IMPACT OF ENERGY BALANCE ON POLYCYSTIC OVARY SYNDROME

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Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age [1], affecting one in five women worldwide [2]. Overweight and obesity increase the prevalence of PCOS, which together with dyslipidemia is considered to be the dominant feature in 40 to 60% of cases [3,4]. Diagnostic criteria include irregular menstruation, androgen excess, and/or polycystic ovaries, with long-term consequences being hyperinsulinemia and infertility [5, 6]. Many studies suggest that metformine and oral contraceptive combinations are commonly prescribed to alleviate reproductive complaints; However, for overweight and obese patients planning pregnancy, weight loss of 5 to 10% through lifestyle modification is recommended as first-line treatment [7-10].

The goal of a weight loss diet is to be in proportion to energy needs and therefore should result in a daily energy deficit that promotes weight loss. If estimated energy requirements are not known, this may lead to poor weight loss and poor adherence to the diet by patients [11].

The only direct method for estimating energy requirements involves caloric titration of food intake over several days or weeks to achieve energy balance [12, 13]. Other objective but indirect methods include doubly labeled water (DLW) and measurement of resting energy values by indirect calorimetry. These methods rely on the assumption that if body mass is stable throughout the observation period, then energy expenditure must be equivalent to energy intake, creating an estimated energy requirement for body mass stability.

Given the cost and ineffectiveness of caloric titration in clinical settings, DLW is considered the gold standard approach because energy expenditure is assessed over several days while individuals continue their usual behavior under free, unmodified conditions. DLW studies also provide a direct assessment of weight stability [14]. However, DLW studies are not cost-effective or practical for use in clinical settings or large-scale studies.

Mathematical equations that calculate energy requirements based on variables such as age, sex, weight, height, and physical activity level are available and have been used in women with PCOS [5,15,16]. In the past decade, the ability of mathematical equations to estimate energy requirements has improved, as several groups have developed equations from DLW data compiled over a 7–14-day period taking into account energy expenditure (including physical activities) [6].

There are insufficient data in the literature to allow any meaningful conclusions to be drawn regarding the relationship between PCOS and energy balance. Furthermore, even if PCOS is indeed associated with energy expenditure (both postprandial and resting state components), it does not necessarily lead to long-term weight gain, especially in adolescents. The central control of components of metabolism, appetite, intestinal peptides and nutrient supply is a very complex to investigate. Thus, the aim of our study was to evaluate the energy parameters in adolescents with PCOS using the indirect calorimetry method.

Research methods

50 adolescents (age 13-19 years) with PCOS of various body weights were studied in a cross-sectional design. 50 adolescents with the same body mass and age without PCOS constituted the control group. PCOS was diagnosed. Energy indicators were determined by the method of indirect calorimetry with REEVUE Metacheck (KORRTM, USA) device. Resting Metabolic Rate (RMR) was determined by the ratio of percentage values of oxygen in inhaled and exhaled air fractions during 10 minutes. Harris and Benedict's mathematical formulas were also used to calculate body energy characteristics (RMRs) taking into account gender, age, body mass, height

and physical activity level, based on which the increased RMR formula was estimated = (RMR-RMRs)/RMRs. Anthropometric parameters were assessed by calculating body mass index taking into account age and gender (percentile tables, WHO, 2002).

The obtained data were statistically processed with the program SPSS22.0. Quantitative variables are presented as the mean standard deviation (SD), the difference of such variables between groups was evaluated by t-test, categorical variables are presented as percentages, and the difference of such variables between groups was evaluated by Chi2-test. The null hypothesis was rejected using the $p<0.05$ criterion.

Results

The distribution of study and control group patients according to body mass percentile is shown in chart #1. As can be seen from diagram #1, the study group consists of both low body weight (36.0%), normal weight (40.0%) and overweight patients (24.0%). In the subgroup of low body mass, the index of BMI was 17.6±1.6 kg/m2, and the percentile of BMI was 12.0±8.2. In the subgroup of normal body mass, the index of BMI was 21.6±1.3 kg/m2, and the percentile of BMI was 55.6±15.7. In the overweight subgroup, BMI was 29.0±5.9 kg/m2, and BMI percentile was 92.6±4.9.

#1BMI percentile in study and control group patients.

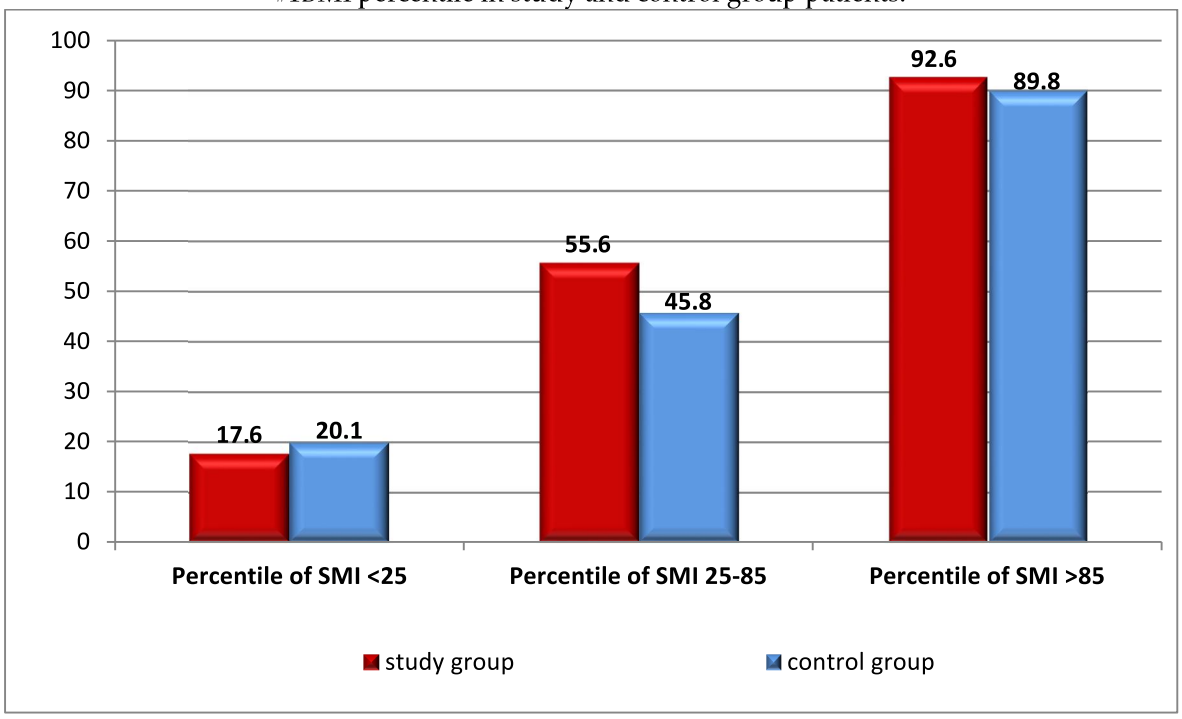

Figure 1. *Anthropometric and energy parameters of study and control group patients.*

As can be seen from Table 1, the RMR rate in both the main study group and the study subgroups of patients with low, normal and overweight body mass was significantly increased compared to the control subgroups. If the RMR rate is compared between subgroups, it is clear that in the study subgroup of overweight and PCOS it is significantly increased compared to the study patients with normal and underweight and PCOS ($p<0.001$), while the rate of the study subgroup of normal weight is not significantly different from the rate of patients with low weight and PCOS ($p=0.254$).

Resting metabolic rate in the RMR groups and statistical test results for their comparison are shown in Table 1.

Table 1.
RMR rate in both the main study group and the study subgroups of patients with low, normal and overweight body mass.

	Research Group		Control Group	
	MEAN	SD	MEAN	SD
RMR	1758.5	363.7	1447.5	149.2
t-test, p	t=5.59, p<0.001			
RMR, low BMI (n=18)	1603.6	274.0	1350.6	178.2
t-test p	t=3.28, p=0.002			
RMR, normal body mass (n=20)	1724.2	356.9	1427.7	154.3
t-test, p	t=3.41, p=0.002			
RMR, high BMI (n=12)	2088.0	327.2	1634.0	185.4
t-test, p	t=4.18, p<0.001			

In the study group, a total of 9 (18%) patients had a decreased indicator compared to the indicators calculated by mathematical formulas, which was considered an energy deficit condition. In the subgroups divided by body mass, this condition was distributed as follows: low mass - 6 (33.3%), normal mass - 3 (15.0%). Such a condition was not observed in people with excess body weight. Figure 2 shows the increase in RMR in study subgroups by body mass.

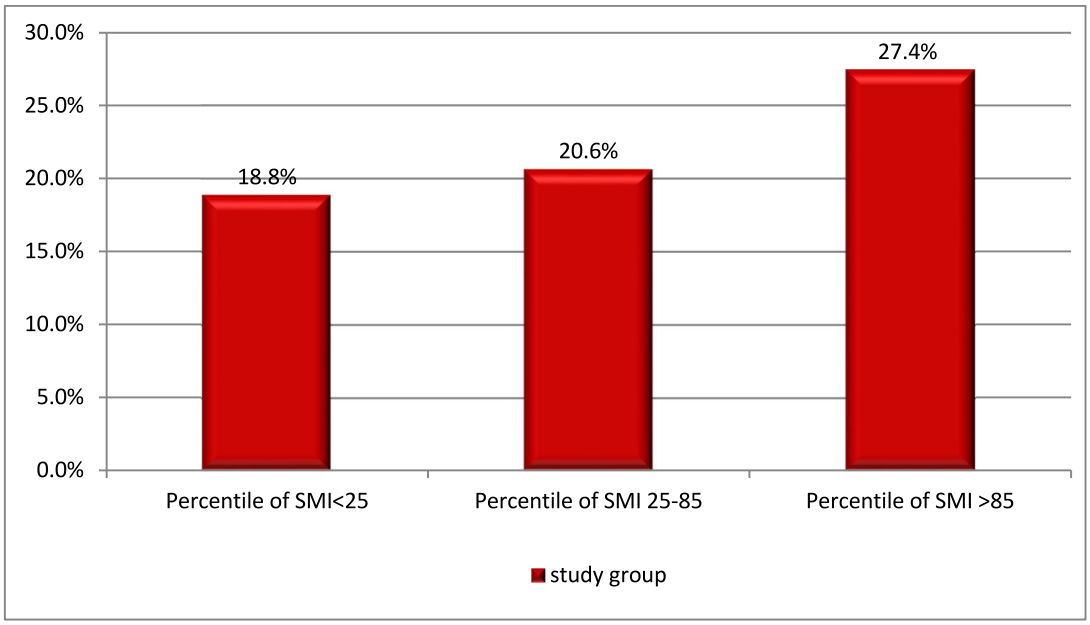

Figure 2. *Increased RMR (%) in study and control group patients.*

Discussion of the obtained results: Long-term energy imbalance can affect body weight. It is therefore important to consider whether PCOS is associated with changes in any aspect of metabolism.

Robinson and co-authors [17] conducted a continuous indirect calorimetric study in a cross-sectional design in 14 women with PCOS compared with 14 controls of the same body mass. Postprandial thermogenesis was significantly lower in PCOS women, and the difference between groups was more pronounced for overweight PCOS women (difference 41.1 kJ). In addition, insulin resistance was correlated with reduced postprandial thermogenesis in the PCOS group [17]. Interestingly, resting energy expenditure was not reliably different between the study groups. Romualdi and co-authors [18] compared 109 PCOS women with 31 control women and showed that resting metabolic rate was significantly elevated in the PCOS group compared to controls.

The developed energy imbalance leads to the redistribution of residual resources to ensure the vital functions of the body [19]. The so-called Secondary functions - ovulation, thyroid function - are

sequestered; The concentration of catabolic agents (estrogens, thyroid hormones, etc.) is reduced; Cortisol levels and the androgen/estrogen ratio increase. Proteins are one of the powerful compounds that participate in the creation of energy balance, synthesis of necessary substances. Achieving energy balance with proper nutrition and circadian rhythm should normalize the main criteria of many conditions - metabolites and excess body mass [20,21]. Research results suggest that PCOS is accompanied by an energy imbalance caused by lifestyle disorders. The result of these conditions is, on the one hand, dysmetabolism, insulin resistance, inflammation, and on the other hand, estrogen deficiency, cervical mucus thinning, glycogen level decrease, mechanical and immune defense weakening.

Conclusion

Based on the research results, it can be concluded that energy imbalance is a possible pathogenetic cause in the development of overweight and PCOS. Obviously, larger randomized clinical trials are needed to turn this assumption into evidence.

XÜLASƏ

Enerji balansının polikistik yumurtalıq sindromuna təsiri

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***Açar sözlər**: polikistik yumurtalıq sindromu, reproduktiv yaş, piylənmə, genetik amil, enerji balansı, pəhriz, həyat tərzi*

Polikistik yumurtalıq sindromunun (PYS) təqdimatı adətən heterojendir, lakin onun etiologiyasının genetik əsası üçün güclü dəlillər mövcuddur. Son genom geniş assosiasiya tədqiqatları (GWAS) klinik təzahürlərin tam spektri üçün ümumi genetik mənşəyi vurğuladı. Əsasən PYS-un heyvan modellərindən də sübut var ki, artıq androgenin təsiri altında epigenetik proqramlaşdırma PYS-un inkişafında həlledici rol oynayır. Lakin, digər mürəkkəb endokrin pozulmalarda (məsələn, CD2, piylənmə) olduğu kimi, genetik təsirlərlə qarşılıqlı əlaqədə olan və epigenetik təsirlərdə dəyişikliklərə səbəb ola bilən mühüm ekoloji amillər, xüsusilə də pəhriz və həyat tərzi var.

РЕЗЮМЕ

Влияние энергетического баланса на синдром поликистозных яичников

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***Ключевые слова**: синдром поликистозных яичников, репродуктивный возраст, ожирение, генетическое происхождение, энергетический баланс, диета, образ жизни*

Проявления синдрома поликистозных яичников (СПКЯ) обычно неоднородны, но имеются убедительные доказательства генетической основы его этиологии. Недавние полногеномные исследования ассоциаций (GWAS) выявили общее генетическое происхождение всего спектра клинических проявлений. Существуют также доказательства, в основном на животных моделях СПКЯ, что эпигенетическое программирование под влиянием избытка андрогенов играет решающую роль в развитии СПКЯ. Но, как и в случае с другими сложными эндокринными расстройствами (например, СД2, ожирением), существуют важные факторы окружающей среды, особенно диета и образ жизни, которые взаимодействуют с генетическими влияниями и могут привести к изменениям эпигенетических эффектов.

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