

# Inositol – A Natural Treatment for Polycystic Ovarian Syndrome?



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Polycystic ovary syndrome (PCOS) is a complex endocrine disorder affecting 18-22% of reproductive-aged women.<sup>1</sup> According to the Rotterdam criteria, PCOS is diagnosed by any two of the following three criteria: oligo- or anovulation, clinical and/or biochemical hyperandrogenism, and polycystic ovaries.<sup>2</sup> Four different phenotypes (A-D) of PCOS are identified assuming these three criteria.<sup>3</sup> Heterogenous PCOS phenotypes might additionally include insulin resistance, hyperinsulinemia, hypertension, dyslipidemia, obesity, hirsutism, acne, infertility, as well as increased risk of metabolic syndrome and type 2 diabetes mellitus,<sup>3</sup> decreased quality of life<sup>4</sup> and impaired psychological function.<sup>5</sup>

As a promise, research suggests supplementing with inositol, former vitamin B-8, can help address various aspects of this condition. Inositol is a six-carbon polyalcohol, hexahydroxycyclohexane, but formally belongs to the sugar family.<sup>6</sup> Nine different stereoisomers of inositol are possible, among which myo-inositol (MI) is the most prevalent in biological systems. Inositol is a constitutive part of cell membranes and acts as an insulin second messenger when modified to inositolphosphoglycans (IPGs), MI-IPG and D-chiro-inositol (DCI)-IPG, involved in activating enzymes that control glucose metabolism.<sup>7</sup> Impaired IPGs pathways have been hypothesized to induce insulin resistance.<sup>8</sup> Additionally, MI and DCI have been shown to be differently enrolled in PCOS etiology and treatment.<sup>9</sup> In the liver, they are both involved in insulin signaling, where MI serves for glucose uptake, whereas DCI

participates in glycogen synthesis. In the ovary, MI is involved in glucose uptake and follicle stimulating hormone (FSH) signaling, while DCI mediates insulin-sensitive androgen synthesis. Treatment with MI has been associated with better oocyte quality compared to application of DCI<sup>10</sup> and it might be a treatment of infertility in PCOS by restoring the frequency of menstrual cycles and eventual pregnancies.<sup>11</sup> On the other hand, treatment with DCI has been associated with improved insulin sensitivity, decreased free circulating testosterone level and increased frequency of ovulation,<sup>8</sup> but the lack of these effects is seen when higher doses of DCI have been administered.<sup>12</sup> According to the „DCI paradox“, since ovary is non-insulin resistant, hyperinsulinemia stimulates epimerase-mediated conversion MI to DCI, which could have consequences on oocyte quality, FSH signaling and androgen production underlying PCOS.<sup>9</sup> Thus, the application of proper MI: DCI ratio (40:1) has been suggested to be the key in PCOS treatment instead of administration of MI or DCI alone. Beside improving insulin level and sensitivity, glucose metabolism, hormonal pattern and infertility, inositol (mostly MI) has been also demonstrated to have beneficial effects on metabolic syndrome characteristics (obesity, lipid profile), to reduce cardiovascular and type 2 diabetes mellitus risk, and even to protect from congenital abnormalities and gestational diabetes.<sup>3,13</sup> Since impaired psychological function has been demonstrated in PCOS<sup>5</sup>, evidences indicating antidepressive, antianxiety<sup>14</sup> and antipanic effects<sup>15</sup> of inositol require further examination due to conflicting results. Assuming all, inositol, as an insulin mimetic or insulin sensitizing agent, might be used for a broad therapeutic advantages regarding almost all endocrine, reproductive and metabolic issues of PCOS.

Interestingly, MI is considered as a prebiotic molecule.<sup>16</sup> It is endogenously produced in the body from glucose-6-phosphate, while DCI is converted from MI by epimerase enzyme.<sup>6</sup> Inositol and his derivates (in the

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form of hexaphosphate, and phytic acid or phytates) are also found in many plants and foods.<sup>17</sup> Natural sources extremely rich in MI are fresh fruits (cantaloupe and citrus fruits, excluding lemon), vegetables (beans and peas, and than leafy vegetables, carrots and corn) and cereals (beans, grains and nuts, particularly oat and bran), while the lowest content of MI is found in milk, meat, fat, and generally processed, frozen or canned food.

Therapeutic doses of inositol are shown to vary from 2 to 4 grams per day, with no adverse effects.<sup>18</sup> Nausea, flatulence, loose stool, and diarrhea are detected at a daily dose of 12g, while higher doses (up to 30g) do not aggravate these gastrointestinal symptoms. Additionally, DCI supplementation has shown dose-dependent harmful effects on oocyte quality and ovarian response in PCOS women without insulin resistance and/or hyperglycaemia undergoing in vitro fertilization procedure.<sup>19</sup>

In conclusion, inositol is promising and generally safe, natural treatment for PCOS, but further research on inositol safety is mandatory due to possible adverse effects when administered in elevated doses. Health professionals should be consulted about appropriate inositol-rich diet or optimal supplementation in the treatment of various PCOS comorbidities. However, the consumption of inositol-rich food is preferred than tablets intake, especially in younger women.

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