

Nutrition Recommendations in Adolescent Presentations of PCOS

Defining PCOS, Etiology, and Characteristics

Polycystic ovary syndrome (PCOS) is an endocrine condition, with estimated prevalence approximately 6-21% of females depending on diagnostic criteria, ethnicity, age, and other factors.ⁱ It is a complex condition, with patients often presenting with a number of imbalances, as shown below, which can overlap and influence one another.

Category	Specific Imbalances
Reproductive/Hormonal	Menstrual dysfunction Infertility/increased pregnancy complications Hyper-androgenism (measured by free testosterone) Hirsutism Acne
Metabolic	Insulin resistance/hyperinsulinemia Dyslipidemia Increased risk factors for: <ul style="list-style-type: none">• Type 2 diabetes mellitus (DM)• Cardiovascular disease (CVD)• Metabolic syndrome (MetS)• Non-alcoholic fatty liver disease (NASH)
Psychological	Anxiety and depression Decreased quality of life Eating disorders Negative body image

Diagnostic criteria have changed and broadened over the years to better capture females with varying symptoms of PCOS.ⁱⁱ

1990: Chronic anovulation and clinical or biochemical hyper-androgenism after exclusion of other causes. (NIH)

2003: The presence of PCOs by ultrasound was added as a third criterion; two of the three criteria required for diagnosis. (Rotterdam European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine Consensus Workshop; ESHRE/ASRM)

2009: Presence of clinical or biochemical hyperandrogenism as the main criterion, followed by one additional criterion, either ovarian dysfunction of oligo-anovulation or PCO morphology by ultrasound, and exclusion of other causes. (Androgen Excess Society)

2012: Adolescent-specific diagnosis criteria were published; oligomenorrhea or amenorrhea should be present for at least 2 years after menarche (or primary amenorrhea at 16 years), both clinical and biochemical hyper-androgenism, and diagnosis of PCOs on ultrasound should include increased ovarian size $>10\text{ cm}^3$. (ESHRE/ASRM)

Diagnosis in adolescents is an ongoing challenge in the field of PCOS, as some primary symptoms (oligomenorrhea/chronic anovulation and multiple ovarian cysts) are similar to those normally occurring during stages of puberty and initiation of menarche. Also, other causes of hyper-androgenism may include late-onset congenital adrenal hyperplasia (CAH), Cushing syndrome, hyper-prolactinemia, hypothyroidism, and ovarian or adrenal tumors, and must be ruled out before diagnosing PCOS.

Treatment Approaches

A greater percentage of females with PCOS are overweight or obese than normal weight. What is unknown is whether obesity leads to PCOS or rather PCOS predisposes a female to excessive weight gain. Research has shown that weight loss of any form, often through healthy diet and exercise approaches, can improve insulin resistance and menstrual dysfunction. Generally, treatment falls into three sectors, which include lifestyle modifications (i.e. dietary interventions and exercise, cognitive behavioral therapy, mindfulness-based therapy, and family support), hormonal contraceptives, insulin sensitizers (i.e. metformin), and androgen receptor blockers (i.e. spironolactone).

According to a comprehensive review, published in 2013 by the Journal of the Academy of Nutrition and Dietetics (JAND), there are no clear guidelines on what diet approach is most optimal in the setting of PCOS. Below are subtle differences in findings between the different diet types studied, which should be interpreted lightly.

Type of diet	Subtle differences in study findings
Monounsaturated fat (MUFA)-enriched diet	Greater weight loss
Low-glycemic index diet	Improved menstrual regularity; greater reduction in insulin resistance, fibrinogen, total cholesterol, and high-density lipoprotein (HDL) cholesterol; improved quality of life
High-carbohydrate diet	Increased free androgen index
Low-carbohydrate diet	Greater reduction in insulin resistance, fibrinogen, total cholesterol, and high-density lipoprotein (HDL) cholesterol
High-protein diet	Improved depression and self-esteem

As insulin resistance is a hallmark feature of PCOS, it is warranted to consider dietary approaches traditionally used in managing diabetes, whether an individual has been diagnosed with diabetes or not.

A 16-day **low-carbohydrate diet** was associated with a greater decrease in surrogate markers of insulin resistance (acute insulin response to glucose) as compared to a MUFA-enriched diet. Likewise, a greater decrease in fasting insulin was seen as compared to a high-carbohydrate, standard-protein, and low-fat diet.

An ad-libitum **low-GI weight-loss diet** was associated with a greater reduction in surrogate markers of insulin resistance (insulin sensitivity index after an oral glucose tolerance test; OGTT) as compared to a conventional healthy ad libitum weight-loss diet.

All diet types initiated, included within this review, resulted in some degree of weight loss and subsequent benefit on presentation of PCOS. Authors concluded that weight loss should be the target of treatment for overweight or obese women diagnosed with PCOS, achieved through a reduction in caloric intake, adequate nutrient intake, and an individualized exercise plan. It must be remembered that co-morbid conditions, etiology of signs and symptoms, and response to treatment are quite variable depending on the patient and treatment plans for PCOS should be individualized. Furthermore, these studies focused on acute changes rather than long term sustainability of diet approaches and various outcomes. Authors further noted that rather than focus on the *type* of diet initiated, it is more important to focus on increasing patient engagement, adherence, motivation, and ability to sustain lifestyle changes.

Nutrition Implications and Recommendations

Impact of medications on nutrition status

Spirolactone. Spirolactone is a potassium-sparing diuretic traditionally used to treat edema associated with hypertension, heart failure, and primary hyper-aldosteronism. It acts to increase sodium and water excretion, while conserving potassium and hydrogen ions, by competing with aldosterone for receptor sites in the distal renal tubules.ⁱⁱⁱ As part of treatment for PCOS, spironolactone is used for managing acne and hyper-androgenism, specifically hirsutism. These are PCOS characteristics often associated with decreased quality of life, anxiety, and body image issues. Spirolactone is an anti-androgen, meaning an androgen receptor blocker, which can reduce concentration of circulating androgens (testosterone, etc.) and thus hormone-mediated hair growth and acne.

Spirolactone can cause side effects including nausea, diarrhea, drowsiness associated with hyperkalemia, and dizziness. It can also cause excessive water and sodium losses, leading to or exacerbating existing dehydration. If hyperkalemia persists, patients may have to follow a potassium-restricted diet, which can impact intake of other vitamins and minerals if patients choose to restrict a wide variety of fruits and vegetables due to a lack of education on sources of potassium. Finally, concerns exist over the negative effects that long-term anti-androgen therapy may have on bone mass.^{iv} Although no definitive research exists, bone mass should be monitored and dietary approaches to increase calcium and vitamin D intake should be advised.

Metformin. Metformin is a medication used commonly in the treatment of non-insulin dependent type II diabetes that cannot be managed through diet and exercise alone.^v It is indicated, off-label, in treatment of PCOS in order to manage insulin resistance, which is a hallmark feature of PCOS and sometimes results in a formal diagnosis of type II diabetes. Metformin acts to decrease hepatic production and intestinal absorption of glucose, and improve insulin sensitivity so that peripheral glucose uptake and utilization is optimized.

In greater than 10% of individuals on metformin, adverse gastrointestinal symptoms such as diarrhea, nausea, vomiting, and flatulence may occur. Taking the medication with food may help to alleviate symptoms. Also, metformin may impair vitamin B12 absorption, particularly in individuals with inadequate vitamin B12 or calcium intake and/or absorption. With long-term metformin use, serum vitamin B12 should be routinely measured and adequate intake via diet should be advised.

Hormonal contraceptives. Hormonal contraceptives (birth control) are indicated in treatment for PCOS, which often contain ethinyl estradiol (estrogen) and progesterone.^{vi} This treatment is used for a similar reason as spironolactone, to reduce levels of circulating androgens and thus treat hormone-mediated hair growth and skin conditions. Some proposed ways in which oral contraceptives act are by reducing production of androgens by the ovaries, adrenal glands, and at receptor level on the skin, in addition to decreasing circulating testosterone through increase in production of sex hormone binding globulins (SHBG).

Oral contraceptives can be difficult to tolerate on an individual basis, causing nausea, loss of appetite, bloating, headaches, depression, and other symptoms that can impact food intake and thus nutrition status.

On a positive note, oral contraceptives may increase HDL cholesterol and reduce risks of iron deficiency anemia if controlling excessive menstrual bleeding. Also, estrogen found in oral contraceptives can play a beneficial role in bone health and reducing risks of osteoporosis, which can be a relevant concern if experiencing amenorrhea or on anti-androgens long-term.

Recommended supplementation

Vitamin D. Theories in the literature suggest vitamin D deficiency may be associated with the adverse factors of PCOS including fertility issues, inflammation, mood disturbances (anxiety and depression), adrenal function, and insulin resistance.^{vii} It would be presumed then that vitamin D supplementation would be beneficial as treatment. However, research is quite inconclusive. From a different perspective – that of obesity – vitamin D is important. Research has shown that vitamin D deficiency is common in overweight or obese individuals due to excess fat tissue limiting bioavailability on absorption.

Future research should further address the role vitamin D in treating factors of PCOS, including insulin resistance, mood disturbances, inflammation, and more. However,

adequate vitamin D plays a significant role in bone health, and as bone health may be concerning in this population, supplementing with vitamin D may be warranted.

Folate. Folate supplementation has been shown to reduce plasma homocysteine (Hcy), high levels of which are associated with increased risk of cardiovascular disease. It has also been associated with increased insulin sensitivity.^{viii}

Omega-3 fish oil. Fish oil, particularly the DHA found in fish oil supplements, may aid in insulin control, improve skin and hair, lower triglycerides and blood pressure, and reduce fatty liver. As an anti-inflammatory polyunsaturated fatty acid (PUFA), DHA has been shown to decrease the production of inflammatory mediators associated with obesity and type 2 diabetes, and the appearance of cardiovascular disease risk factors.^{ix}

Other nutrients. Zinc supplementation has been associated with reduced fasting plasma glucose, reduced serum insulin, and reduced serum triglycerides.^x Additionally, selenium supplementation has been associated with similar results to that of zinc, with reductions seen in serum insulin and serum triglycerides.^{xi} However, more research is needed before supplementation is advised.

Dietary approaches for insulin resistance and PCOS

As was stated earlier in this review, a variety of dietary approaches in treatment of PCOS and comorbid conditions have been studied in the literature for their ability to lower insulin resistance, promote weight loss, and more. Across all diets, weight loss and a reduction in insulin resistance was seen, with other measures varying across diet types. However, it should be remembered that these are single studies all with limitations, ranging from small sample sizes, varying definitions of diet types, and varying diet adherence (i.e. *ad libitum* versus set energy parameters).

Heart Healthy + consistent carbohydrate = D.A.S.H. The D.A.S.H. diet – Dietary Approaches to Stop Hypertension – has been shown to play a beneficial role in weight loss and glycemic control for individuals with type 2 diabetes. The basis of this eating plan is a diet rich in fruits and vegetables; whole grains; low fat or fat free dairy; lean meats, fish, and poultry; nuts; and beans. It advises limited red meat, processed foods, and sweets, and is thus low in total and saturated fat, sodium, and added sugars. It is rich in potassium, magnesium, and calcium. It advises whole grains over refined grains and other foods high in refined sugars. Whole grains have a lower glycemic index and increased fiber content, which plays a role in glycemic control. Also, by following a balanced plate approach – half your plate fruits and non-starchy vegetables, one quarter whole grains, and one quarter lean protein – individuals will be maintaining a diet fairly consistent in carbohydrate content. Adequate lean protein at each meal and snack will also help to maintain glycemic control. Finally, the D.A.S.H. diet has been successful in promoting weight loss due to the lack of a feeling of “restriction.”

A number of studies have looked at efficacy of the D.A.S.H. diet in adolescents for a range of conditions, from treating hypertension and hyperlipidemia to high cholesterol and diabetes

mellitus, with the overarching result of weight loss seen in the majority findings. In particular, these results were seen in The SEARCH for Diabetes in Youth Study, published in 2011.^{xii} Results also suggested a causal relationship between D.A.S.H. adherence and Hemoglobin A1C, though this could be related to “general health behaviors and quality of diabetes care.” Regardless, glycemic control and decreased lipid levels appear to be related.

Role of antioxidants. While limited research exists to address antioxidant use in PCOS, some studies suggest that antioxidant supplementation may improve insulin sensitivity. Furthermore, the association between antioxidants and reduced oxidative stress and inflammation found in cardiovascular disease and other chronic diseases is a compelling reason to think there may be a role in PCOS treatment. Many antioxidants are proposed in the research, though for the purpose of this review, cinnamon will be a primary focus.
Cinnamon

A 2014 study found that cinnamon administration to women with diagnosed PCOS for 6 months significantly improved menstrual cyclicity as compared to placebo controls, though no difference was seen in insulin resistance or serum androgen levels.^{xiii}

A 2016 review found conflicting findings between studies looking at various polyphenols – tea and coffee, chocolate and cocoa, cinnamon, grape, pomegranate, red wine, berries, and olive oil – and enhanced glycemic control.^{xiv} It is suggested that dietary polyphenols may have anti-inflammatory effects in addition to effects on glucose transport and insulin secretion. Specifically, they may inhibit alpha-amylase and alpha-glucosidase, inhibit SGLT1, stimulate insulin secretion, reduce hepatic glucose production, and enhance insulin-dependent glucose uptake.

Additional research is ongoing looking at the role of soy, organic meats, organic dairy, and other antioxidants in alleviating symptoms and comorbidities associated with PCOS.^{xv}

Conclusion

PCOS in adolescence has a number of comorbid conditions that can persist into adulthood and worsen, resulting in type 2 diabetes, cardiovascular disease, hypertension, non-alcoholic fatty liver disease, and more. Anxiety, depression, decreased quality of life, and poor body image can be equally as detrimental disturbances to live with. It is important to not only participate in medical management but also engage in lifestyle changes for weight loss at an early stage following diagnosis of PCOS. Research regarding a number of dietary interventions and supplement use is ongoing and still conflicting, suggesting that the evidence-based treatment approaches already being used for weight loss and type 2 diabetes management may be the best routes. Specifically for adolescents and young women, type 2 diabetes may not yet be present and the focus should be more on managing insulin resistance and maintaining a healthy weight. The D.A.S.H. diet supports these goals well, and is safe to initiate in this age group for weight loss and glycemic control, without being overly restrictive. Antioxidant supplementation may be warranted, though more research is needed. Daily vitamin D and fish oil supplements are safe at prescribed doses,

indicated on manufacturers' labels, and beneficial as an adjunct therapy in PCOS as evidenced by the research.

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^{vi} Oral contraceptives. *Up To Date*. http://www.uptodate.com/contents/overview-of-the-use-of-estrogen-progestin-contraceptives?source=search_result&search=estrogen&selectedTitle=3%7E150

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^{xiv} Kim Y, Keogh JB, Clifton PM. Polyphenols and Glycemic Control. *Nutrients*. 2016 Jan 5;8(1). pii: E17.

^{xv} Polycystic Ovarian Syndrome: Condition Care Guide. Dr. Andrew Weil. Website. Accessed at <http://www.drweil.com/drw/u/ART03160/Polycystic-Ovarian-Syndrome-PCOS.html>.