

Polycystic Ovarian Syndrome: Role of Nutrition, Vitamins, and Minerals—Myoinositol and Vitamin D3

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The pathophysiology of polycystic ovarian syndrome (PCOS) is multifactorial and is still an enigma. Impaired ovarian steroidogenesis, insulin resistance (IR), neuroendocrine defects, and increased cortisol metabolism-related adrenal hyperandrogenism are most important mechanisms. Although the triggering cause of PCOS is currently unknown, androgens and insulin are two key factors in its pathogenesis. Therefore, treatment of PCOS involves improvement of hyperandrogenism and hyperinsulinemia. Nutrients act as cofactors in maintaining functions of insulin and androgen receptors. Deficiencies of myoinositol and vitamin D can lead to PCOS pathogenesis-related complications. Therefore, nutritional supplementation may contribute to overcome complications of PCOS such as immature oocyte, IR, hyperandrogenism, and oxidative stress.

This review emphasizes the importance of various micro-nutrients in management of PCOS.

VITAMIN B

Vitamin B6 and vitamin B12 have significant roles in homocysteine (Hcy) regulation. In the pathophysiology of PCOS, a positive correlation has been reported between IR and elevated Hcy levels.^{1,2} Kaya et al. demonstrated that IR, obesity, and increased Hcy levels were related to low serum insulin B12 concentrations in women with PCOS. In order to reduce elevated levels of serum Hcy, folic acid supplementation for 3 months produced effective results, especially in women without IR.

Metformin inhibits the binding intrinsic factor-B12 complex and its receptor, and also serum vitamin B12 and folic acid levels decrease during metformin therapy. Metformin increases Hcy levels. Supplements of vitamins had no effects on androgen and lipid levels in the pathophysiology of PCOS.³

VITAMIN A

Obesity and abnormal glucose metabolism are associated with elevated retinol-binding protein 4 (RBP4) levels in overweight women with PCOS. Another RBP4-based study reported the measurement of RBP4 expression in isolated subcutaneous and omental adipose tissue from women with PCOS.⁴

VITAMIN D

Measurement of D3 inhibits inflammatory progress in the pathogenesis of PCOS. Moreover, vitamin D3 treatment plays a vital role in folliculogenesis due to decreasing elevated anti-mullerian hormone levels.⁵ Interestingly, Jafari-Sfidvajani et al.⁶ demonstrated that vitamin D supplementation in PCOS caused no statistically significant differences in the androgen profile when combined

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with a low-calorie diet; however, an improvement in menstrual frequency was observed. A cross-sectional study reported that lower vitamin D was linked with IR as a result of the pathophysiology of PCOS.⁷ Vitamin D3 inhibits inflammatory progress in the pathogenesis of PCOS.

VITAMIN E

Vitamin E (400 IU) and omega-3 fatty acid (1,000 mg) cosupplementation in women with PCOS for 12 weeks provided significant improvement in IR and androgen levels.⁸

INOSITOL

Inositol provides improvement in reproductive abnormalities, causes decreased androgen levels, and improves insulin levels. Myoinositol (MI) provides healing in hyperandrogenism and IR-associated parameters.

ALPHA LIPOIC ACID

Alpha lipoic acid decreased number of ovarian cysts and increased progesterone levels. At the metabolic perspective, IR significantly improved in the patients with PCOS, and impaired lipid metabolism was significantly changed.⁹

BIOFLAVONOID

This includes anthocyanides, flavan-3-ols, flavanones, flavones, flavonols, and isoflavones. Romualdi et al.¹⁰ showed that 36 mg/day soy isoflavone genistein treatment in women with PCOS for 3 months provided a significantly improved lipid profile. However, hyperinsulinemia, anthropometric measurements, hyperandrogenism, and reproductive abnormalities did not change significantly.

CARNITINE

Women with PCOS have significantly decreased serum total L-carnitine levels when compared to healthy women.¹¹ Fenkci et al.¹¹ considered that lower L-carnitine level could be linked with hyperandrogenism and IR. Some antidiabetic agents used for PCOS treatment are associated with carnitine metabolism. Piaglitazone administration for 16 weeks in obese premenopausal patients with PCOS led to increased fasting concentrations of free carnitine.¹² Study by Dunning and Robker¹³ concluded L-carnitine influenced oocyte quality.

Randomized clinical trial in clomiphene-resistant women with PCOS reported that using both clomiphene citrate and L-carnitine provided thicker endometrium, higher estradiol concentrations, higher pregnancy rates, and improved lipid profiles compared to clomiphene citrate treatment alone. L-carnitine supplementation (250 mg per day) for 12 weeks improved mental health and oxidative stress parameters¹⁴

OMEGA-3 FATTY ACID

Omega-3 is associated with regulation of abnormal gene expression in the pathophysiology of PCOS. Omega-3 EPA in doses of 25 to 100 µg in granulosa cell culture resulted with higher insulin growth factor (IGF)-1 expression and lower cyclooxygenase 2 (COX2) expression. IGF-1 is an essential compound of follicular differentiation and COX-2 contributes to oocyte maturation.¹⁵

CONCLUSION

Nutrition-associated signaling pathways play a central role in the regulation of ovarian follicle growth and ovulation rates. Vitamin and mineral supplements have a definite role in PCOS-related symptoms, bringing out good oocytes. Hyperinsulinemia, hyperandrogenism, increased body mass index, and cardiovascular disorders are also improved. Psychological issues associated with PCOS are also improved.

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