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# STUDY OF THE EFFECTIVENESS OF DIET THERAPY IN THE CORRECTION OF METABOLIC PARAMETERS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME AND INSULIN RESISTANCE

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**Summary.** Taking into account the importance of correction of metabolic parameters in PCOS, diet therapy is offered. Diet therapy is appropriate as the first stage of treatment in patients with PCOS and IR, but the optimal diet has not been determined at the moment [8].

**Purpose:** to conduct an analysis of studies on the effectiveness of various types of diet therapy.

**Materials and methods.** 12 articles from 2020 to 2022 were analyzed.

**Research results and their discussion.** A review and analysis of a cohort study on the effects of a ketogenic diet (KD), in which 14 overweight women with a diagnosis of PCOS participated [1]. The main argument for the use of KD in PCOS and IR is physiological ketosis [4], which occurs as a result of a low carbohydrate content in the diet, which in turn reduces the level of circulating insulin, and therefore the receptor for insulin-like growth factor type 1. As a result, production of androgens in both ovaries and adrenal glands is inhibited.

The results of a 12-week study suggest that a ketogenic diet is appropriate for correcting metabolic disorders and obesity in PCOS and IR.

The Mediterranean diet (MED) has proven to be one of the most effective diets in the treatment of metabolic and reproductive problems in women with PCOS and IR [5].

*The results of the research showed that both approaches to diet therapy are productive in normalizing metabolic processes. It is worth noting that the group of patients who used the MED/LC diet combination showed excellent results in the normalization of the menstrual cycle (86.7% recovered a regular menstrual cycle).*

**Conclusions.** *The advantages of KD are a good result in reducing weight and anthropometric indicators in a short period of time. The most promising in the context of PCOS and IR treatment with further introduction into the patients' lifestyle is the Mediterranean diet.*

**Key words:** *polycystic ovary syndrome, insulin resistance, diet therapy, Mediterranean diet, ketogenic diet, a low-carbohydrate diet, a low-fat diet, HOMA*

**Introduction.** Polycystic ovary syndrome (PCOS) is a neuroendocrine syndrome characterized by a menstrual cycle disorder mainly in the form of oligo-opsomenorrhoea or amenorrhoea, hyperandrogenism, infertility, changes in metabolic parameters against the background of a large number of cystic-atretic follicles in the ovaries [1].

One of the pathophysiological links in the development of the syndrome is a violation of the circadian rhythm of the secretion of gonadotropin-releasing hormone (LH-RH), as a result of which the production of luteinizing hormone (LH) increases and the secretion of follicle-stimulating hormone (FSH) is limited. Under the action of FSH, aromatases and enzymes that transform androgens into estrogens are formed in the granulosa cells of the ovaries. In PCOS, there is a deficiency of FSH and an excess of LH, due to which the ovaries produce an increased amount of androgens [2].

Patients with PCOS who suffer from obesity develop insulin resistance (IR), which in this case is manifested as a result of a decrease in the immune response to circulating insulin [3]. Summarizing all the studies, several mechanisms of IR formation in patients with PCOS can be distinguished: genetic predisposition, violation of insulin secretion by beta cells of the pancreas, peripheral insulin resistance caused by the action of androgens on skeletal muscles, violation of insulin metabolism in the liver, serine phosphorylation of the insulin receptor, and others disturbance in the way of insulin signal transduction into the cell. An important role in the development of IR belongs to hyperandrogenism [4], since androgens change the structure of muscles due to the predominance of type 2 muscle fibers, which are less sensitive to insulin. History of obesity, most often visceral, worsens insulin sensitivity in approximately 50% of patients [5]. Insulin also increases the activity of cytochrome P450c17, increasing the production of ovarian and adrenal androgens [6].

Taking into account the importance of the correction of metabolic parameters in PCOS, a number of measures of both medicinal nature and non-medicinal means (diet therapy, physical exercise, phytotherapy) are proposed [7,8].

Diet therapy is appropriate as the first stage of treatment in patients with PCOS and IR, but the optimal diet has not been determined at the moment [9]. Also, for the first stage of treatment, it is recommended to use metformin, but this drug is not without side effects [10].

**Purpose:** to conduct an analysis of current medical research on the effectiveness of various types of diet therapy as an initial method of treatment in women with PCOS and IR, their effect on the normalization of the menstrual cycle, correction of metabolic disorders and reduction of the level of IR. Emphasize the need to acquaint women with

PCOS and IR and their treating physicians with the importance of correcting the way and diet as a sufficiently effective and safe method of treatment.

**Materials and methods.** 12 articles from 2020 to 2022 were analyzed with keywords: PCOS, IR, diet therapy, MED, KD, LC, LF, HOMA, for which a review of the available literature was conducted in PubMed, National Library of Medicine, Medscape and 1660 articles were found.

**Research results and their discussion.** A review and analysis of a closed cohort study on the effects of a ketogenic diet (KD), in which 14 overweight women with a diagnosis of PCOS participated [11].

Visceral adipose tissue has a high sensitivity to the lipolytic action of catecholamines and a low sensitivity to the antilipolytic action of insulin, providing good susceptibility to the hormonal changes that often accompany abdominal obesity. Increased lipolytic activity in visceral adipose tissue leads to the fact that a large amount of free fatty acids enters the portal system. Infiltration of the liver with fats leads to a violation of its function, in particular, the metabolism of insulin itself. This is accompanied by the development of system HI. The arrival of increased concentrations of free fatty acids in the liver stimulates the synthesis and release of low-density lipoproteins rich in triglycerides. An increase in the content of free fatty acids in the blood contributes to the insulin resistance of skeletal muscles due to the competition between glucose and free fatty acids in the glucose-fatty acid cycle, that is, inhibits the absorption and utilization of glucose by muscles, contributing to the development of hyperglycemia. Free fatty acids first have a stimulating, and then a lipotoxic effect on beta cells of the pancreas. An excess of free fatty acids stimulates gluconeogenesis, increasing the production of glucose by the liver [11]. Therefore, the development of visceral obesity in patients with PCOS supports a vicious circle of metabolic disorders caused by HI.

The main argument for the use of KD in PCOS and IR is physiological ketosis [12], which occurs as a result of a low carbohydrate content in the diet, which in turn reduces the level of circulating insulin, and therefore the receptor for insulin-like growth factor type 1. As a result, production of androgens in both ovaries and adrenal glands is inhibited. A positive effect is also provided by oxidative stress, a decrease in the number of circulating lipids and markers of inflammation.

The results of the 12-week study, shown in Table 1, indicate that the ketogenic diet is appropriate for the correction of metabolic disorders and obesity in PCOS and IR. However, it should be emphasized that there is no reliable information about the absence of side effects in the long term.

Table 1

Metabolic biomarkers before and after 12 weeks of KD

	Before	After
Glucose (mmol/l)	5,10 ± 0,25	4,64 ± 0,24
Insulin (μU/ml)	12,62 ± 0,48	11,31 ± 0,60
Index HOMA	2,85 ± 0,15	2,32 ± 0,13
Triglycerides (mmol/l)	2,31 ± 0,40	1,87 ± 0,27
Total cholesterol (mmol/l)	5,36 ± 0,36	4,72 ± 0,33

Table 1 continuation

	Before	After
LDL (mmol/l)	3,11 ± 0,60	2,33 ± 0,17
HDL (mmol/l)	1,79 ± 0,41	2,02 ± 0,43

The table was created based on the data of the study of Antonio Paoli, Laura Mancin, Maria Cristina Giacona, Antonino Bianco & Massimiliano Caprio. *Journal of Translational Medicine. Effects of a ketogenic diet in overweight women with polycystic ovary syndrome. J Transl Med.* 2020; 18: 104. Published: 27 February 2020. doi: 10.1186/s12967-020-02277-0 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7045520/#CR1>

However, in this study, there is no information about the effect of KD on the menstrual cycle and infertility in women with PCOS and IR. The given data indicate an effective reduction of anthropometric indicators. The Mediterranean diet (MED) has proven to be one of the most effective diets in the treatment of both metabolic and reproductive problems in women with PCOS and IR [13]. In particular, many biomolecules that are present in the products of the Mediterranean diet contribute to the reduction of hyperandrogenism in PCOS. One of the components of the diet are grapes, dry red wine and certain berries that contain the substance resveratrol [2]. The effect of resveratrol on target cells and its biochemical mechanism are shown in Figure 1.

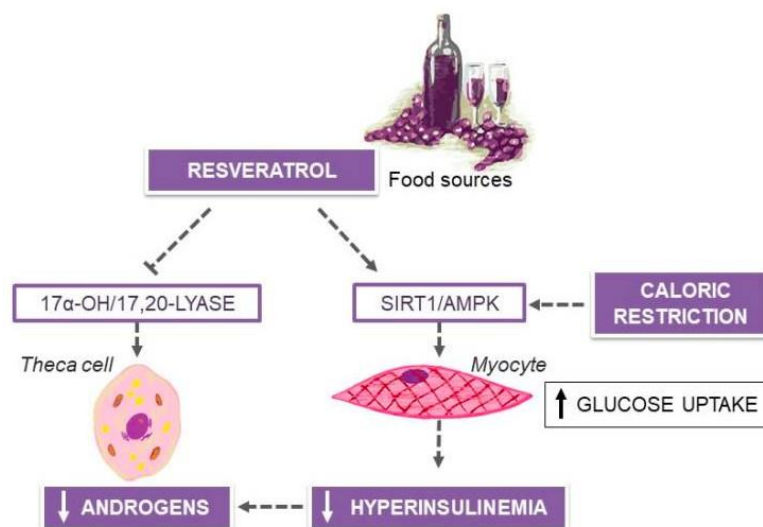


Fig. 1. Resveratrol from grapes, berries, and wine and alleviation of hyperandrogenism in polycystic ovary syndrome. SIRT1 - sirtuin 1; AMPK - AMP-activated protein kinase.

Figure taken from research by Maria MirabelliFrancesco Saverio Brunetti, Valentina Maggisano, Diego Russo, Daniela Patrizia Foti, and Antonio Brunetti. *Mediterranean Diet Nutrients to Turn the Tide against Insulin Resistance and Related Diseases.Nutrients.* 2020 Apr; 12(4): 1066. Published online 2020 Apr.

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Resveratrol inhibits the proliferation of ovarian thecaluteal cells and the enzyme 17α-hydroxylase/C17-20-lyase, which weakens the synthesis of androgens. Another mechanism of resveratrol is its effect on the activation of AMPK and sirtuin 1 receptors in cells such as myocytes. This process contributes to the development

of a decrease in the level of insulin, which also has an indirect effect on the decrease in the level of androgens [12].

Based on the above, it can be assumed that combinations of certain diets will have a greater effect on the organism of women with PCOS and IR than the use of each diet separately.

Thus, a closed cohort study of 72 women with PCOS and IR, without burdened anamnesis from other systems and organs, showed a higher level of effectiveness of the combination of the Mediterranean diet (MED) in combination with a low-carbohydrate (LC) diet in contrast to the independent use of a low-carbohydrate diet fat content (LF) [13].

Changes in laboratory parameters before and after adherence to the MED/LC diet combination compared to the LF diet are shown in Table 2.

Table 2

#### Index of glycolipid metabolism at the beginning and after the intervention

	Group LF		Group MED/LC	
	Before	After	Before	After
Glucose (mmol/l)	5,17 ± 0,47	5,22 ± 0,47	5,32 (4,95-5,62)	4,97 (4,45-5,38)
Insulin (μU/ml)	18,90 (14,80-23,45)	13,49 (9,75-19,45)	21,7 ± 7,62	13,18 ± 5,58
Index HOMA	4,00 (3,39-5,43)	3,06 (2,24-4,33)	5,17 ± 1,7	2,94 ± 1,36
Triglycerides (mmol/l)	4,95 ± 1,02	4,55 ± 0,82	5,05 (4,50-5,76)	4,05 (2,98-4,82)
Total cholesterol (mmol/l)	1,48 (1,17-2,60)	1,10 (0,88-1,94)	1,67 (1,02-2,14)	1,03 (0,76-1,33)
LDL (mmol/l)	2,84 ± 0,88	2,43 ± 0,83	3,06 (2,6-3,52)	2,44 (1,91-2,91)
HDL (mmol/l)	1,21 (0,96-1,37)	1,27 (1,05-1,34)	1,09 (0,95-1,28)	1,14 (0,95-1,28)
Prolactin (ng/ml)	11,28 (7,91-15,39)	13,52 (8,93-17,75)	12,36 (9,36-15,51)	12,56 (9,48-15,51)

The table was created based on data from the research of Shanshan Mei, Jie Ding, Kaili Wang, Zhixin Ni and Jin Yu. Mediterranean Diet Combined With a Low-Carbohydrate Dietary Pattern in the Treatment of Overweight Polycystic Ovary Syndrome Patients. *Front Nutr.* 2022; 9: 876620. Published online 2022 Apr doi:10.3390/nut12041066 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7230471/>

The results of the research showed that both approaches to diet therapy are productive in normalizing metabolic processes. It is worth noting that the group of patients who used the combination of the MED/LC diet showed excellent results in the normalization of the menstrual cycle (86.7% restored a regular menstrual cycle) and the restoration of reproductive function after previous failed pregnancy attempts. Evaluating the results shown in Table 2, it can be said with confidence that the use of diets as a method of treatment has its own, not only theoretical, but also clinical justifications, since hormone levels and anthropometric indicators were normalized compared to the input data of the study. This gives reason to popularize the use of diets as an advanced method of treatment for women with PCOS and IR, which does not have any side effects and has great prospects in the future [13].

**Prospects for further scientific research.** As a result of women not following the correct lifestyle, which includes moderate physical activity and a balanced diet, the number of cases of obesity, which is one of the factors in the development of IR and PCOS, is increasing. Therefore, these concepts are directly proportional, and over time, the spread of this condition will not only cause a woman's own discomfort and the development of background diseases, but also cause an increase in expenses for insurance medicine and treatment.

Summarizing all of the above, prevention exchange and metabolic disorders in PCOS is properly selected diet therapy, taking into account the personal health characteristics of each woman.

### Conclusions

1. For the effective treatment of PCOS with IR, it is necessary to reduce the negative impact of the IR factor and, as a consequence, hyperandrogenism. Diet therapy is the main initial and effective stage of treatment of this disease.

2. The advantages of KD are a good result in reducing weight and anthropometric indicators in a short period of time. However, there are not enough studies on its effectiveness in the correction of gynecological disorders. The disadvantages of this diet are negative effects on the gastrointestinal tract and urinary system.

3. The Mediterranean diet is the most promising in the context of PCOS and IR treatment with subsequent introduction into the lifestyle of patients. Numerous studies have shown its influence on the regulation of disorders that occur with PCOS and IR at the biochemical level.

4. The combination of a Mediterranean diet and a low-carbohydrate diet has proven to be one of the most effective ways to correct not only obesity in women with PCOS and IR, but also the menstrual cycle and reproductive function of this patient group.

5. Properly selected diet therapy has a positive effect on the general condition of the body, has practically no side effects and reduces the need for pharmacological interventions in the treatment of PCOS with IR.

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