

Know your Enemy: The Rationale of Using Inositol in the Treatment of Polycystic Ovary Syndrome

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The Polycystic Ovary Syndrome (PCOS) is defined, according to Rotterdam's criteria proposed by the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine [1,2], by the identification of two out of following parameters: oligo-anovulation; hyperandrogenism (clinical or biochemical); the presence of 12 or more follicles in each ovary measuring 2-9 mm in diameter, and/or an increased ovarian volume (>10 ml). PCOS affects about 4-8% of the women in reproductive age [3], causing anovulatory cycles in the 74% of the cases, insulin-resistance in the 42% and hyperandrogenism in the 48% [4]. PCOS in our opinion could be considered as the result of concurrent endocrinological alterations, which affects each other. First of all, obesity affects the 35% of PCOS patients [5] and provoke multiple metabolic and endocrine dysfunctions: fatty tissue, in fact, behaves as non-classical endocrine organs and secretes specific cytokines and chemokines [6] which stimulate the androgens production by adrenal cortex and ovaries [7]; on the other hands, adipocytes' mediators seems to alter the hypothalamus-hypophysis-gonads regulation system, causing high and constant production of Luteinizing Hormone (LH). This may accounts, at least in part, for the typical inhibition of the ovarian follicular maturation in PCOS patients [8]. Moreover, metabolic profile is strictly connected to gonadal function [9]: in PCOS patient's insulin-resistance is commonly associated with hyperinsulinemia [10], and the latter acts synergistically with LH to enhance the androgen production of theca cells [11]. Furthermore, it is able to reduce circulating levels of Sex Hormone Binding Globulin (SHBG), leading to increased levels of free testosterone [12]. Considered altogether, these evidences led to the use of insulin sensitizing drugs to stem the symptoms of this pathology. To date, different Inositol isoforms seems to increase insulin action on various tissues and, in this way to improve the ovulatory function and to inhibit or limit the production of testosterone [13]. Moreover, the use of Inositol may improve the possibility of spontaneous ovulation and regular menstrual cycles, as well as to increase the production of progesterone in the luteal phase of female infertile patients with PCOS [14]. Inositol is a polyalcohol classified as insulin sensitizer and existing as nine stereoisomers, two of which, D-Chiro-inositol [15-18] and Myo-Inositol [14,19-22], are currently used in PCOS treatment. Myo-Inositol, which is the most abundant form of inositol in humans, is converted to D-Chiro-inositol by an insulin-dependent epimerase [23]. These two stereoisomer showed an insulin-like action in vivo exerting the function of insulin mediators as inositolphosphoglycans (IPGs) [24]. In our experience, both Inositol isoforms are effective in improving ovarian function and metabolism of patients with PCOS, although Myo-Inositol shows the most marked effect on the metabolic profile, whereas D-Chiro-Inositol reduces more hyperandrogenism [25].

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