

APPLICATION OF THIOCTIC ACID IN WOMEN WITH POLYCYSTIC OVARY SYNDROME AND NORMAL BODY WEIGHT

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ABSTRACT

27 women with polycystic ovary syndrome and normal body weight were divided into 2 groups. Within 1 year, the patients of the main group (n = 16) received a high-protein diet for 2100 calories in combination with thioctic acid, 600 mg per day (Berlition, 300 mg 1tab × 2 times a day or 300mg, 2 tab 30 minutes before breakfast for 1 year). Anthropometric examination, determination of the level of basal and stimulated blood plasma insulin during the oral glucose tolerance test (OGTT), calculation of the insulin resistance index (HOMA-IR), the volume of the ovaries, the thickness of the endometrium according to ultrasound were performed baseline and after 1 year of treatment. As a result of therapy with thioctic acid in the main group, the basal and stimulated insulin levels of blood plasma, the HOMA-IR index, the volume of the right and left ovaries decreased, the dominant follicle appeared. These changes were achieved against the background of weight gain (in the norm range), an increase of estrogen levels and endometrial thickness in most patients.

KEYWORDS: Thioctic Acid, Hyperinsulinemia, Polycystic Ovary Syndrome & Normal Body Weight

INTRODUCTION

It is convincingly proved that hyperinsulinemia is one of the main causes of the development of the polycystic ovary syndrome (PCOS) [3,5,6]. Insulin sensitizers (metformin) are now successfully used for treatment in adolescent girls with PCOS, contributing to the normalization of the menstrual cycle and weight loss [4]. A number of studies have demonstrated that the use of thioctic acid in obese individuals and/or overweight once reduces both basal and stimulated hyperinsulinemia, which leads to a decrease in insulin resistance an improvement in lipid and carbohydrate metabolism, a reduction in body weight [3,5,6].

The aim of the study was to evaluate the effect of thioctic acid on the level of basal and stimulated insulin plasma, the HOMA-IR index, the volume of the ovaries in women with PCOS and normal body weight.

MATERIALS AND METHODS

A prospective, controlled, randomized trial included 27 women with PCOS and normal body weight aged, from 18 to 31 years (mean age 21.46 ± 1.19 years). Randomization of patients in the main and control groups was carried out by using a table of random numbers. The criteria for inclusion in the study were: PCOS, $BMI \geq 18.5$ and $< 25 \text{ kg} / \text{m}^2$, the signing of voluntary informed consent for participation in the study. Exclusion criteria were: age of patients under 18 years of age, pregnancy, intake of oral contraceptives within 3 months before the start of the study, severe physical illness,

alcohol and/or drug abuse, patient's failure to study, body mass index ≥ 25 kg / m².

The main group consisted of patients (n = 16) who received a high-protein diet for 2100 calories in combination with thioctic acid (Berlition, 300 mg, 2 tablets in the morning 30 minutes before breakfast or 300 mg x 2 times a day for 1 year. Patients of the control group (n = 11) were only on the high protein diet for 2100 calories during the entire study period.

Diet for 2100 calories included 3 main meals with high protein content and mandatory intake of milk fat (daily 200g of 9% fat cottage cheese, 20g of 82.5% fat butter, 2.5-3.5% fat of milk or kefir 150- 200ml per day, 50-100g of meat in ready form, mainly beef or rabbit meat), 50-100g of legumes (peas, beans) with good tolerability. Light digestible carbohydrates in pure form were excluded from the diet. Difficult digestible carbohydrates (porridge with milk) accounted for not more than 50% of the daily ration. Obligatory was the reception of fresh vegetables and fruits at least 500 g per day.

Initially and after 1 year of treatment, patients underwent anthropometric examination (measurement of height, weight, waist circumference, the body mass index according to the Quetelet formula (body weight (kg)/height² (cm)), laboratory studies (basal and stimulated blood plasma insulin during oral glucose tolerance test (OGTT), the insulin resistance index (HOMA-IR), transvaginal ultrasound of the genitals on the 2nd-5th day of the ovarian-menstrual cycle were calculated. Diagnosis of PCOS was carried out according to the recommendations proposed in 2003 by the Joint Congress of the European Society for Human Reproduction and the American Society for Reproductive Medicine in Rotterdam. Blood plasma glucose (reference interval (RI) 3.9-5.9 mmol/L) was determined by the glucose oxidase method glucose oxidase method using Sentinel Diagnostics reagents (Italy) on the Konelab analyzer (Thermo Fisher Scientific, Finland). Blood plasma insulin (RI 3.0-25.0 μ U/ml) was studied by means of an enzyme immunoassay using ELECSYS Insulin reagents using the Roche Diagnostics Cobas e 411 (Roche, Switzerland). Insulin resistance (IR) was determined by the formula: HOMA IR = Fasting glucose (mmol/L) x Fasting insulin (μ U / ml)/22.5, where ≥ 2.7 corresponded to IR.

The results obtained during the study were processed using the Statistica 6.0 software package. The possibility of using parametric statistics methods was confirmed by the Kolmogorov-Smirnov test. A comparison of the results obtained as the mean values \pm error of the mean ($M \pm m$) in the coupled populations was performed using the Wilcoxon T test. The values obtained for $p < 0.05$ were considered reliable.

RESULTS OF THE STUDY

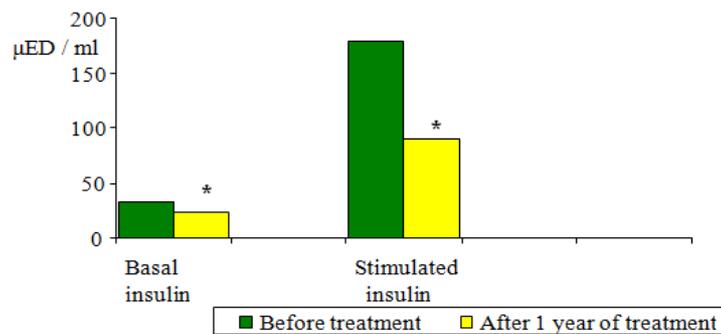
Initial demographic, clinical and laboratory indicators in the compared groups were comparable. There were no significant intergroup differences in sex, age, BMI. In this connection, it was possible to explain the changes in the parameters in the dynamics of observation and treatment by the effect of therapy. In women with PCOS, there were various violations of the ovarian-menstrual cycle: oligoovulation (n = 4, 14.8%); amenorrhea (n = 2, 7.4%); algodismenorrhea (n = 2; 7.4%); anovulatory cycles (n = 22; 81.5%). All women had initial hyperinsulinemia: basal (n = 7; 25.9%), postprandial (n = 8; 29.6%) or their combination (n = 12; 44.4%). When we analyzed the results of the study a significant positive dynamics in comparison with the initial data was revealed (see Table 1).

Table 1: Dynamics of Carbohydrate Metabolism in Patients with Polycystic Ovary Syndrome Initially and After 12 Months of Treatment with Thioctic Acid

Index	Main Group Initially, (N=16)	Control Initially, (N=11)	The Main Group After Treatment, (N=16)	Control After Treatment, (N=11)
Glucose basal, mmol / l	4,55±0,20	4,29±0,11	4,81±0,17	4,31±0,17
Glucose stimulated, mmol / l	5,43±0,34	5,73±0,34	5,92±0,31	5,45±0,42
Insulin basal, µEq / ml	33,59±5,91	32,16±4,88	23,25±4,12 ¹	33,07±4,65
Insulin stimulated, µEq / ml	178,81±36,7	172,19±28,9	90,48±17,43 ²	165,44±30,1
HOMA IR	6,62±1,23	6,73±1,69	4,12±1,04 ³	6,25±0,98

Annotation: ¹ - T=26, p<0,05; ² - T=0, p<0,01; ³ - T=22,5, p<0,05

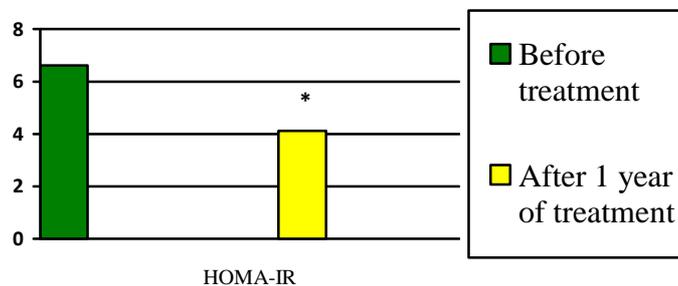
The mean value of basal insulin decreased by 30.8% (T Wilcoxon test = 26, p <0.05). Stimulated insulin decreased by 49.4% (T Wilcoxon test = 0, p <0.05) in the main group. In the control group significant changes in these indicators were not observed. The obtained data are presented in Figure 1.



Annotation: * - p<0,05, in comparison with baseline indicators

Figure 1: Dynamics Basal and Postprandial Blood Plasma Insulin Levels in Women After 1 Year of Treatment with Thioctic Acid (600 Mg / Day) and with High-Protein Diet for 2,100 Calories

In the main group, a significant reduction in the HOMA-IR index by 37.8% was obtained in the main group (T Wilcoxon test = 22.5, p <0.05). In the control group, significant changes in the mean value of the insulin resistance index were not detected (Figure 2).

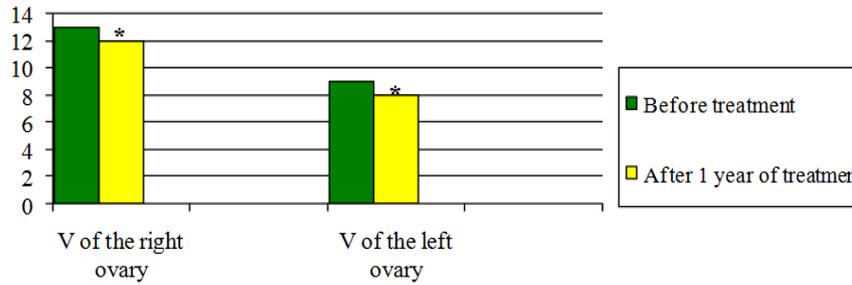


Annotation: * - p<0,05, in Comparison with Baseline Indicators

Figure 2: Dynamics of the Level of HOMA-IR Index in Women with Polycystic Ovary Syndrome After 1 Year of Treatment with Thioctic Acid (600 Mg / Day) and High-Protein Diet for 2100 Calories

Treatment with thioctic acid in combination with diet for 2,100 calories in women with normal body weight improved menstrual function and favorably affected the average volume of the ovary. In the main group, all women normalized their duration and resolved the frequency of the ovarian-menstrual cycle. Three patients (n = 3, 18.8%) had a dominant follicle.

A year after the treatment in the main group, a statistically significant decrease in the mean volume of the right ovary by 30.2% and the mean volume of the left ovary by 26.3% was obtained (T Wilcoxon test = 0, p <0.01 in both cases). In the control group, such positive results were absent after 1 year of diet therapy. The obtained data are presented in Fig. 3.



Annotation: * - p<0,001, in Comparison with Baseline Indicators

Figure 3: Dynamics of the Mean Value of the Volume of the Right and Left Ovaries in Patients with Polycystic Ovary Syndrome After 1 Year of Treatment with Thioctic Acid (600 Mg / Day) and a High-Protein Diet for 2100 Calories (According to Ultrasound Data)

Table 2: Dynamics of Ultrasound Parameters of Genitals, Mean Estradiol and Body Weight in Patients with Polycystic Ovary Syndrome After 12 Months of Treatment with Thioctic Acid

Index	Main Group Initially, (N=16)	Control Initially, (N=11)	The Main Group After Treatment, (N=16)	Control After Treatment, (N=11)
Volume of the right ovary, cm ³	13,42±0,81	12,9±0,65	9,37±0,9 ¹	13,22±0,9
Volume of the left ovary, cm ³	12,02±0,75	12,66±0,42	8,85±0,65 ²	12,45±0,33
Presence of a dominant follicle,%(n)	6,25 (1)	9 (1)	25 (4)	9 (1)
Thickness of the endometrium	5,72±1,18	5,61±1,27	5,9±1,42	5,88±1,34
Estradiol, pmol / l	152,62±51,3	150,23±47,8	370,76±71,15 ³	154,19±50,2
Weight, kg	21,94±0,68	21,52±0,7	22,94±0,70 ⁴	21,78±0,19

Annotation: ¹ - T=0, p<0,01; ² - T=0, p<0,01; ³ -T=22,5, p<0,05; ⁴ -T=7, p<0,01

The data in Table 2 confirmed that treatment with the thioctic acid and diet for 2,100 calories in individuals with PCOS and normal body weight may simultaneously lead to an increase in the thickness of the endometrium, plasma estradiol level, Normalization of the ovary volume against the background of an increase in the body weight of the subjects within normal values.

DISCUSSIONS

It has been proved that thioctic (α -lipoic) acid increases the bioavailability of glucose in insulin-dependent and non-insulin-independent tissues. It interacts with the receptors of the ventromedial nucleus of the hypothalamus through suppression of the hypothalamic activity of adenosine monophosphate kinase, which leads to an anorexigenic effect and an increase in the rate of thermogenesis [1,2]. Thioctic acid increases the production and activity of insulin receptor tyrosine kinase, which increases the sensitivity to insulin in the fat and muscle tissues, and the rate of gluconeogenesis in the liver decreases. Alpha-lipoic (thioctic) acid can function as a partial agonist of PPAR gamma nuclear receptors, which ultimately increases the activity of GLUT-1 and GLUT-4 glucose transducers, reduces leptin gene expression, reduces the level of tumor necrosis factor alpha, which together reduces insulin resistance[8]. Thioctic acid can be the drug of choice in patients with PCOS and nonalcoholic fatty liver disease [9]. According to our results, treatment with a thioctic acid in combination with a high protein diet for 2,100 calories in patients with PCOS and normal body weight proved to be very effective. It helps to reduce the levels of basal and stimulated insulin of blood plasma, HOMA-IR index, a significant reduction in the average volume of ovaries, the appearance of ovulatory cycles. These results are similar to the treatment of thioctic acid in obese and PCOS[5]. For patients with normal body weight and PCOS is very important to increase the level of estradiol, the thickness of the endometrium, body weight is within the normal range. Insulin resistance in these women is associated with the presence of central obesity. Apparently, to confirm this fact in women with PCOS and normal body weight, it is necessary to calculate not only BMI but also to measure the waist circumference.

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