

The stabilizing effect of dehydroepiandrosterone on clinical parameters of metabolic syndrome in patients with schizophrenia treated with olanzapine – a randomized, double-blind trial

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Summary:

Objectives: Epidemiological studies have shown that low levels of dehydroepiandrosterone might increase the risk of developing metabolic syndrome. The aim of this study was to evaluate whether dehydroepiandrosterone supplementation in schizophrenic patients treated with olanzapine would influence the anthropometric and biochemical parameters of metabolic syndrome.

Methods: Male schizophrenic patients (no=55) participated in a twelve-week, randomized, double blind, placebo controlled study. They received 100 mg dehydroepiandrosterone (DHEA) or placebo as an augmentation of olanzapine treatment (an average dosage 15 mg/day). Main outcomes of the study were changes in lipid profile, fasting glucose levels, body mass index and waist circumference values.

Results: Forty five patients completed the study. There were no major changes in the overall cholesterol value, HDL cholesterol, LDL cholesterol or triglycerides in either group. The results of the repeated measures analysis of the system: fasting glucose level 2x, (at the beginning and end of the study), 2x (the study group and the control group), showed a significant interaction ($F = 5.7$, $df = 1.000$ $p = 0.021$). The blood glucose level was decreased in the DHEA group. Furthermore, increases in waist circumference ($\Delta = -1.11$, $t = -2.87$; $df = 20$; $p = 0.01$) and BMI value ($\Delta = -0.48$, $t = -2.38$; $df = 19$; $p = 0.028$) were observed in the placebo group.

Conclusions: Dehydroepiandrosterone supplementation results in stabilization of BMI, waist circumference and fasting glycaemia values in schizophrenic patients treated with olanzapine. To confirm the insulin-like effect of dehydroepiandrosterone, long-term research concentrating on the evaluation of glucose metabolism has to be performed.

Key words: dehydroepiandrosterone, metabolic syndrome, schizophrenia

Introduction

Metabolic syndrome is a construct created for the assessment of risk factors of atherosclerotic disease and type 2 diabetes. According to the current International Diabetes Federation (IDF) guidelines a criterion for the diagnosis of metabolic syndrome is central obesity, and two of the following four factors: raised triglycerides, increased systolic and diastolic blood pressure, reduced HDL cholesterol and raised fasting plasma glucose level [1]. Glucose and lipid metabolism abnormalities are observed 2–3 times more often in patients diagnosed with schizophrenia and schizoaffective disorder than in the overall population [2]. A metabolic syndrome, including a considerable weight increase, occurs in the course of treatment with many atypical antipsychotics and becomes evident after the first 10 weeks of treatment [3]. Weight increase has been observed in the majority of schizophrenic patients ($n = 1432$) treated with both first and second generation antipsychotics [4]. Among young antipsychotic naïve patients diagnosed with a first episode of schizophrenia, dyslipidemia (i.e. reduced HDL cholesterol, and raised triglycerides) has been observed more often than in the general population [5] and worsens in the course of pharmacological treatment. Nowadays, metabolic abnormalities diagnosed in schizophrenic patients are considered as: genetically determined (especially visceral obesity), a part of the clinical picture of schizophrenia, a lifestyle consequences resulting from decreased physical activity and the result of antipsychotic pharmacotherapy [6]. The above abnormalities are also considered an effect of the increased vulnerability to stress of schizophrenic patients (resulting in excessive activity of the hypothalamic-pituitary axis) [6]. Nevertheless, metabolic abnormalities and clinical diabetes are observed more often in patients diagnosed with schizophrenia than in the overall population, even in people who have never been treated with antipsychotics [6].

Olanzapine is one of the most effective atypical antipsychotics, and can prevent a relapse of schizophrenia in a long-term observation. In the CATIE trial olanzapine has proved to be significantly better than other antipsychotics concerning the period of time from its introduction until the termination of antipsychotic treatment for a number of reasons [7]. However, olanzapine treatment is followed by a greater weight increase – basic symptom of metabolic syndrome – than is seen with the use of other antipsychotics (except clozapine) [8].

In the CATIE trial it was shown, that in as many as 30% of patients treated with olanzapine experienced more than a 7% weight increase compared to the primary values [9]. According to another study, olanzapine treatment may be related to a significant body mass increase of 0.9 kg/month or up to as much as 6–10 kg over a one year observation period [10]. It is assumed that the reason for the body weight increase during olanzapine treatment lies in the stimulation of appetite and an increased insulin resistance. The postulated etiopathogenic mechanism of this phenomenon is probably antagonism against the histamine H1 and serotonin 5-HT_{2C} receptors. This may lead to stimulation of the appetite and be followed by binge eating [11, 12]. The search for new solutions

that could prevent the development of the metabolic syndrome during treatment with both olanzapine and other atypical antipsychotic agents continues. A range of substances which clinical effects included inhibition of excessive appetite or anti-diabetic properties have been examined. These included: amantadine, topiramate, fenfluramine, reboxetine, fluoxetine, fluvoxamine, sibutramine, orlistat and metphormine [13–17]. None of these substances has been recommended for metabolic syndrome that occurs in the course of antipsychotic pharmacotherapy. Fenfluramine and sibutramine have been withdrawn from the market because of their significant adverse effects. None of the substances newly registered for the treatment of obesity (phentermine, diethylpropion, phendimetrazine, lorcaserin or benzphetamine) [18] has been evaluated for effectiveness in the treatment of symptoms of metabolic syndrome in schizophrenic patients.

Dehydroepiandrosterone is a steroid hormone with weak androgenic properties produced by the adrenal cortex, and, in small amounts, by the gonads. It is a precursor for other steroid hormones, including oestrogens and androgens [19]. Dehydroepiandrosterone has been examined for years for its systemic antiatherosclerotic properties in order to increase insulin sensitivity and prevent the development of metabolic syndrome components. In experimental studies it has been proved that administering DHEA has a positive effect against obesity symptoms, atherosclerosis, osteoporosis, Hyperlipidemia, and diabetes [20]. In a series of experiments, it has been confirmed that DHEA supplementation promotes insulin sensitivity in laboratory animals, although the mechanism of this phenomenon is not elucidated yet [21–24]. In another experimental study, it has been shown that DHEA administration leads to body weight decrease and reduced food intake in diabetic rats; it also contributes in reducing serum glucose levels in diabetic animals [25, 26]. It is assumed that DHEA acts through modulating the activity of liver enzymes responsible for gluconeogenesis, preventing atrophy of the islets of Langerhans, (or even increasing their volume) along with increasing insulin secretion, which has been proven in histological examination [21, 20, 27]. On the other hand, it has been shown in in-vitro studies that DHEA administration can cause the opposite outcome, that is, deterioration of the glycemic mechanism control and the functionality of islets of Langerhans' cells [28].

In recent experimental studies it has been proven that DHEA has antiatherosclerotic properties, imitating the properties of insulin by stimulating the production of both nitrogen and endothelium [29]. Additionally, DHEA's antiatherosclerotic mechanism could be linked to the presence of its characteristic receptors in the smooth muscle tissue of human blood vessels. It has been also demonstrated that DHEA inhibits the proliferation of muscle cells, and reduces arteriosclerosis via these receptors [30]. It is known that DHEA's properties are independent of its conversion to oestrogens, however, a detailed antiatherosclerotic mechanism of DHEA is still unknown [31]. In in-vitro trials it has been shown that DHEA can inhibit adipogenesis in human subcutaneous tissue. This effect has not been confirmed for subcutaneous adipose tissue [32].

Clinical and epidemiological studies have shown a relationship between a low dehydroepiandrosterone level and cardiovascular diseases, especially coronary arte-

ry disease. In the prospective Massachusetts Male Aging Study, conducted on men aged 40–70 ($n = 1167$), the patients with the highest serum dehydroepiandrosterone and dehydroepiandrosterone sulfate were at the highest risk for developing coronary artery disease in a 9-year observation period [33]. Another prospective study of men aged 69–81 ($n = 2644$) revealed that a low concentration of dehydroepiandrosterone might result in an increased risk of mortality due to heart failure or other diseases [34]. In a similar cohort prospective study (Study of Health in Pomerania) of 1004 men aged 20–79, a relationship between a low level of serum DHEA-S and incidental metabolic syndrome was not observed after five years. Such a dependency has been observed only for a low testosterone level [35]. Nevertheless, DHEA-S is metabolized in the human body to testosterone and the concentration of both hormones in serum can be correlated. In prospective women studies it has been noted that the concentration of DHEA and DHEA-S is not predictive for coronary artery disease [36].

A high level of free dehydroepiandrosterone is related to a lower body weight, both in men and women, and a reduced accumulation of abdominal adipose tissue in men [36]. However, there have been rare reports linking high levels of DHEA and increased insulin resistance, higher body mass index (BMI), and higher triglyceride and cholesterol levels in postmenopausal women [37].

Despite the development of new antipsychotics, olanzapine is one of the best antipsychotics which prevents schizophrenia relapse over a long-term observation period. Nevertheless, it increases the risk of developing metabolic syndrome. The objective of this study is to assess how the administration of dehydroepiandrosterone (100 mg/day) can affect the diagnostic parameters of metabolic syndrome in schizophrenic men treated with olanzapine.

Material

The study was conducted on male patients aged 18–65 diagnosed with schizophrenia or schizoaffective disorders according to ICD-10 criteria. The patients could not have been treated with clozapine before and at the time of inclusion to the study required neuroleptic treatment. The group consisted of 55 patients, out of which 27 were randomized into the DHEA subgroup and 28 to the placebo group. The trial was conducted between October 7th 2008 and June 30th 2011. All participants gave informed consent to participate in a study. The dehydroepiandrosterone and placebo were prepared and coded by Lekam LTD. The trial was accepted by the Committee on Bioethics of the Institute of Psychiatry and Neurology (Decision No 28/2007, 2006-11-9).

Method

The study was constructed as a 12-week double blind randomized trial in two parallel groups of patients using DHEA or placebo. In cases in which the patient had been treated with olanzapine before, treatment was continued at a stable dose. In cases

where olanzapine treatment was newly introduced, it was continued until a stable dose of antipsychotic was achieved (defined as no need for a change in the dosage of olanzapine for at least 6 weeks). After that period, the patients were randomly assigned to one of two groups receiving either DHEA or placebo. The randomization was generated based on a computer-generated list of random numbers $\langle 1, 2 \rangle$, where each new patient received the subsequent number on the list. For the first two weeks of the study, patients received 50 mg of DHEA or placebo. If it was well tolerated, the dosage was titrated up to 100 mg/day and continued until the end of the study protocol. The screening procedure consisted of a detailed medical interview and a physical examination (including height, weight, and waist circumference), ECG, laboratory tests: blood morphology, AspAt, AlAt, GGTP, bilirubin, sodium, potassium, urea, creatinine, PSA and a general urine examination. In order to determine the occurrence of parameters of metabolic syndrome the levels of: overall cholesterol, triglycerides, HDL cholesterol, LDL cholesterol and fasting blood glucose were determined. Also, the waist circumference and BMI value were assessed. Exclusionary criteria included the presence of psychiatric disorders other than schizophrenia (according to ICD-10), significant somatic disorders (including benign prostatic hyperplasia), current endocrine therapy, major aberrations in laboratory tests, excessive use of alcohol and other psychoactive substances. Additional disqualifying criteria included: major symptoms of olanzapine intolerance or the occurrence of side effects of dehydroepiandrosterone.

The statistical analysis included only the results from those patients who completed the study.

To describe the study groups, descriptive statistics such as mean and standard deviation were used (taking into account the standard error of the mean).

Kolmogorov-Smirnov test was conducted in order to determine whether the distribution of investigated variables did not differ from a normal distribution. All tested variables were not significantly different from a normal distribution with the exception of BMI and triglycerides values.

For parametric variables analysis of variance with repeated measurements and Student's t-test were used. For variables that did not meet the assumption of normality of distributions further analysis was performed using Mann-Whitney U test and Wilcoxon signed-rank test, which confirmed the obtained results. The detailed results are presented in tables, as mean values, taking into account the standard deviation and standard error of the mean. The significance of differences between the mean scores in each group was determined by Student's t-test equality of means for independent groups.

Results

The basic data on the physical state of the participants before the study were the following: mean weight of 85.5 kg in the placebo sub-group and 84.74 kg in the DHEA sub-group; mean estimated waist circumference of 93.4 cm for the placebo sub-group and 95.85 cm for the DHEA sub-group; and mean BMI of 27.4 for the placebo sub-

group and 26.98 for the DHEA subgroup. The groups did not differ statistically in the primary parameters connected with the occurrence of metabolic syndrome, i.e. BMI, waist circumference, serum lipoprotein level and fasting blood glucose. Similarly, no differences between the groups were observed in the hormonal profile of the participants, i.e. levels of DHEA-S, cortisol, estradiol, testosterone, prolactin, luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Initially only nine patients met the criteria of metabolic syndrome (table 1).

Table 1. A comparison of the initial clinical parameters of metabolic syndrome for the DHEA sub-group and the placebo sub-group

Data on the initial clinical parameters of metabolic syndrome	Placebo N= 28			DHEA N = 27			P
	Mean	SD	SE	Mean	SD	SE	
Weight (kg)	85.57	13.58	2.56	84.74	13.10	2.52	ns
Waist circumference (cm)	93.46	10.02	1.89	95.85	9.20	1.77	ns
BMI	27.40	4.76	0.91	26.98	4.55	0.87	ns
Overall cholesterol (mg/ml)	196.02	29.36	5.65	197.40	28.75	5.53	ns
HDL cholesterol (mg/ml)	43.94	10.00	1.89	45.44	10.48	2.01	ns
Triglycerides in the serum (mg/dl)	134.55	71.82	13.57	135.17	103.00	20.20	ns
LDL cholesterol (mg/dl)	121.15	28.52	5.39	125.72	27.58	5.30	ns
Fasting glucose level (mg/ml)	88.69	11.37	2.15	95.04	15.43	2.97	ns
DHEA-S (ng/ml)	2665.21	1424.46	269.19	2484.23	1796.12	352.24	ns

SD – standard deviation; SE – mean standard error; p – statistical significance of a difference

The study was completed by 45 patients out of 55, i.e. 81.5% of the randomized patients. The study was not completed by 6 patients from the placebo sub-group and 4 patients from the DHEA sub-group, respectively. None of the patients were excluded from the study due to the occurrence of major side effects of dehydroepiandrosterone or olanzapine. An analysis conducted using a Student's t-test did not show the occurrence of statistically important differences between the mean BMI measurements in the DHEA subgroup at the end of the trial compared to its beginning. However, in the placebo subgroup the mean BMI value increased ($t = -2.38$; $df = 19$; $p = 0.028$). This difference in the mean BMI value ($\Delta = +0.48 \text{ kg/m}^2$) was small enough to be of no medical importance. Similarly, the occurrence of statistically important differences between mean measurements of waist circumference in the DHEA subgroup was not noted. However, in the placebo subgroup the mean value of waist circumference increased to a statistically significant degree ($t = -2.87$; $df = 20$; $p = 0.01$). Again, the difference in mean value of waist circumference ($\Delta = +1.11 \text{ cm}$) for the placebo subgroup was not clinically important.

There were no differences of statistical importance between the mean measurements of: overall cholesterol level, triglycerides level, HDL cholesterol level, or LDL

cholesterol level from the beginning and the end of the trial in the DHEA subgroup compared to the placebo subgroup. One major difference referred to the mean values of blood fasting glucose levels which, in the placebo subgroup, increased to a statistically significant degree, while they remained unchanged in the DHEA subgroup (table 2).

Table 2. A comparison of metabolic syndrome parameters at the beginning and end of the trial

Parameters related to metabolic syndrome	Placebo			DHEA		
	Day 1 Mean (SD)	Day 82 Mean (SD)	Student's t-test	Day 1 Mean (SD)	Day 82 Mean (SD)	Student's t-test
BMI	27.15 (4.90)	27.63 (4.78)	t = -2.38 df = 19 p = 0.028	27.03 (4.20)	26.63 (3.64)	t = 1.30 df = 22 p = 0.20
Waist circumference (cm)	93.38 (11.18)	94.50 (11.11)	t = -2.86 df = 20 p = 0.010	95.95 (8.55)	95.30 (7.14)	t = 1.06 df = 22 p = 0.30
Overall cholesterol (mg/ml)	194.03 (24.64)	201.40 (26.85)	t = -1.42 df = 20 p = 0.16	192.13 (25.87)	192.92 (34.62)	t = 1.175 df = 22 p = 0.863
Triglycerides in the serum (mg/dl)	110.88 (34.47)	110.86 (43.23)	t = 0.002 df = 20 p = 0.998	143.62 (113.19)	137.62 (76.19)	t = 0.415 df = 19 p = 0.683
HDL cholesterol (mg/ml)	45.54 (9.42)	46.42 (8.45)	t = -0.58 df = 20 p = 0.564	45.28 (10.44)	45.59 (11.80)	t = -0.153 df = 22 p = 0.88
LDL cholesterol (mg/dl)	122.58 (27.65)	129.38 (24.36)	t = -1.44 df = 20 p = 0.164	122.40 (25.72)	120.42 (25.36)	t = 0.336 df = 22 p = 0.74
Fasting blood glucose level (mg/ml)	88.00 (11.37)	92.46 (10.90)	t = 3.248 df = 21 p = 0.004*	96.76 (15.43)	94.37 (11.85)	t = 0.965 df = 22 p = 0.345

SD – standard deviation; df – degrees of freedom; t – result of Student's t-test; p – level of significance

Additionally, an analysis of the repeated measurements in the system: the level of overall cholesterol 2x, the level of HDL cholesterol 2x, the level of LDL cholesterol 2x, the level of triglycerides 2x, and the fasting blood glucose level 2x (i.e. measurements at the beginning and end) x 2 group (the group under trial and the control group) was made (table 3).

Table 3. The results of the analysis of the repeated measurements in the system: the level of overall cholesterol 2x, the level of HDL cholesterol 2x, the level of LDL cholesterol 2x, the level of triglycerides 2x, and the fasting blood glucose level 2x (i.e. measurements at the beginning and end) x2 group (the group under trial and the control group).

Parameters related to metabolic syndrome.	Day of the study	Placebo		DHEA		ANOVA
		Mean	SD	Mean	SD	
Overall Glucose (mg/ml)	1	88.00	12.39	96.76	15.41	F = 5.7
	82	92.46	10.90	94.37	11.85	p = 0.021*
Overall Cholesterol (mg/ml)	1	194.03	24.64	194.13	25.87	F = 0.958
	82	201.40	26.85	196.97	31.09	p = 0.333
HDL Cholesterol (mg/ml)	1	45.42	9.42	45.28	10.44	F = 0.05
	82	46.42	8.45	45.59	11.80	p = 0.824
LDL Cholesterol (mg/ml)	1	122.58	27.65	122.40	25.72	F = 1.322
	82	129.38	24.36	120.42	25.36	p = 0.257
Triglycerides (mg/ml)	1	110.88	34.47	110.86	43.23	F = 0.132
	82	143.62	113.19	137.62	76.19	p = 0.718

SD – standard deviation; F – ANOVA result; p – level of significance

The results did not show any simple effect or an interaction effect of statistical importance in reference to the following variables: the level of overall cholesterol, the level of HDL cholesterol, the level of LDL cholesterol, and the level of triglycerides. A statistical interaction effect was shown only for the fasting blood glucose level $F(1.43) = 5.7$. The mean glucose values in the placebo subgroup increased, whereas in the DHEA subgroup they decreased.

Discussion

Administration of dehydroepiandrosterone had no major effects on the elements of metabolic syndrome. One can infer that DHEA supplementation resulted in a stabilizing influence on the BMI value, waist circumference, and fasting blood glucose level (the mean values of these variables in the DHEA subgroup remained stable, whereas they decreased in the placebo subgroup). Additionally, using a different statistical method, i.e. a one-way analysis of variance, it was shown that the mean fasting blood glucose levels in the DHEA subgroup slightly decreased, whereas in the placebo subgroup they increased. Nevertheless, the changes in the described parameters were slight enough to determine them as of no clinical value, and they should be treated as a preliminary result for further research.

Epidemiological trials have shown that low blood dehydroepiandrosterone levels are related to increased risk of cardiovascular diseases [38]. Increased DHEA and DHEA-S levels were related to lower concentrations of blood plasma lipoproteins,

especially triglycerides [36]. A number of trials of the clinical effects of DHEA supplementation have been performed in men and women of various ages. However, most of the trials that confirmed the positive effects of DHEA supplementation on the occurrence of metabolic syndrome were performed in small study groups. One placebo-controlled trial based on larger study group, referring to a group of 39 healthy men, showed reduction in body weight, overall cholesterol level and HDL cholesterol [39]. However, the lack of a positive effect of DHEA supplementation on the lipid profile reflects the results of a majority of randomized trials, in which DHEA (25–100 mg/day) was used in order to stabilize/enhance lipid profile values. Most randomized trials carried out on groups larger than twenty persons have not shown any between group differences in the stabilization of the lipid profile between DHEA and placebo, either in healthy men or in men diagnosed with hypercholesterolemia [40–43].

Among the above described parameters of metabolic syndrome, only fasting blood glucose level showed a statistically significant interaction. The mean glucose values increased in the placebo subgroup and decreased in the trial group. Nevertheless, the mean decrease in the glucose value was slight (not exceeding 2.5 mg/dl); thus, it had no clinical significance in the course of the twelve week observation period. Basing on the literature concerning various study populations, no conclusions can be drawn regarding the influence of dehydroepiandrosterone on glucose metabolism. In the insulin resistant group, administration of DHEA did not result in an increase in insulin sensitivity; only a tendency towards enhanced insulin sensitivity was observed [44]. In the trial carried out by Strous et al., in which an olanzapine was augmented with DHEA or placebo in a group of schizophrenic patients, a stabilization of the fasting blood glucose level in the DHEA subgroup in relation to the placebo subgroup (evaluated with a glucose tolerance examination) was observed. Nevertheless, the effects of such augmentation in relation to the lipid profile were not evaluated [45]. The results of this trial concerning the effect of dehydroepiandrosterone on glucose metabolism should also be interpreted with caution, due to the fact that a low sensitivity method was used. The evaluation of glucose metabolism was not the primary objective of our trial but solely a secondary outcome. For that reason we have focused on the assessment of the fasting blood glucose level without using more sensitive methods to evaluate glucose metabolism (i.e. glycated haemoglobin level, insulin level, and the glucose tolerance test).

No differences in the mean values of BMI or waist circumference in the DHEA subgroup were observed. In the placebo subgroup the mean BMI value and the waist circumference increased to a statistically significant degree. In both cases the differences in the mean values were not clinically important despite being statistically significant (BMI increased by 0.48 kg/m²; waist circumference increased by 1.11 cm). Therefore, a stabilizing effect of the administration of DHEA on anthropometric measures of metabolic syndrome in patients treated with olanzapine can be assumed. On the basis of the existing research, no effect of administering 50 mg DHEA in order to reduce adipose tissue was observed in a group of 13 men and 17

women [46] or in a group of 140 men and 140 women [43]. A significant effect of dehydroepiandrosterone supplementation has only been observed in one study with a dose of 50 mg/day in 18 persons (both women and men) compared to 10 persons in control group, regarding the radiologically evaluated overall volume of the adipose tissue [47].

Despite the fact that experimental trials indicate the possibility of utilizing dehydroepiandrosterone supplementation to stabilize the appetite and reduce body weight as well as blood glucose levels (especially in diabetic animals), the results of the clinical trials do not confirm the antiatherosclerotic and insulin-like effects of this substance. To summarize the above-presented results, it must be emphasized that the trial did not confirm the occurrence of a significant clinical effect of DHEA on the level of blood plasma lipoproteins or anthropometric measures of metabolic syndrome (i.e. waist circumference and BMI). Some stabilizing effect of DHEA on anthropometric measures of metabolic syndrome and a statistically significant effect on fasting blood glucose level was observed.

Among the main limitations of our study, the relative insensitivity of the methods used to assess glucose metabolism should be mentioned. We relied only on the measurement of fasting blood glucose levels without using more sensitive methods such as measurements of glycosylated haemoglobin, insulin, or the glucose tolerance test. In addition, due to the small number of recruited patients with clinical symptoms of metabolic syndrome, we failed to restrict the selection criteria of the research group only to patients with metabolic syndrome. This would allow for a better assessment of the effects of dehydroepiandrosterone on the examined parameters of metabolic syndrome. Another limitation of the study may have been connected to the small size of the study group. This could affect the errors of inference using ANOVA experiment on only 45 patients.

Conclusions

Dehydroepiandrosterone supplementation at a dose of 100 mg in schizophrenic men treated with olanzapine in a twelve-week observation period:

1. Did not result in any changes in biochemical parameters related to the diagnosis of metabolic syndrome, i.e. overall cholesterol level, the level of HDL cholesterol, the level of LDL cholesterol, and triglycerides.
2. It resulted in a statistically significant decrease in the fasting blood glucose level.
3. It resulted in stabilization of anthropometric parameters related to the diagnosis of metabolic syndrome, i.e. waist circumference and BMI (the parameters remained constant in the DHEA subgroup though they increased in the placebo subgroup).

The results of this trial reflect the unclear conclusions of the literature data, among which the most important clinical advantage of dehydroepiandrosterone supplementation has been observed for anthropometric measures of metabolic syndrome (i.e. visceral obesity), especially in insulin-resistant persons. Further studies based on long term

observation using more sensitive tools of glucose metabolism have to be performed in order to confirm the insulin-like effects of dehydroepiandrosterone.

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