.4 (p=0.009) after treatment, which is statistically significant.

2) HOMA index before treatment was mean 27.74 after treatment it increased despite of reduction to 23.8 (p=0.995), which is statistically not significant. So here HOMA index did not have beneficial effect in PCOD cases.

3) LH/ FSH Ratio were mean 2.32 before treatment. After treatment it reduced to mean 2.10 (p=0.001), which is statistically significant. This indicates MI is helpful in correcting hormonal dysfunction of PCOD.

4) Prolactin Levels were mean 19.73 before MI treatment. It increased to 21.69 (p=0.420) which is statistically not significant.

Discussion

There is data suggesting MI is useful to varying extent in cases of PCOD. Improvement in Insulin sensitivity, weight loss, menstrual regularity, ovulation by hormonal dysfunction is studied. Costantino et al. recruited 42 patients treated with MYO showed there was no change in the fasting plasma insulin and glucose concentration. AUC, for both insulin and glucose, decreased during the oral glucose tolerance. There was no change in the fasting plasma insulin and glucose concentration. Ovulation was restored in 16 (69.5%) women treated with MYO group. Genazzani AD et al. studied effect of MI in 20 patients compared with placebo. After 12 weeks of treatment, they found that LH, Prolactin, T, insulin levels, LH/FSH results were significantly reduced. Insulin sensitivity results were significantly improved. Menstrual cyclicity was restored in all amenorrheic and oligomenorrheic subjects.

Gerli et al. The BMI decreased significantly in the MYO group (p = 0.04). No change was observed in the waist-to-hip ratio.

Raffone et al. showed that MYO slightly improves pregnancy rate compared to metformin. no side effects were reported.

Conclusions

MI did better in this study in regard to BMI & LH/FSH ratio but there is not significant change in HOMA index & prolactin levels. Being physiological component It may be considered one of the supportive option in PCOD treatment schedule.

References