Dietary interventions in the treatment of women with polycystic ovary syndrome

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Abstract

Women with polycystic ovary syndrome (PCOS) are characterized by several hormonal and metabolic disturbances, which interact with each other. Diseases such as overweight or obesity in these women further lead to the development of metabolic complications and its consequences such as type 2 diabetes mellitus (T2DM) and cardiovascular disease. Modification of dietary habits in women with PCOS may have favourable effects on their hormonal and metabolic profile. Dietary treatment of women with PCOS should be based on a balanced diet taking into consideration the dietary fibre and polyunsaturated fatty acids consumed. Also, enrichment of the diet with the long chain polyunsaturated fatty acids may have favourable effects. The decrease in the energy intake is mandatory in PCOS women with accompanying overweight or obesity. In addition, regular physical activity has also beneficial effects on the metabolic disturbances in these patients.

Key words: polycystic ovary syndrome, metabolic disturbances, dietary intervention.

Introduction

Polycystic ovary syndrome (PCOS) is the most frequent endocrinopathy in women of reproductive age. It affects from 5% to 10% of the female population and is the most common cause of infertility. The symptoms characteristic of this syndrome include: clinical or biochemical hyperandrogenism, oligo- or anovulation and the presence of polycystic ovaries in transvaginal ultrasonography (TV USG). Disturbances of the carbohydrate and lipid metabolism are also very frequent in PCOS, which is associated with the development of type 2 diabetes mellitus (T2DM) and cardiovascular disease in later life [1]. Therefore, treatment of women with PCOS should not only concentrate on lowering high androgen levels and restoring ovulatory menstrual cycles, but should also take into consideration all the metabolic disturbances present in this endocrinopathy [2]. In particular, non-pharmacological methods concentrating on diet and eating habits of these patients should be implemented. Appropriate dietary interventions in these women based on adequate energy intake and proper macronutrient content will usually not only improve the metabolic disturbances but also can lead to the normalization of hyperandrogenaemia in these patients.

Diagnostic criteria for polycystic ovary syndrome

Polycystic ovary syndrome includes a number of endocrine and metabolic disturbances associated with increased ovarian androgen production. In 1935, Stein and Leventhal reported a number of symptoms related to the presence of cystic changes in the female gonads, including hyperandrogenism, secondary amenorrhea and ensuing infertility. Since then the criteria for the diagnosis of PCOS have been repeatedly modified [1]. Now, PCOS is diagnosed according to the consensus established in 2003 in Rotterdam by the experts of the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM). According to these “Rotterdam criteria”, PCOS is diagnosed in a woman who presents at least two out of three of the following symptoms: (1) oligo- or amenorrhea, which is a result of oligo- or anovulation; (2) biochemical hyperandrogenemia and/or clinical hyperandrogenism; and (3) the presence of polycystic ovaries in the TV USG. Additionally, other causes of hyperandrogenism such as non-classical congenital adrenal hyperplasia (NCCAH), androgen secreting tumours, Cushing disease and caus-
es of oligomenorrhea such as hyperprolactinaemia and hypothyroidism must be excluded [3]. Nevertheless, according to the experts of the Androgen Excess and PCOS Society (AE & PCOS) in women presenting with oligo- or amenorrhea and polycystic ovaries in the TV USG but without biochemical or clinical hyperandrogenism, PCOS should not be diagnosed [4].

Pathogenesis of polycystic ovary syndrome

In recent years numerous studies have focused on the pathogenesis of PCOS, however its cause is still unknown. The main cause of PCOS development seems to be the genetic predisposition, but environmental factors such as high energy diet and low physical activity also play an important role in its pathogenesis. Insulin resistance and hyperinsulinaemia related to overweight and obesity, especially visceral obesity, are the main link in endocrinological disturbance development in numerous cases of PCOS [5]. The important factors in insulin resistance development are the local inflammation and hormonal disturbances of adipose tissue. A proinflammatory cytokine – tumour necrosis factor α (TNF-α) plays the key role in the insulin resistant function disturbances. Tumour necrosis factor α inhibits tyrosine autophosphorylation in IRS-1 and increases serine phosphorylation in the intracellular part of the insulin receptor as well as suppresses expression of the glucose transporter (GLUT 4) [6]. Hyperinsulinaemia, as a consequence of insulin resistance, decreases hepatic production of the sex hormone binding globulin (SHBG), which increases serum concentrations of bioavailable testosterone. Additionally, it has been shown that increased serum insulin levels enhance ovarian and adrenal androgen production [7]. High insulin levels increase pituitary LH secretion, which cause increased androgen synthesis in the theca cells which in turn disturb folliculogenesis, that is the cause of anovulation [6]. In addition, insulin resistance and hyperinsulinaemia are associated with metabolic disturbances, such as hyperglycaemia, hypertriglyceridaemia, increased serum LDL-cholesterol levels and hypertension development [8].

Metabolic disturbances related to overweight and obesity in polycystic ovary syndrome

Over a half of the PCOS women are overweight or obese. Obesity, especially visceral obesity, is the reason for metabolic disturbances and impaired quality of life [9]. Additionally, obesity per se impairs ovulation and therefore causes menstrual irregularities and infertility [7]. It has been suggested that hormonal and metabolic implications of the visceral fat per se induce and exacerbate the symptoms of PCOS [7]. During the 3rd ESHRE/ASMR Consensus in Amsterdam, the consequences of PCOS have been listed. These were decreased quality of life, fertility problems, increased risk of T2DM, cardiovascular disease and cancer (i.e. endometrial and breast cancer) development. All are regarded as a late consequence of this syndrome. It should be noted that obesity per se can play an independent role in the development of the metabolic and reproductive symptoms of PCOS. In addition, obesity also has a negative effect on pharmacological treatment of PCOS [10]. The main cause of weight gain in women with PCOS is a positive energy balance and intensified at a later period by insulin resistance and hyperinsulinemia resulting in the reactive hypoglycaemia and increased consumption of snacks rich in simple carbohydrates between the main meals [11].

Women with polycystic ovary syndrome frequently also have other metabolic syndrome components such as increased arterial blood pressure and low serum HDL-cholesterol concentrations as well as higher triglyceride levels [9]. The dyslipidaemia is the effect of visceral obesity, insulin resistance and environmental factors. Low physical activity and diet rich in saturated fats and simple carbohydrates play an important role in lipid disturbances in PCOS women. In addition, they increase serum total and LDL cholesterol levels as well as apolipoprotein CIII (Apo CIII). Apo CIII inhibits the activity of the lipoprotein lipase blocking the Apo CII (essential enzyme activator), that impairs the metabolism of very-low density lipoproteins (VLDL) and triglycerides. In addition, Apo CIII inhibits Apo B and Apo E, ligands of the lipoprotein receptors resulting in the increase in serum LDL-cholesterol concentrations. Moreover, due to the insulin resistance, increased serum glucose concentrations also increase Apo CIII synthesis. The result of the rise of atherogenic molecule concentrations promotes inflammation in the endothelial cells and increases the risk of cardiovascular disease development [12].

Body mass reduction in polycystic ovary syndrome treatment

Lifestyle modification, such as changes of dietary habits and increasing physical activity should be the first recommendation in the treatment of overweight or obese PCOS women [18]. Regular physical activity decreases body mass and helps maintain this effect as well as improves well-being. However, the lack of a recommendation on the optimal type, duration and frequency of physical activity in PCOS women [19].

It has been shown that dietary modification and increase in physical activity (alone or in a combination) improves the hormonal profile in PCOS women by a de-
crease in insulin resistance resulting in restoration of regular menses [20]. In addition, physical activity decreases fat mass, especially visceral fat, and prevents the loss of free fat mass [17]. It has been observed that 10% reduction of baseline body mass decreased blood pressure and serum glucose and lipid levels. However, Olszanecka-Glinianowicz et al. [21] have shown that 12% body mass reduction in PCOS women obtained by low energy diet (1200-1600 kcal) and regular physical activity (30–40 min per day) resulted in a decrease in serum triglycerides and increase in SHBG levels but serum glucose concentrations or hormonal profile have not changed. Therefore, these authors suggest that a moderate body mass reduction is not sufficient to obtain a full therapeutic effect. In contrast, Thomson et al. [22] assessed the effect of high protein (30% of energy intake) low energy diet (1200-1400 kcal) without or with regular physical activity (5 sessions a week), which revealed that 10% body mass reduction resulted in a decrease in blood pressure and serum fasting glucose, insulin and testosterone levels as well as an increase in circulating SHBG levels. In addition, the restoration of ovulatory cycles was observed. It should be noted that regular physical activity cause higher fat mass and lower free fat mass reduction. Moran et al. [23] suggested that short-term meal replacement enhanced body mass reduction in PCOS. In addition, a moderate decrease in simple carbohydrate and fat is also effective in the body mass maintenance and improvement of carbohydrate metabolism as well as decrease in serum testosterone concentrations [24].

Dietary interventions in the treatment of women with polycystic ovary syndrome

The aim of dietary treatment is to supply an adequate quantity of macro-, micronutrients and energy for the optimal health status and decrease the risk of the diet-related disease development. In PCOS, the main aim of dietary interventions is the body mass reduction, especially the visceral fat, which decreases insulin resistance and improves the hormonal and metabolic profile. Short-term recommendations in overweight and obese PCOS women are focused on body mass reduction, which usually decreases disease symptoms and restores regular menses. Meanwhile, the aim of long-term interventions is to maintain reduced weight and decrease the risk of T2DM and coronary heart disease as well as cancer development [13]. It has been shown that the type of the ingested foods may have a great impact on fertility in these PCOS women. It has been observed that an increased consumption of animal protein and carbohydrates with a high glycaemic index (GI) can disturb ovulation in PCOS women. It has also been suggested that severity of PCOS symptoms is associated with dietary factors [14]. Thus, appropriate dietary interventions in this group of patients is indisputably an important part of PCOS treatment. However, it is distressing that obese PCOS women frequently do not follow diet recommendations. It has been shown that in PCOS women the percentage of daily energy intake from carbohydrates is diminished due to the increased fats consumption [15]. Therefore, the dietary recommendation should include both quality and quantity macronutrients, especially carbohydrates and lipids. The level of energy intake should be individualized according to the body mass and the level of physical activity. A daily deficit of energy equal to 200 kcal is sufficient for the protection of body mass gain. A deficit of 500 kcal to 1000 kcal per day is recommended to decrease body mass by 0.5 kg and 1.0 kg weekly, respectively. The negative energy balance should be obtained not only by restriction on energy intake but also by increasing energy expenditure as a result of physical activity [16]. It was shown that individualized diet and physical activity recommendation in the long term result in body mass reduction and restoration of regular menses [17].

The role of carbohydrates in the dietary treatment of women with polycystic ovary syndrome

High simple carbohydrate diets have unfavourable effects on postprandial serum glucose and insulin concentrations as well as serum triglyceride and HDL-cholesterol levels. However, it was shown that carbohydrates with a low glycaemic index (GI) improve insulin sensitivity and increase HDL-cholesterol concentrations. Meanwhile, carbohydrates with a high GI increase insulin resistance. In addition, data from epidemiological studies show that diets with a low GI decrease the risk of T2DM and cardiovascular disease development [25]. It has also been suggested that diets based on products with a low GI decrease the risk of endometrial cancer development in PCOS women indirectly by decreasing BMI, hyperinsulinaemia and hyperandrogenaemia [26]. In turn, use of a diet with a low glycaemic load (GL) is associated with a significant body mass reduction and its maintenance as well as lower postprandial hyperinsulinaemia in PCOS women. Marsh et al. [13] revealed that low GI diet has significantly improved insulin sensitivity compared with a classical balanced diet. In addition, use of this diet is associated with frequent restoration of regular menses (95% of women treated with low GI diet compared to 63% women treated with classical balanced diet), probably due to improvement of insulin sensitivity and androgen decrease. Moreover, the favourable effect of this diet on the lipid profile was observed [13]. However, this evidence is not sufficient to confirm that low carbohydrate
diet offers benefits other than weight loss obtained during the conventional low energy diet [18].

**High protein diets in the treatment of women with polycystic ovary syndrome**

The results of some studies suggested that high protein and low carbohydrate diets have a beneficial effect in PCOS by a significant decrease in body mass and visceral fat accumulation as well as improvement of glucose metabolism. However, recently dietary guidelines have recommended that protein should constitute not more than 20% of total daily energy intake. Nevertheless, it seems that a short-term increase in protein consumption may be considered a part of a dietary plan to facilitate body mass reduction and improve insulin sensitivity [16]. Sørensen *et al.* [27] have shown a significantly higher body mass reduction and decrease in body fat, waist circumference as well as serum fasting glucose levels in PCOS women treated with high protein diet (> 40%) than in a group consuming diet with normal protein content (< 15%). However, the changes of serum testosterone and SHBG concentrations did not differ between the study groups. It should be noted that numerous studies comparing the high protein diets with normal protein diets showed no differences in body mass reduction and metabolic profile in PCOS women. Moran *et al.* [28] have shown that diet of about 1400 kcal/day, regardless of protein content (30% and 15%) causes a similar weight loss, decrease in fat tissue content lowering plasma triglycerides and total cholesterol and insulin levels. Toscani *et al.* [29] and Thomson *et al.* [30] have also shown no differences in decrease in serum insulin, testosterone and markers of endothelial dysfunction levels between obese PCOS women treated with low calorie diet (1400 kcal), high-protein diet (30%) or normal protein diet and physical activity. It should be noted that despite a significant decrease in body mass during treatment with high-protein diets, their implementation should be cautious due to potential adverse effects on the renal function and bone mass density. Moreover, use of high protein diets is associated with a decrease in cereal, vegetable and fruit (the main source of fibre, vitamins and minerals) consumption. In addition, an increased risk of cardiovascular disease and endometrial cancer development in subjects consuming high protein diets was described [25].

The role of lipids in the dietary treatment of women with polycystic ovary syndrome

Dietary lipids play a significant role in several different health aspects. The n-3 polyunsaturated fatty acids (PUFA) for example are the precursors in the synthesis of prostaglandins and eicosanoids, which in turn regulate inflammatory reactions. Consumption of n-3 long-chain fatty acids decreases the concentrations of serum triglycerides and increases HDL-cholesterol levels. Population studies show that the consumption of sea fish rich in long chain polyunsaturated fatty acids (LC-PUFA) decreased the risk of cardiovascular diseases [31]. Therefore, it seems that the supplementation of diet with the n-3 PUFA in women diagnosed with PCOS will have favourable metabolic and cardiovascular effects. Implementation of a Mediterranean diet rich in monounsaturated fatty acids (MUFA), might also be beneficial in women with PCOS. This hypothesis is based on the observations that obesity and insulin resistance is less prevalent among Italian compared to American women diagnosed with PCOS. In contrast, excess consumption of all fatty acids impairs insulin sensitivity and leads to the development of obesity. Therefore, total dietary fat content should not exceed 30% of the daily energy intake and less than 10% with saturated fatty acids [16]. Phelan *et al.* [32] have shown a significant correlation between serum n-6 fatty acids and androgen levels in women diagnosed with PCOS. Meanwhile, higher n-3 fatty acid concentrations are associated with a favourable lipid profile (lower serum triglycerides and higher HDL-cholesterol concentrations) in women diagnosed with PCOS. These authors also found that dietary supplementation of n-3 LC-PUFA decreases the bioavailability of testosterone in PCOS women [32]. In turn, Kasim-Karakas *et al.* [33] observed that the replacement of saturated fatty acids with unsaturated by the implementation of walnuts as a source of linoleic (LA) and α-linolenic acid (ALA), leads to favourable changes in the lipid profile of PCOS women. Moreover, significantly lower serum concentrations of free fatty acids and ketone bodies and non-significantly lower triglycerides, total cholesterol and higher HDL-cholesterol were found. Furthermore, consumption of walnuts increased serum concentrations of LA and ALA but was not accompanied by the increase in eicosapentaenoic (EPA), docosahexaenoic (DHA) and arachidonic acid (AA) levels. In addition, serum fasting and 2 h after a glucose load (OGTT), glucose levels increased, despite the described potential favourable effects of the PUFA on insulin sensitivity and carbohydrate metabolism [33]. It may be an effect of higher total fat content up to 39% of the daily energy intake. Meanwhile, Cussons *et al.* [34] found that n-3 LC-PUFA decreased a liver fat deposit in non-alcoholic fatty liver disease (NAFLD), serum triglycerides and glucose concentrations as well as arterial blood pressure [34]. Kalgaonkar *et al.* [35] compared the effects of consumption of walnuts and almonds as a source of PUFA and MUFA, respectively, on the metabolic and hormonal
profile in PCOS women. They showed that nutrient consumption is associated with a significant increase in serum LA and ALA concentrations. However, similarly to the results obtained by Kasim-Karakas et al. [33], serum concentrations of EPA and DHA have not changed. In a group of PCOS women consuming walnuts, serum SHBG and adiponectin concentrations increased while serum LDL-cholesterol and ApoB levels decreased. Meanwhile, in a group of PCOS women consuming almonds in serum AA, adiponectin and SHBG concentrations increased and as a consequence, free androgen index values (FAI) decreased. Despite an increase in serum adiponectin levels, insulin sensitivity has not changed. In addition, no significant decrease in the serum proinflammatory cytokines [interleukin (IL)-6, IL-1 and TNF-α] and C-reactive protein (CRP) levels was observed. Thus, the authors of this study concluded that the addition of walnuts, as a source of PUFA, to the diet of PCOS women may improve the lipid and hormonal profile and as a consequence, decrease the risk of cardiovascular disease development [35]. Studies which assessed the effects of diets rich in MUFA compared to diets rich in carbohydrates, show that MUFA consumption improves the lipid profile decreasing serum triglycerides and increasing HDL-cholesterol concentrations. However, the favourable effect on insulin sensitivity is inconsistent. It must be stressed that the favourable changes in the lipid profile were not observed when the total fat intake was above 38%. In addition, the higher caloric density of meals rich in unsaturated fatty acids is associated with an increased risk of weight gain and related metabolic disturbances [25].

Conclusions

Lifestyle modifications focusing on the implementation of a well-balanced diet and physical activity should be the first-line therapy in women diagnosed with PCOS. Unfortunately, there are no guidelines available concerning the best dietary approach in these patients. Several dietary modifications are taken into consideration according to the results of short-term interventional studies. Additionally, apart from focusing on the alleviation of clinical signs of hyperandrogenism, we must also take into consideration long-term effects on diminishing the risk of T2DM, coronary heart disease and oestrogen-dependent neoplasms (i.e. endometrial and breast cancer). Dietary treatment of women diagnosed with PCOS should be based on balanced diet taking into consideration the glycaemic index of the consumed carbohydrates. Also, enrichment of the diet with the long chain polyunsaturated fatty acids, especially n-3 may have favourable effects. The decrease in the energy intake is mandatory in overweight or obese PCOS women. In addition, regular physical activity has also beneficial effects on weight reduction and improvement of metabolic disturbances in these patients.

Disclosure

Authors report no conflict of interest.

References


