

**EFFICACY OF MYO-INOSITOL AND D-CHIRO-INOSITOL COMBINATION ON MENSTRUAL CYCLE REGULATION AND IMPROVING INSULIN RESISTANCE IN YOUNG WOMAN WITH POLYCYSTIC OVARY SYNDROME (CASE STUDY)**

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**Abstract:** Polycystic ovary syndrome is a complex condition characterized by oligo/amenorrhea, signs of hyperandrogenemia (hirsutism, acne, alopecia) and ovaries that on ultrasound show the presence of multiple cysts, characteristically distributed in the periphery of the ovary (known as the "string of pearls" sign.) The clinical presentation of PCOS varies widely. To establish a diagnosis of polycystic ovary syndrome, it is necessary to have at least two of the three so-called Rotterdam criteria, which include:

1. Irregularities of the menstrual cycle - oligomenorrhea, amenorrhea or prolonged menstrual bleeding.

2. Hyperandrogenemia (proven clinically or laboratory) - hirsutism is the most common clinical presentation of hyperandrogenemia and occurs in up to 70% of women with this syndrome. Evaluation of hirsutism is with use of a modified Ferriman-Gallwey score system. With this system we evaluate hair growth in seven regions: upper lip, chin/face, chest, back, abdomen, arms and thighs. In about 90% of women that have normal menstrual cycle and hirsutism, during an ultrasound exam, it can be found that they have polycystic ovaries.

3. Polycystic ovaries (presence of  $\geq 12$  follicles 2-9 mm in size and/or ovarian volume  $> 10$  mL)

The most of the patients with PCOS have insulin resistance that leads to hyperinsulinemia. A paradox present in PCOS patients is that the ovaries remain insulin sensitive despite the universal insulin resistance.

The increased androgen production is not so much due to remained insulin sensitivity of the ovaries as to compensatory hyperinsulinemia. Compensatory hyperinsulinemia increases pulsatile secretion of GnRH which can cause increased secretion of LH and lower the secretion of FSH.

Insulin resistance and compensatory hyperinsulinemia affect about 65-70% of women with PCOS, of which 70-80% are obese and 20-25% are of normal body mass.

The most authors suggest that that insulin resistance is the primary defect in patients with PCOS and hyperandrogenemia is secondary to that

Our purpose is to evaluate the efficacy of treatment with myo-inositol (MI) and D-chiro-inositol (DCI) in ratio 40:1, in the therapy of polycystic ovary syndrome (PCOS).

Case study of 22 year-old female who presented to the clinic for irregular menstrual cycle, acne and hirsutism. Transvaginal ultrasound showed anteverted uterus, proliferative endometrium d-7mm and more than 12 antral follicles on right and left ovary. Hormonal investigations showed increase fasting insulin level and testosterone level. She was advised to start treatment with combination of myo-inositol and D chiro-inositol (ratio 40:1) 2 g per day during three months.

Hormonal investigation after 3 months treatment with myo-inositol/D- chiroinositol showed a decrease in the values of IRI 9.3 uU/ml, Testosteron 48.8ng/dl, Prolactine 19.3ng/ml. Also the treatment with combination of myo-inositol/D- chiroinositol in ratio 40:1 contributed to regulation of menstrual cycle.

Myo-inositol and D-chiro-inositol in combination (40:1 ratio) are effective in regularizing menstrual cycles in PCOS patients, improving insulin resistance and decreasing of hyperandrogenemia.

The combination of myo-inositol/D- chiroinositol (40:1) ratio should be considered as first line treatment in women with PCOS.

**Keywords:** PCOS, inositols, insulin resistance, hyperandrogenemia, anovulation

## 1. INTRODUCTION

PCOS is a complex condition with features of oligomenorrhoea/amenorrhoea, anovulation, and signs of androgen excess (hirsutism, acne, male type baldness) and multiple cysts in ovaries. It is the most common cause of infertility due to anovulation.

Approximately 60 – 70% of women with PCOS have insulin resistance. Pancreas reacts on IR as insulin deficiency and that leads to increased insulin secretion. Increased insulin stimulates pulsatile secretion of GnRH that stimulates secretion of luteinizing hormone (LH). Excess of LH increases the production of androgens from theca cells of ovary leading to hyperandrogenism (acne, hirsutism). Increased androgen production prevent maturation of one dominant follicle and that's why the most of the patients with PCOS are facing anovulation and menstrual irregularity. Treatment depends on age of the patient and clinical features. We use anti androgens and hormonal contraceptives for cycle regulation and to lower androgens. Women that face infertility need ovulation induction such as Clomifen citrate or gonadotropins..

For a long time, metformin as a insulin sensitizer agent was a choice in PCOS management in women with insulin resistance. The treatment with metformin shows improvements in clinical features of PCOS but the most of the patients on Metformin are complaining about gastrointestinal adverse events, such as diarrhea and abdominal bloating.

Lately myo-inositol (MI) has been used more and more in the treatment of PCOS patients, due to its satisfying results and the absence of side effects. Inositol is a hexahydroxycyclohexane, a 6-carbon ring compound with a hydroxyl group attached to each carbon of the ring. There are nine possible stereoisomers of inositol. Two of them, MI and DCI have the ability to reduce insulin resistance and that's why they are considered beneficial to PCOS patients. MI and DCI play the role of insulin's second messengers and mediate different insulin actions. Concentration of MI is higher in tissues that have high glucose utilization and it has a main function to control the uptake of glucose into cells, and DCI is mainly involved in glycogen storage.

## 2. CASE STUDY

The patient is a 22 year-old female who presented to the clinic for irregular menstrual cycle, acne and hirsutism. She stated that two years ago she was taking oral contraceptives for six months. During the treatment with contraceptive pills, acne and hirsutism were reduced but after she stopped taking the hormonal therapy she faced the same problem. Transvaginal ultrasound showed anteverted uterus, proliferative endometrium d-7 mm and more than 12 antral follicles on right and left ovary. Hormonal investigations: FSH 6.9mIU/ml, LH 7mIU/ml, IRI 20.3 uU/ml (1.1-17uU/ml), Testosterone 58.3 ng/dl (9-56ng/dl), Prolactin 40.9ng/ml (<25ng/ml). OGTT fasting glucose 5.72 mmol/l, 120' 6.22mmol/l. Because the results from the hormonal investigations showed increased range of fasting insulin and increased range of testosterone, she was advised to start treatment with combination of myo-inositol and D chiroinositol (ratio 40:1) 2 g per day during three months. After the treatment she stated that her menstrual cycle was regular during this three months (30 days duration) and she had significant improvement with her problem with acne. Hormonal investigation after 3 months treatment with myo-inositol/D- chiro-inositol showed a decrease in the values of IRI 9.3 uU/ml, Testosterone 48.8ng/dl, Prolactin 19.3ng/ml

## 3. RESULTS

Hormonal investigation after 3 months treatment with myo-inositol/D- chiroinositol showed a decrease in the values of IRI 9.3 uU/ml, Testosterone 48.8ng/dl, Prolactin 19.3ng/ml. Also the treatment with combination of myo-inositol/D- chiroinositol in ratio 40:1 contributed to regulation of menstrual cycle.

## 4. DISCUSSIONS

Current studies suggest that central feature of PCOS are insulin resistance and compensatory hyperinsulinemia. Insulin resistance in PCOS however tends to be tissue selective. Despite the insulin resistance in metabolic tissues, the paradox is that the ovaries remain insulin sensitive and that leads to hyperinsulinemia-induced hyperandrogenemia in PCOS patients. In the ovary, MI enhances the action of FSH and DCI down-regulates the activity of aromatase enzyme (which main function is to convert androgens into estradiol) and that causes excessive production of insulin-dependent testosterone.

MI is found in follicular fluid and improves oocyte quality. When the concentration of MI in the follicular fluid is reduced (which is the case in PCOS patients), the activation of epimerase is excessive and that leads to an excess of DCI, an increase in insulin resistance and an increase in the concentration of LH. In the PCOS patients the conversion of MI in DCI is decreased and that means that combined supplementation of MI/DCI should be considered and may help to regulate their concentration..

## 5. CONCLUSION

Myo-inositol and D-chiro-inositol in combination (40:1 ratio) are effective in regularizing menstrual cycles, improving insulin resistance in patients with polycystic ovary syndrome and decreasing hyperandrogenemia. The combination of myo-inositol/D-chiroinositol (40:1) ratio should be considered as first line treatment in women with PCOS.

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