Review Article

Dietary Options in Polycystic Ovary Syndrome (PCOS)

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Abstract

Poly Cystic Ovary Syndrome is the hormonal imbalance that is by and large considered to affect more or less 10% of the female population. PCOs is more common in obese and overweight women, which further increases androgen secretion causing impaired metabolism and reproductive functions. Women with PCOS are at increased risk of developing cardiovascular diseases, dyslipidemias, hypertension and type II diabetes Mellitus. Weight reduction is difficult to achieve in obese women with PCOS than normal individuals. So a comprehensive lifestyle intervention program including individualized diet with moderate energy restriction based on basic healthy eating principles, at least 30 minutes moderate physical activity 3-5 days a week and behavior modification approach is required. Hypocaloric diets along with modification of carbohydrates have found to be effective. Selection of foods among low glycemic load (GL) and high fiber foods and replacing fats with polyunsaturated fats may be a helpful strategy in PCOS patients.

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Introduction

Poly Cystic Ovary Syndrome is the hormonal imbalance that is by and large considered to affect more or less 10% of the female population.[1] Poly Cystic Ovary Syndrome is regarded as a hetrogenous endocrine disorder further recognized as reproductive and metabolic. Reproductive accounts for anovulation, oligomenorrhea/amenorrhea, infertility, and androgen excess evident as hirsutism whereas metabolic depicts insulin resistance, dyslipidemia, and obesity.[2] Women with PCOS are at increased risk of developing cardiovascular diseases, dyslipidemias, hypertension and type II diabetes Mellitus[3] as shown in Fig. 1. It is also associated with emotional disturbances, including depression, anxiety and other mood disorders.[4] Metabolic disturbances, mainly insulin resistance and hyperinsulinemia, are recognized as key features responsible for altered androgen production and metabolism.[5] PCOs is more common in obese and overweight women, which further increases androgen secretion causing impaired metabolism and reproductive functions.[6]

Due to anovulation, polycystic ovary syndrome (PCOS) is considered the most common cause of female infertility in child-bearing age women.[7] Insulin resistance and compensatory hyperinsulinemia play major pathogenic roles in PCOs. Insulin may act directly and/or indirectly, via pituitary, to stimulate androgen secretion in ovaries. Menstrual dysfunction, chronic anovulation, hirsutism and hyperandrogenism are some of the well-documented clinical symptoms of PCOs.[8] These clinical symptoms are the four main features of PCOs and may be considered as hyperandrogenic disorder.[9] The early symptoms of the PCOs generally start around menarche followed by cha-

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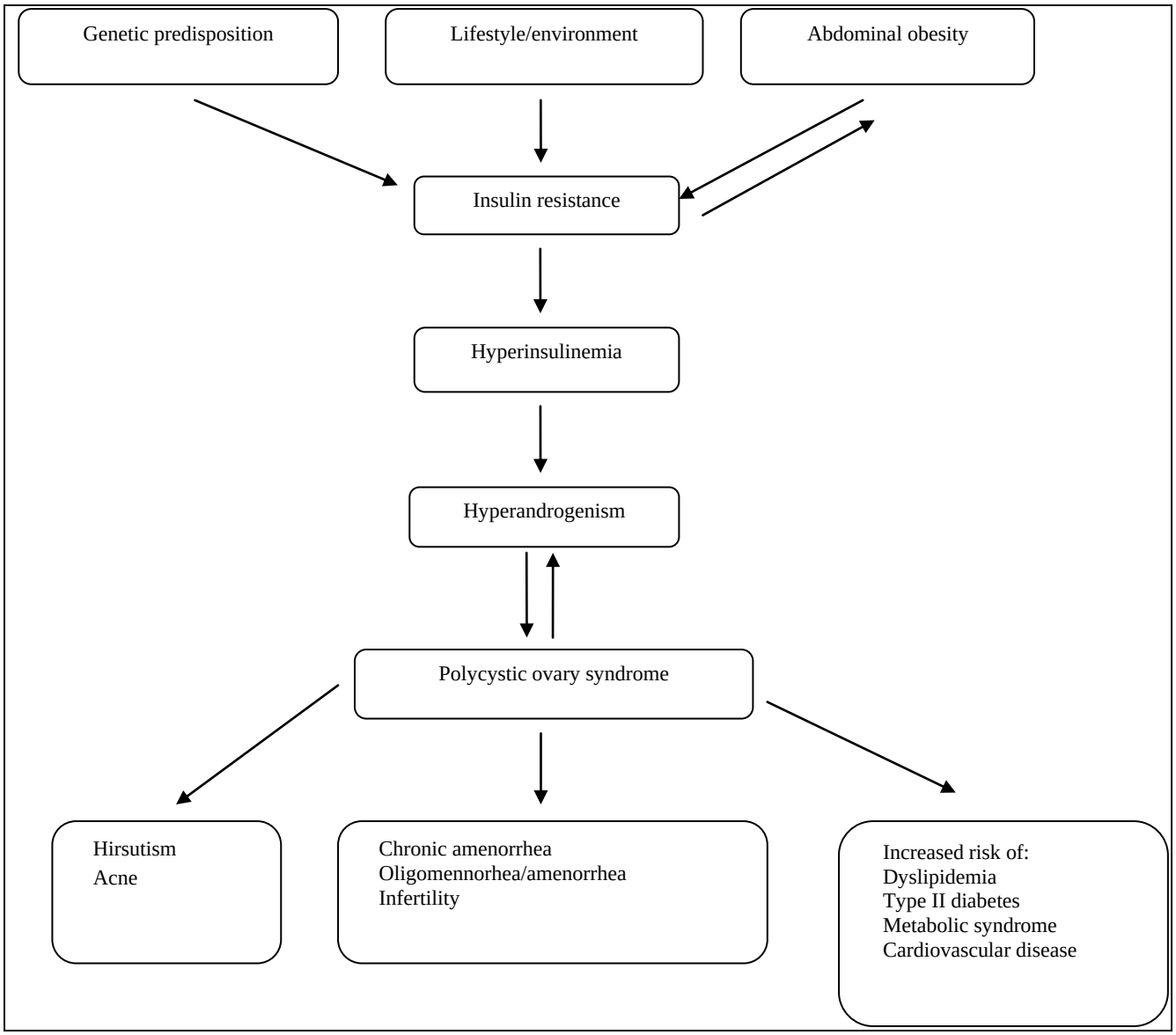

Fig. 1: *Pathways to Insulin Resistance and Polycystic Ovary Syndrome.*

racteristic endocrine abnormalities as hypersecretion of androgens and (LH) luetinizing hormones.[10] The clinical features of PCOS are diverse and complicated and may alter throughout the lifecycle, starting from puberty to postmenopausal age.[11] This indicates an important factor in the evaluation of the PCOS throughout life and implies that the PCOS by itself may not be a hyperandrogenic disorder exclusively restricted and relevant to young and fertile-aged women but may also have some health implications later in life.[12]

Diagnosis of Poly Cystic Ovaries Syndrome

Chronic anovulation and hyperandrogenism and other related features including acne, hirsutism, and male pattern baldness was the earlier criteria for diagnosing PCOS, as defined by the 1990 National Institutes of Health–National Institute of Child Health and Human Development conference. It excluded other associated disorders such as Cushing's syndrome and congenital adrenal hyperplasia (13). The more recent "Rotterdam criteria" revised by Rotterdam European Society for Human Reproduction/American Society of Reproductive Medicine (ASRM) extended the National Ins-

Table 1: *Summary of Different Dietary Interventional Studies in Polycystic Ovary Syndrome.*

Dietary Interventions	Subjects (n)	Duration	Baseline BMI (kg/m)2	Weight Loss Achieved	FML	FBG	Fasting Insulin	Serum Lipids	FT	SHBG	MC	Hirsutism	Reference
Low carbohydrate, ketogenic diet <20 g carbohydrates/ day No caloric restriction	11	24 weeks	> or =27	12%	N/A		↓	N/S	↓	N/A	N/A	N/S	Mavropoulos et al. (2005)
5950-6150 kJ/d Diet 1: High carbohydrate (55%) with high GI Diet 2: High carbohydrate (55%) with low GI Diet 3: High protein (25%) with high GI Diet 4: High protein (25%) with low GI	129	12 weeks	> or =25	... ...	↓ ↑ ↑ N/A	↓ ↓ ↓ ↓	↓ ↓ ↓ ↓	N/S ↓ ↑ N/S	N/A N/A N/A N/A	N/A N/A N/A N/A	N/A N/A N/A N/A	N/A N/A N/A N/A	McMillan-Price et al. (2006)
High protein (30% protein, 40% carbohydrate, 30% fat) 5000-6000 kj/d DO DA DC	94	20 weeks	> or =25	8.9 ± 1.6 10.6±1.7 8.7 ± 1.7	N/S ↑ ↑	↓ ↓ ↓	↓ ↓ ↓	↓ ↓ ↓	↓ ↓ ↓	↑ ↑ ↑	↑ ↑ ↑	N/A N/A N/A	Thomson et al. (2008)

Dietary Interventions	Subjects (n)	Duration	Baseline BMI (kg/m)2	Weight Loss Achieved	FML	FBG	Fasting Insulin	Serum Lipids	FT	SHBG	MC	Hirsutism	Reference
700 kcal reduction from diet, addition of 240 kcal from whey protein or simple sugars	24	2 months	25-40	3.3± 0.8 1.1 ± 0.6	↑ N/S	N/S N/S	N/S N/S	↑ N/S	N/S N/S	N/A N/A	N/A N/A	N/A N/A	Kasim-Karakas et al. (2009)
1200-1400 kcal/d Follow-up by 500 kcal energy deficit and mild physical activity Group 1* (persistence) Group 2 (partial) Group 3 (complete) Composition not specified	65	6 months 20.4±12.5 months Follow-up	≥ 25	12.7±7.3 15.3±8.6 14.1±7	N/A N/A N/A	N/S ↓ ↓	↓ ↓ ↓	↓ ↓ ↓	P/I P/I Normal	N/S N/S ↑	P/I P/I Normal	P/I P/I Normal	Pasquali et al. (2011)
Low GL (45% carbohydrate, 35% fat, 20% protein) vs. low fat (55% carbohydrate, 25% fat, 20% protein)	16	6 months	≥ 85th percentile	1.2±0.8 4.8±1.6	↑ ↑	N/S ↓	↑ ↓	↓ N/S	N/S N/S	N/S N/S	N/A N/A	N/A N/A	Wong et al. (2015)

GI, glycemic index; GL, glycemic load; BMI, body mass index; FML, fat mass loss; FBG, fasting blood glucose; FT, free testosterone; SH BG, serum hormone binding globulin; MC, menstrual cyclicity; N/A, not available or measures; N/S, not significant; P/I, partial imp rovement; DO, diet only; DA, diet and aerobic exercise; DA, diet and combined aerobic-resistance exercise

*women reclassified into 3 groups according to persistence, partial or complete disappearance of PCOS features after follow-up.

titutes of Health definition to include 2of 3 of the following features: (1) clinical or biochemical evidence of hyperandrogenism (2) oligomenorrhea or amenorrhea; and (3) polycystic ovary morphology as visualized by ultrasound.[14]

Relationship of Obesity and PCOS

PCOS is a disorder associated with (and worsened by) obesity. Obesity is common in PCOS and mostly morbidly obese women develop this disease. Studies showed that hyperandrogenemia could aggravate central obesity in women. Androgen promoted visceral fat deposition in females.[15] Obesity and specifically abdominal obesity are main features in PCOS (16) and is observed in 35 – 60% of cases.[13] It exacerbates the reproductive, metabolic, and psychological factors associated mainly by insulin resistance.[17,18] Abdominal obesity is associated with modifications of both synthesis and metabolic clearance rates of sex hormones and reduced serum sex hormone-binding globulins (SHBG) levels. Tissue metabolism regulation can be effected by androgens in abdominally obese women with PCOS.[12] Insulin resistance further leads to obesity in women with PCOS. In insulin resistant states, non-esterified fatty acids released from the muscle and adipose tissues provide substrate for triglyceride production in the liver.[19] Pathogenetic factors like insulin resistance and associated hyperinsulinaemia are now acknowledged as key features in determining hyperandrogenism in the majority of PCOS women, predominantly if obesity is present.[20] Hyperinsulinemia and insulin resistance predispose both normal and overweight women with PCOS to obesity by insulin's anabolic effects as well as changes in eating behavior.[21] As high blood androgen levels results in more cravings of carbohydrates, which is evident by a study indicating greater intake of specific high glycemic-index foods including white bread and potatoes by women with PCOS as compare to healthy group.[22]

There is also twice the risk of metabolic syndrome in adult woman with PCOS than general population[23] and its frequent features like insulin resistance, dyslipidemia, glucose intolerance, central obesity and hypertension are common in PCOS.[24] Many patients with PCOS show central obesity, a frequent feature of metabolic syndrome as compare to peripheral fat deposition.[21] Obesity is also associated with anovulation, miscarriage, or late pregnancy complications such as pre-eclampsia and gestational diabetes.[13]

Weight Management in PCOS

Due to the relationship of obesity and insulin resistance with PCOs, dietary modification, increased physical activity and weight management is recommended as initial management for women with PCOs.[25,26] Weight management refers to prevention of excess weight gain or attaining and maintaining healthful weight in overweight individuals (Moran, Pasquali et al. 2009). Lifestyle management approach consisting of dietary, exercise, and behavioral therapy is helpful in achieving lasting weight loss.[27] Regular moderately intense physical activity for 3o minutes atleast 3 days per week is recommended for weight loss and long-term weight management.[28] It is observed that even 5 – 10% reduction of initial weight returns ovulatory function in anovulatory females with PCOS[29] and results in improvement of all the symptoms of PCOs.[13,30,31] Weight loss not only decrease insulin resistance, serum androgen levels, the number of ovarian cysts and ovarian size but also improves ovulation, fertility (Kasim-Karakas, Cunningham et al. 2007) and menstrual function.[32] However, weight reduction and maintenance of weight loss has found to be extremely difficult in obese women with PCOS.[20]

Role of Diet in Management of PCOS

The initial management for overweight women affected by PCOS, with or without insulin sensitivity, is a balanced diet, along with lifestyle management which permits weight loss in all age groups.[33] Lifestyle management refers to intake of healthy diet, regular exercise and maintenance of healthy body weight.[34] In assessment of a link between diet and PCOS, the main focus of many studies is the most favorable dietary macronutrient composition with other dietary approaches, including low-glycemic Index, low-glycemic load, high-protein, low-carbohydrate, high monounsaturated fatty acids (MUFA) diet or modified fatty acids diets to improve the insulin resistance and obesity. These projected diets are considered having potentially more positive hormonal effects or to be more effective in achieving and maintaining lasting weight loss in PCOS but more research is needed in this regard.[26,35] In the general population, recommendations for macro-nutrients is high-carbohydrate (approximately 50 – 60%), moderate-protein (approximately 15%), moderate-fat (approximately 30% of energy, saturated fat approximately 10% of total fat, < 300 mg cholesterol daily) and with increased consumption of

fiber, fruits and vegetables, and whole-grain breads and cereals, along with regular exercise.[26,36] However, a clear dietary composition and recommendation for improvement of hormonal, metabolic, reproductive and psychological factors associated with PCOS,[27] a sustainable weight loss and long term prevention of type 2 diabetes, CVD and certain hormone dependent cancers is still not developed.[37]

Following dietary options are prescribed for PCOS.

Hypocaloric Diet

Many studies have focused on reduced energy diets regardless of their composition (high protein or high carbohydrates) for a short duration of time and found them effective in weight loss and improvement of metabolic and hormonal abnormalities in PCOS.[31] In normal individuals, a reduction of 500 kcal per day is desirable to lose 0.5 kg per week, while a 1,000 kcal deficit is required for 1 kg weight loss per week.[38] Hypocaloric diets (500–1000 kcal/day reduction) for a duration of 6 – 12 months are effective options for weight loss in PCOS and have found to be helpful in 7–10% body weight reduction.[26] In a calorie restricted diet (5000–6000 kJ/d) for 20 weeks, significant decrease in insulin resistance, fasting glucose and insulin, triglycerides, total cholesterol, testosterone and increase in SHBG levels and reproductive functions have been observed in PCOS patients with and without exercise both. They are also effective in weight and total fat reduction.[39] The long term effects of these diets are not well studied. In a study to observe the long term effect of reduced energy diets (1200 – 1400 kcal/day) for 6 months and then follow up with 500 kcal/day and physical activity for 20.4 ± 12.5 months showed varied responsiveness in disappearance of certain PCOS features like hyperandrogenism and menstrual cyclicity, while only one third women achieved full recovery.[40]

Low Carbohydrate, Low-GI, Low-GL, High Fiber Diet

Recent studies have shown a greater improvement in insulin resistance, weight loss and androgen levels achieved through low-carbohydrate diets. Different dietary regimens have been used with varying degrees of carbohydrate restriction.[41] In a pilot study to evaluate the effect of low carbohydrate, keto-genic diet on PCOS, as low as 20 grams/day carbohydrates for 24 weeks showed significant decrease in fasting insulin (54%), body weight (12%) and testosterone levels (22%).[42] In another study following a low-carbohydrate (43%), high monounsaturated fats (MUFA) diet, subjects showed lower fasting insulin and acute insulin response to glucose (AIRg) in 16 days while hormonal levels and fasting glucose levels remained unaffected.[43]

Dietary fiber has also regulatory effect on metabolism of hormones as it reduces the insulin secretion by slowing the rate of glucose absorption after a meal.[20] Fiber intake has also shown positive correlation with serum SHBG levels. Modern diets having low fiber and high refined carbohydrates induces insulin resistance and obesity.[44]

Glycemic index is the value that tells how rapidly a specific carbohydrate will raise the blood sugar level, while glycemic load is calculated by multiplying the glycemic index with number of grams of carbohydrates and dividing by 100. The benefits of low glycemic index foods on insulin sensitivity and weight loss are studied in PCOS and non PCOS women. As hyperinsulinemia after a high carbohydrate meal is a marked feature in majority of women with PCOS, a low glycemic load food may be helpful in this regard.[45] Low glycemic load foods have found to be effective in weight reduction[46] and improved hyperinsulinemia in non PCO over weight individuals.[47] Greater insulin sensitivity and lower high-sensitivity C-reactive proteins (hsCRP) are observed in PCO women as well with high protein, low glycemic load foods.[48] In a recent study weight loss and reduction in body fats was observed in adolescents with PCOS with consumption of low glycemic load and low fat diets both but there was not any effect on androgenism.[49] In a comparative study of low G-I diet with conventional diet, significant improvement in insulin sensitivity and menstrual cyclicity was observed.[45]

High-Protein Diet

Various short term studies have investigated effect of high-protein diets along with low-calorie or low-carbohydrate diets on PCOS patients. These enviable outcomes may be due to low-carbohydrate, keto-genic diet to some extent, as high glucose intake is significantly related to hyperinsulinemia, high glycemic index and glycemic load.[42] Increased dietary protein to carbohydrate ratio have found greater weight loss and fat mass loss and improvement in glucose metabolism in 6 months period.[50] In a 2-months study to evaluate

the weight loss in overweight PCOS patients, a hypocaloric diet with protein supplementation was found to be more effective in weight loss and fat mass loss than the same diet with simple sugars supplementation. Reduction in HDL cholesterol, total cholesterol and apo-B levels were more profound in high-protein group as compare to high-sugar group, however there were not marked changes found in insulin resistance or serum androgen levels.[51]

High protein diets have also found to be effective in weight loss regardless of any exercise regimen in PCOS patients. In a 20-weeks lifestyle interventional study, Thomson et al (2008) studied the effect of high-protein diet having 30% energy as proteins, 40% as carbohydrates and 30% as fats, alone and combined with aerobic and aerobic-resistant exercise in ninety four over-weight and obese subjects with PCOS. All interventions helped in weight reduction but no additional hormonal, cardiometaboilc and reproductive improvements were found in either group.[39]

The satiety feeling associated with high protein diets have also considered to be helpful in improving psychological well-being as compare to high-carbohydrates diets.[52] Protein intake suppresses ghrelin, modestly longer than glucose, causing a prolonged satietogenic effect.[53]

Low Fat Diet

Low fat diets have shown weight loss in obese individuals and prevented weight gain in normal in normal individuals.[54] Low fat diets have also been used for weight loss purposes in women with PCOS but have shown similar reduction in weight, abdominal fat and improvement in insulin sensitivity as compared to low carbohydrate diets.[30] In different randomized trials, low fat diets have shown greater reduction in total and LDL cholesterol in normal individuals as compare to low carbohydrate diets which showed beneficial effect in HDL cholesterol and triglyceride levels, while there was no difference in weight reduction and other metabolic risk factors in both diets.[47,55] In a recent study, to evaluate the effect of low-glycemic load diet vs. low fat diet on hyperandrogenism in over weight and obese adolescents with PCOS, no diet was found to be more beneficial than other in both interventions in 6 months period, while both were equally effective in weight loss.[49] Low fat diets have varied effects on PCOS symptoms. In a study to examine the effects of high-fat (62% fat, 24% carbohydrate) and low-fat (6% fat, 81% carbohydrate) test meals, reduced suppression of testosterone levels and increased postprandial glucose and insulin levels were found for the low-fat meal.[56]

Omega-3 Polyunsaturated Fatty Acids (n-3 PUFAs)

In recent studies, increased omega-3 PUFAs especially α-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) intake seems the most widespread approach for managing PCOS in obese and non-obese patients both.Omega-3 polyunsaturated fatty acids (n-3 PUFAs) are found in fatty fish, nuts (especially walnuts), nuts butters and seed oils. In contrast high n-6 fatty acid intakes are related to high levels of circulating plasma androgen level. Omega-3 fatty acids have also found to be important in reduction of hepatic lipogenesis, plasma triglycerides, hypertension and other cardiometabolic risk factors in obese women with PCOS.[57] In adipose, skeletal and heart muscles long chain Omega 3 fatty acids found in fish oil raises extracellular lipolysis by lipoprotein lipase and increases β-oxidation in hepatic and skeletal muscle which is helpful in reduced fatty acids supply to the liver. In this way fish oil is effective in lowering hepatic triglyceride production in insulin resistant patients.[19]

Plasma n-6: n-3 PUFA ratios have also exhibited a great effect on plasma androgen concentrations. According to researches, women with a higher plasma n-6: n-3 PUFA ratio demonstrate higher plasma androgen levels.[58] Supplementation of omega-3 PUFAs to PCOS subjects has showed significant decrease in insulin resistance, BMI, testosterone (androgen) levels and increase in sex hormone-binding globulin (SHBG) levels.[59,60] While increased dietary PUFAs intake have also shown significant metabolic and endocrine effects in patients with PCOS.[61] In a study of comparison between long chain PUFAs and essential PUFAs effects on PCOS, Fish oil (a rich source of the long chain n-3 PUFAs; EPA and DHA) and flaxseed oil (a rich source of the essential n-3 PUFA, ALA) both showed separate metabolic and endocrines effects, so they should not be used as substitute for each other.[2]

Conclusion

As obesity is directly linked to all symptoms of PCOS including insulin resistance, hyperandrogenemia, men-

strual cycle, ovulation and fertility, a sustained weight loss should be the first treatment of PCOS. Weight reduction is difficult to achieve in obese women with PCOS than normal individuals. So a comprehensive lifestyle intervention program including individualized diet with moderate energy restriction based on basic healthy eating principles, atleast 30 minutes moderate physical activity 3 – 5 days a week and behavior modification approach is required. A hypocaloric diet along with modification of carbohydrate have found to be effective. Selection of foods among low glycemic load (GL) and high fiber foods and replacing fats with polyunsaturated fats may be a helpful strategy in PCOS patients. There is considerable difference in research literature regarding an optimal dietary composition or standard guidelines in management of weight loss and weight maintenance in such patients. Several dietary approaches have been researched in PCOS but formal evidence-based clinical practice guidelines should be developed.

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