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**Sposób żywienia, aktywność fizyczna i skład ciała a wybrane
parametry metabolizmu u pacjentek z zespołem policystycznych
jajników**

Diet, physical activity and body composition in relation to selected
metabolic parameters in patients with polycystic ovary syndrome

Rozprawa doktorska na stopień doktora
w dziedzinie nauk medycznych i nauk o zdrowiu
w dyscyplinie nauki o zdrowiu
przedkładana Radzie Dyscypliny Nauk o Zdrowiu
Warszawskiego Uniwersytetu Medycznego

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Warszawa, 2023



Abstract

Dissertation title: Diet, physical activity and body composition in relation to selected metabolic parameters in patients with polycystic ovary syndrome.

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age. Insulin resistance (IR) is suggested to play a crucial role in the pathogenesis of PCOS and is associated with the risk of ovulatory disorders. It can be presumed that there is a complex relationship between abnormal adipose tissue metabolism, abdominal obesity, ovulatory disturbances, oxidative stress, hyperandrogenism and insulin resistance in the course of PCOS.

Recommendations regarding the treatment of PCOS have emphasized the great importance of lifestyle interventions in the management of this disease. This doctoral thesis, consisting of three literature review papers and three original research papers, analyzes the importance of diet, physical activity and nutritional status in relation to metabolic disturbances accompanying PCOS, with a particular emphasis on insulin resistance.

Aim

The primary aim of the study was to analyze the impact of diet, physical activity and nutritional status on metabolic disturbances accompanying polycystic ovary syndrome with a particular emphasis on insulin resistance.

Specific objectives of the study were to: assess the association between milk and dairy product consumption and the risk of carbohydrate metabolism disorders and ovulatory disorders, evaluate the influence of dietary factors on adiponectin levels and the risk of ovulatory disorders, in PCOS patients to investigate the relationship between diet, physical activity and insulin resistance and the concentrations of adipokines (adiponectin, leptin, and resistin) secreted by adipose tissue, determine the potential use of HOMA-AD (*the homeostatic model assessment - adiponectin*) as a substitute marker for HOMA-IR (*the homeostatic model assessment of insulin resistance*) in assessing insulin resistance, assess the relationship between abdominal obesity and the type of abdominal fat distribution and the occurrence and severity of insulin resistance, evaluate the relationship between abdominal obesity and diet and physical activity, and assess the association between anthropometric and body composition parameters, with a particular emphasis on abdominal obesity and antioxidant defense parameters.

Materials and Methods

The study group consisted of 56 women aged 18-40 diagnosed with PCOS. A control group of 33 healthy women of the same age was also included.

Anthropometric measurements were conducted and body composition analysis, including abdominal adipose tissue (visceral and subcutaneous), was assessed using bioelectrical impedance. Additionally, fasting blood samples were collected from each participant to measure glucose and insulin levels, adipokines, hormones and oxidative defense markers. Insulin resistance was evaluated based on the following parameters: HOMA-IR, HOMA-AD, and the L/A ratio (*leptin to adiponectin ratio*), with the following cut-off points: HOMA-IR ≥ 2.5 ; HOMA-AD ≥ 6.26 ; and L/A > 2.2 .

To assess dietary habits, an original food frequency questionnaire was used, considering products with either a positive or negative association with tissue insulin sensitivity. A point-based method was used to determine the adherence level to the recommended diet for insulin resistance. Physical activity was measured using the Actigraph GT3X-BT activity monitor.

Results

In the literature review constituting the introduction to the study, it was observed that the relationship between milk and dairy product consumption and the risk of carbohydrate metabolism disorders is unclear. This relationship appears to primarily depend on the quantity and type of dairy products in the diet. While these products do not seem to have a negative impact on women's fertility, there is an adverse effect noted regarding the consumption of low-fat dairy products on the risk of ovulatory disorders. Furthermore, it was found that diet is a significant factor affecting both adiponectin levels and the risk of ovulatory disorders.

In the study, it was observed that in the PCOS group a higher level of physical activity (expressed as MVPA, *moderate-to-vigorous physical activity*) was associated with lower HOMA-IR ($t=-2.109$; $p=0.038$). Furthermore, in the PCOS group, a higher level of physical activity (expressed as MVPA) translated into a greater odd of a normal HOMA-IR level (OR 1.012, 95% CI 1.003-1.021; $p=0.01$). Such associations were not observed between physical activity and other IR parameters or adipokines, nor between diet and all IR parameters and adipokines. Moreover, a strong correlation was noted between HOMA-IR and HOMA-AD values in women with PCOS, with IR being more frequently identified when using HOMA-AD.

Women with PCOS and abdominal obesity exhibited statistically significantly higher fasting insulin levels ($p < 0.001$; $p = 0.007$; $p < 0.001$ and $p = 0.005$, respectively) and significantly higher values of the HOMA-IR, HOMA-AD and L/A ratio compared to non-centrally obese PCOS women. There was a statistically significantly higher frequency of insulin resistance, measured by HOMA-IR, HOMA-AD and the L/A ratio, in PCOS women with increased content of visceral adipose tissue, an elevated VAT/SAT ratio (*visceral to subcutaneous fat ratio*), and a higher WHR (*waist-to-hip ratio*) compared to women with normal values of these parameters. Furthermore, women with insulin resistance diagnosed using all indicators had significantly higher VAT (*visceral adipose tissue*) and SAT (*subcutaneous adipose tissue*) content, as well as higher VAT/SAT and WHR ratios than women without insulin resistance. It was also observed that the VAT/SAT ratio was the best predictor of insulin resistance diagnosed with HOMA-IR and HOMA-AD. On the other hand, VAT $> 120 \text{ cm}^2$ proved to be the best and strongest predictor of insulin resistance measured by the L/A ratio, while VAT/SAT most significantly increased the odds of abnormal HOMA-AD values.

It was observed that higher adherence to the diet recommended in IR was significantly associated with lower VAT content ($t = -2.635$; $p = 0.011$), SAT content ($t = -2.905$; $p = 0.005$), and WHR values ($t = -2.631$; $p = 0.011$). Additionally, a higher level of vigorous physical activity was significantly associated with lower VAT content ($t = -2.277$; $p = 0.027$), SAT content ($t = -2.028$; $p = 0.048$), the VAT/SAT ratio ($t = -2.280$; $p = 0.027$) and WHR ($t = -2.421$; $p = 0.019$). Furthermore, higher adherence to the recommended diet in IR translated into 43% higher odds of having normal VAT content (OR 1.427, 95% CI 1.091–1.868; $p = 0.009$) and 33% higher odds of having a normal WHR value (OR 1.325, 95% CI 1.023–1.716; $p = 0.033$). Additionally, higher levels of vigorous physical activity were associated with an increased odd of having normal VAT (OR 1.063, 95% CI 1.007–1.122; $p = 0.028$) and VAT/SAT (OR 1.057, 95% CI 1.006–1.110; $p = 0.028$) values. Moreover, multivariate analysis indicated that diet was a factor independent of physical activity, that increased odds of normal VAT content (OR 1.430, 95% CI 1.097–1.864; $p = 0.008$), VAT/SAT (OR 1.273, 95% CI 1.003–1.615; $p = 0.047$) and WHR (OR 1.322, 95% CI 1.025–1.704; $p = 0.031$).

It was observed that the concentrations of GSSG (*oxidized glutathione*) and Keap1 (*Kelch-like ECH-associated protein 1*) were significantly higher, while the R ratio (*reduced glutathione to oxidized glutathione ratio*) was significantly lower in the serum of women with VAT/SAT > 0.9 compared to the group with normal values of this indicator. Similar differences were found for GSSG and the R ratio between the WHR ≥ 0.85 and WHR < 0.85 groups

(respectively, $p < 0.05$ and $p < 0.01$). Furthermore, all antioxidant defense parameters were correlated with anthropometric and body composition parameters. Negative correlations were observed between the R ratio and body weight, BMI (*body mass index*), WHR, VAT, SAT, VAT/SAT ratio and total body fat, while positive associations were found with lean body mass and total body water content. Conversely, inverse relationships were noted between the level of GSSG and the aforementioned body composition parameters.

Conclusions

The literature review revealed that despite inconsistent research results, milk and dairy products are significant components of the PCOS women diet. Furthermore, dietary habits play a substantial role in modulating adiponectin levels and influence the risk of ovulatory disorders.

In the study, it was demonstrated that physical activity is associated with reduced insulin resistance in women with PCOS and a lower risk of abdominal obesity. On the other hand, diet appears to be a key factor in the therapeutic management of women with central fat accumulation. Moreover, abnormalities in body composition, especially abdominal obesity, increase the risk of insulin resistance and are linked to the dysfunction of antioxidant defense parameters. Therefore, diet and physical activity are essential components of the therapeutic approach for women with PCOS and every woman with this condition should receive counsel regarding lifestyle modifications to prevent metabolic complications.