EFFECT OF TRANSDERMAL TESTOSTERONE OR ALPHA-LIPOIC ACID ON ERECTILE DYSFUNCTION AND QUALITY OF LIFE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT
Erectile dysfunction (ED) is the inability to develop and/or maintain an erection that is sufficient for satisfactory sexual intercourse. The prevalence of erectile dysfunction in diabetic men is 28-75%, this percentage rising with patient’s age and duration of diabetes. The aim of the present study was to investigate erectile dysfunction and quality of life in patients with type 2 diabetes mellitus (T2DM) after treating them with transdermal testosterone or with alpha-lipoic acid.

MATERIALS AND METHODS: The effect of a 12-week treatment with transdermal testosterone or alpha-lipoic acid on the erectile function and quality of life of 45 men with ED and T2DM was studied in a randomized, prospective, open clinical, comparative study. The parameters we measured in the patients were body weight and body mass index (BMI); the albumin, lipids, HbA1C, testosterone (T), sex hormone-binding globulin (SHBG), follicle stimulating hormone (FSH), luteinizing hormone (LH) and microalbuminuria levels; the International Index of Erectile Function (IIEF) and Health related quality of life (SF-36) questionnaires were completed to evaluate ED and quality of life before and after 12 weeks of treatment with alpha-lipoic acid (600 mg, parenterally, for 7 days, followed by 600 mg received per os) or with transdermal testosterone in a dose of 50 mg daily.

RESULTS: Testosterone treatment decreased BMI significantly (p < 0.01), increased testosterone concentrations (p < 0.01) and raised the SHBG levels (p < 0.05), improved the glycemic control and lipid profile (total cholesterol, p < 0.05; HDL cholesterol, p < 0.05; triglycerides, p < 0.05). The patients treated with alpha-lipoic acid had their BMI (p < 0.01), HbA1C (p < 0.01), total cholesterol (p < 0.01), HDL-cholesterol (p < 0.01) and triglycerides (p < 0.01) significantly reduced. The indicators for ED in both groups were also statistically significantly improved. There was improvement for all patients’ self-assessment score for “physical functioning” (p = 0.001), for “role limitations due to physical health” (p < 0.001) and for “general health perception” (p = 0.021).

CONCLUSIONS: Transdermal testosterone and alpha-lipoic acid have a tangible beneficial effect on erectile dysfunction and on metabolic disorders in T2DM patients and can be used to treat such patients.

Key words: erectile dysfunction, type 2 diabetes mellitus, testosterone, alpha-lipoic acid, quality of life

INTRODUCTION
Erectile dysfunction is defined as the inability to attain or maintain an erection sufficient for satisfactory sexual performance.1 The considerable advances in understanding the pathogenesis of this disorder has made it possible to reassess as organic process related those cases of ED that were previously classified as psychogenic in etiology. Erectile function depends on the complex interactions between a number of psychological, neurological, vascular and endocrine factors. It is well known that androgens play a key role in the physiology of erectile function.2 Their gradually decreasing levels and the greater rate of occurrence of ED with age are well documented.3,4 There is still no conclusive data about any correlation between testosterone levels and ED.5 There are studies on testosterone replacement therapy in hypogonadal men that have reported improvement
in the erectile function. But still no dose-dependent effect has been reported at different levels of testosterone both within the reference limits and when it exceeds the normal values. A meta-analysis of 17 randomized, placebo-controlled trials of the effects of testosterone on the sexual function indicates that while testosterone replacement therapy in hypogonadal men has improved sexual function, addition of testosterone in eugonadal men has no effect on erectile function. So, the role of androgens in erectile function remains controversial.

There is a growing body of evidence that suggests a correlation of androgens, testosterone in particular, with metabolic syndrome and an increased risk of developing diabetes and/or cardiovascular disease. ED occurs in 28-75% of men with diabetes, this percentage rising with age and duration of diabetes. The etiology of ED in type 2 diabetes is often multifactorial and includes poor metabolic control, diabetes induced micro- and macrovascular changes, neuropathy, hypogonadism, or a combination of all these factors. Most of these conditions are difficult to treat. Erectile dysfunction not only accompanies cardiovascular diseases and diabetes, but it may also be their first manifestation.

ED is a serious problem for men and for public health in general; it affects millions of people and their quality of life. It has been increasingly attracting considerable interest recently as life expectancy of the population increases and the related issue of maintaining sexual interest. Poor quality of life has an impact not only on the happiness of an individual, but also on their participation in the work process, their social behaviour, the ease, etc.) that required constant therapy.

The aim of the present study was to investigate erectile dysfunction and quality of life in patients with relatively well controlled type 2 diabetes mellitus prior to and after treating them with transdermal testosterone or alpha-lipoic acid for 12 weeks.

MATERIALS AND METHODS

We studied the effect of 12-week treatment with transdermal testosterone or alpha-lipoic acid on erectile function and quality of life of patients with well controlled type 2 diabetes in a randomized, prospective, open clinical study. We examined 45 men with type 2 diabetes mellitus and ED hospitalized and followed up in the Clinic of Endocrinology and Metabolic Disorders, Plovdiv Medical University, over a period of 4.5 years. The study comprised of patients aged 40 to 60 years with duration of diabetes less than 5 years, and on continuous metformin therapy in a dose of 1500-2550 mg/day and HbA₁C ≤ 7.5%. The main requirement that the patients needed to meet was cohabitation with a permanent partner for at least 12 months. Consultations were carried out with a neurologist and a urologist as early as 5 days prior to the commencement of the study. Other endocrine disorders leading to ED were excluded. The study excluded patients receiving hypoglycemic therapy, patients with uncontrolled dyslipidemia, patients with overt microangiopathy (high-degree microalbuminuria, proliferative retinopathy, severe polyneuropathy), patients lacking history evidence and clinical data about macroangiopathy, patients with concomitant disorders (arterial hypertension, ischemic heart disease, etc.) that required constant therapy.

The patients were randomized to receive either alpha-lipoic acid or testosterone gel in the order they were included in the study.

We measured the following parameters: body weight, BMI, albumin, lipid profile, HbA₁C, testosterone, SHBG, FSH, LH and microalbuminuria. Clinical determinations of albumin and the lipid profile were carried out using Konelab 60i analyser (Thermo Electron Corporation, Finland). The gonadotropic hormones, the FSH and the LH, were determined using a microparticle enzyme immunoassay, and the testosterone and the SHBG - using an enzyme linked immunosorbent assay. Using the values for albumin, testosterone and SHBG we calculated the free and bioavailable testosterone by the Internet-based free access formula or using a special digital calculator. The study was approved by the Plovdiv Medical University Ethics Committee. The patients receiving testosterone therapy were also tested for the prostate-specific antigen. After establishing the hormonal status, evaluating the level of diabetes control and the late degenerative complications that were present we infused alpha-lipoic acid intravenously (600 mg for 7 days); this was followed by alpha-lipoic acid (600 mg) per os or transdermal testosterone in a dose of 50 mg/day for 12 weeks. The preparations used were Androgel® (Abbott) and Thiogamma® (Woerwag Pharma). Both drugs can be bought over the counter in the pharmaceutical outlets.

All patients completed the IIEF and SF-36 questionnaires validated for Bulgaria at baseline.
and at the end of the study. Erectile function was evaluated using the IIEF questionnaire taking the score from the answers to questions Nos 1, 2, 3, 4, 5 and 15 and including patients with a score under 25 points. Quality of life was assessed by means of the questionnaire “Health related quality of life”, popularly known as SF-36. SF-36 allows the clinicians to get reliable information about the functional health and well-being as seen by the patient. The responses to the questions in the questionnaires show the patient’s self-assessment of their physical and mental condition in 8 domains: physical functioning, role limitations due to physical health, emotional well being, role limitations due to emotional problems, bodily pain, vitality, social functioning, general health perception. These domains are grouped into 2 major sections, physical health and mental health, which combine in a total final score or “quality of life”.

Statistical analysis
Statistical analysis was performed using the SPSS statistical package, version 17.0 for Windows (IBM Acquires SPSS Inc., Somers, NY, USA) and STATISTICA, version 7.0 for Windows (StatSoft Inc, Tulsa, OK, USA). The results of the quantitative variables are presented as mean ± the standard error. For all comparisons, p < 0.05 was the significance level at which the null hypothesis is rejected. The Kolmogorov-Smirnov test was used to check the normal distribution and the homogeneity of the variables. We used parametric and nonparametric statistical methods: the t-criterion and the paired Student’s t-test; monofactorial and multifactorial logistic regression; analysis of variance and correlation analysis.

Results
At baseline the study included 57 patients, and of these 45 were treated successfully. Of these 45 patients 19 were on transdermal testosterone, and 26 were treated with alpha-lipoic acid. Of the 57 men with ED that were screened at baseline, only 4 sought medical advice on this occasion before being diagnosed with diabetes. The disease history of patients showed that almost all patients included in the study (51 men, 89.47%) had the symptoms of ED before being diagnosed with T2DM.

The two groups were age, BMI, and \( \text{HbA}_1\text{C} \) matched (Table 1). Of the 45 patients that completed the study, 26 (57.78%) were obese in varying degrees, 14 (31.11%) were overweight and only 5 (11.11%) had a normal body weight. Sixteen patients (35.56%) had their total cholesterol level higher than 5 mmol/l and 15 (33.33%) had HDL-cholesterol level < 1 mmol/l. The study included patients with type 2 diabetes with satisfactory control (HbA\text{1C} ≤ 7.5%) without arterial hypertension, 40 (88.89%) of them met the diagnostic criteria for metabolic syndrome.

The laboratory parameters for all patients and for patients divided into subgroups by received therapy, testosterone gel or alpha-lipoic acid, are presented in Table 1.

Serum levels of total testosterone in the majority of patients (77.78%) were in the “low normal” range (in the lower third of the norm), 17.78% with levels below 2 nmol/l, 4.44% - less than 1.8 nmol/l, LH levels in all being within the reference limits.

We found a significant positive correlation of BMI with \( \text{HbA}_1\text{C} \) (\( r = 0.452, p = 0.001 \)) and a negative correlation with testosterone (\( r = -0.468, p = 0.001 \)), SHBG (\( r = -0.315, p = 0.027 \)) and the bioavailable testosterone (\( r = -0.368, p = 0.009 \)). A finding worthy of note is the statistically significant negative correlation of testosterone with \( \text{HbA}_1\text{C} \) (\( r = -0.332, p < 0.05 \)) and the positive correlation with SHBG (\( r = 0.449, p = 0.001 \)). Bioavailable testosterone shows similar correlations just like total testosterone.

Treatment with testosterone gel resulted in a significant reduction of BMI (\( p < 0.01 \)), an increase of the testosterone levels (\( p < 0.01 \)), an increase in SHBG (\( p < 0.05 \)), better glycemic control and lipid profile (total cholesterol - \( p < 0.05 \), HDL-cholesterol - \( p < 0.05 \), triglycerides - \( p < 0.05 \)) (Table 1). When the group was divided into 2 subgroups based on the median of testosterone (testosterone = 2.73 nmol/l), we found a statistically significant difference in the levels of LH and testosterone before and after treatment. In the group with lower testosterone levels we found that it increased statistically significantly (2.03 ± 0.07 nmol/l vs. 2.54 ± 0.08 nmol/l; \( p = 0.002 \)), coupled with the significantly lower values of LH (3.74 ± 0.5 IU/l vs. 3.09 ± 0.5 IU/l; \( p = 0.039 \)). In the group with higher testosterone levels these parameters changed at a lower statistical significance for testosterone (3.36 ± 0.2 mmol/l vs. 3.82 ± 0.2 mmol/l; \( p = 0.018 \)) and with no statistical significance for LH (3.57 ± 0.4 IU/l vs. 3.35 ± 0.5 IU/l; \( p = 0.285 \)). There was a difference in the absolute values for the other laboratory parameters but it failed to reach statistical significance.

In the alpha-lipoic acid-treated group there was a significant decrease of BMI (\( p < 0.01 \)), \( \text{HbA}_1\text{C} \) (\( p <
0.01), total cholesterol (p < 0.01), HDL-cholesterol (p < 0.01) and triglycerides (p < 0.01) and a significant increase of HDL cholesterol (p < 0.01).

The distribution of patients by severity of ED was as follows: 7 men (15.55%) had moderate erectile dysfunction, 34 (75.56%) had mild to moderate dysfunction and 4 (8.89%) had mild dysfunction.

The IIEF questionnaire enables an assessment not only of the erectile function of patients, but also of some additional indicators such as orgasmic function, sexual desire, intercourse satisfaction and overall sexual satisfaction. Results from the answers given for the five domains in the questionnaire are presented in Table 2.

We found a statistically significant improvement in the means of ED indicators in both groups of patients (testosterone treated and alpha-lipoic acid treated patients). Considerable improvement with varying degrees of statistical significance was found in the orgasmic function, sexual desire, intercourse satisfaction and overall sexual satisfaction. It is impossible to draw any definitive conclusions as to the therapeutic effects of the two drugs based on the replies to questions in IIEF due to significant differences in the baseline parameters (their absolute values) between the two groups. The effect of the treatment in percent for each domain in IIEF is presented in Fig. 1. From the data for the percent-

### Table 1. Some clinical and laboratory parameters of the patients before and after treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total (n = 45)</th>
<th>Testosterone gel (n = 19)</th>
<th>Alpha-lipoic acid (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
<td>Before treatment</td>
</tr>
<tr>
<td>Age (years)</td>
<td>50.86 ± 0.73</td>
<td>51.58 ± 0.92</td>
<td>50.40 ± 1.04</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>3.84 ± 0.39</td>
<td>3.54 ± 0.67</td>
<td>4.03 ± 0.48</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>32.05 ± 0.89</td>
<td>31.11 ± 0.73*</td>
<td>31.89 ± 1.39</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>7.10 ± 0.09</td>
<td>6.64 ± 0.09**</td>
<td>7.06 ± 0.13</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>41.51 ± 0.58</td>
<td>42.12 ± 0.48</td>
<td>41.21 ± 0.68</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>5.51 ± 0.11</td>
<td>5.12 ± 0.07**</td>
<td>5.23 ± 0.17</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>1.11 ± 0.04</td>
<td>1.15 ± 0.04**</td>
<td>1.16 ± 0.08</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>2.36 ± 0.22</td>
<td>2.17 ± 0.17**</td>
<td>2.08 ± 0.22</td>
</tr>
<tr>
<td>Testosterone (ng/ml)</td>
<td>2.78 ± 0.11</td>
<td>2.96 ± 0.10**</td>
<td>3.03 ± 0.16</td>
</tr>
<tr>
<td>Free testosterone (ng/ml)</td>
<td>0.103 ± 0.02</td>
<td>0.076 ± 0.001</td>
<td>0.12 ± 0.03</td>
</tr>
<tr>
<td>Bioavailable testosterone (ng/ml)</td>
<td>1.70 ± 0.07</td>
<td>1.64 ± 0.12</td>
<td>1.75 ± 0.09</td>
</tr>
<tr>
<td>SHBG (nmol/l)</td>
<td>17.72 ± 0.87</td>
<td>18.17 ± 0.78*</td>
<td>19.81 ± 1.14</td>
</tr>
<tr>
<td>Microalbuminuria (μg/min)</td>
<td>16.56 ± 1.93</td>
<td>16.88 ± 1.45</td>
<td>13.74 ± 1.83</td>
</tr>
</tbody>
</table>

* p < 0.05; ** p < 0.01 intragroup significance.

### Table 2. Results from the answers given for the five domains in the IIEF questionnaire before and after treatment

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Total (n = 45)</th>
<th>Testosterone gel (n = 19)</th>
<th>Alpha-lipoic acid (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
<td>Before treatment</td>
</tr>
<tr>
<td>Erectile function</td>
<td>15.67 ± 0.33</td>
<td>18.20 ± 0.37**</td>
<td>15.95 ± 0.48</td>
</tr>
<tr>
<td>Orgasmic function</td>
<td>7.27 ± 0.13</td>
<td>8.02 ± 0.16**</td>
<td>7.11 ± 0.23</td>
</tr>
<tr>
<td>Sexual desire</td>
<td>7.14 ± 0.14</td>
<td>8.29 ± 0.14**</td>
<td>6.95 ± 0.22</td>
</tr>
<tr>
<td>Intercourse satisfaction</td>
<td>10 ± 0.3</td>
<td>10.87 ± 0.31**</td>
<td>8.67 ± 0.46</td>
</tr>
<tr>
<td>Overall satisfaction</td>
<td>7.44 ± 0.12</td>
<td>8.23 ± 0.15**</td>
<td>7.39 ± 0.23</td>
</tr>
</tbody>
</table>

* p < 0.05; ** p < 0.01 intragroup significance.
age improvement in the various indicators we can note the significant increase in sexual desire in the testosterone treated patients (27.2%) with relatively less improvement in orgasmic function (7.31%) and overall sexual satisfaction (8.28%). In the group treated with alpha-lipoic acid the erectile function improved by 17.42%, the orgasmic function - by 12.21%, and the overall sexual satisfaction - by 12.05%.

All in all, as determined by IIEF, none of the patients included in the study could restore their normal erectile function. At study end there was only 1 (2.22%) man with moderate dysfunction, 23 patients - with mild to moderate dysfunction - 23 (51.11%) and with a mild dysfunction - 21 (46.67%).

The statistical analysis of all patients showed no significant relationship between erectile dysfunction and the clinical and laboratory parameters, including age and duration of diabetes. The linear regression analysis with erectile function as dependent variable and all measured parameters as independent variables showed that age was the only statistically significant predictor for ED (Beta = 0.306; p = 0.046). As for the other sexual function parameters we found a strong correlation of sexual desire with total testosterone levels (r = 0.671, p < 0.001) and bioavailable testosterone (r = 0.710, p < 0.001), and negative correlation with HbA1C (r = -0.294, p = 0.040). We found a negative correlation between erectile function and orgasmic function (r = -0.305, p = 0.033). The correlation between intercourse satisfaction and the overall sexual satisfaction became positive after treatment. After testosterone treatment the correlation between the erectile function and the orgasmic function also became positive (r = 0.507, p = 0.027), while after the alpha-lipoic acid treatment the correlation remained negative (r = -0.395, p = 0.031).

The results of the completed SF-36 for all patients are shown in Fig. 2 and Table 3. For the entire group there was improvement in the self-assessment for “physical functioning” (p = 0.001), for “role limitations due to physical health” (p < 0.001) and for “general health” perception (p = 0.021). This resulted in a statistically significant improvement in the physical (p < 0.001) and mental (p = 0.021) health and ultimately to a significant improvement in quality of life (p < 0.001). The patients treated with testosterone gel had a statistically significant improvement in the “role limitations due to physical health” (p = 0.007) and improvement of border significance for “physical functioning” (p = 0.059). General physical health improved significantly (p = 0.001), as well as the final result of the test (quality of life) (p = 0.001). In the alpha-lipoic acid treatment group there was improvement in “physical functioning” (p = 0.007), in “role limitations due to physical health” (p < 0.001) while the change in the “general health perception” had a borderline significance (p = 0.058). There was also a significant improvement in “general health” (p = 0.001), the final result of the test (“quality of life”) (p = 0.001) and borderline significant improvement in the “general mental health” (p = 0.058) (Fig. 2).

The score for ED correlates significantly positively with the quality of life (r = 0.439; p = 0.002), vitality (r = 0.424; p = 0.003), physical functioning (r = 0.335; p = in 0.021) and negatively with bodily pain (r = -0.346; p = 0.017). The correlation with mental health is borderline (r = 0.286; p = 0.052). ED predictors were determined by regression analysis: BMI, bioavailable testosterone, age, total testosterone in a combination had the highest significance (p = 0.012). Predictors of ED can also be the summarising domains in SF-36: physical health, mental health and overall score. Quality of life, however, is closely associated with ED and it would be logical to believe that the initially manifested problem determines the other. In other words, ED has a negative impact on quality of life and the deteriorating quality of life leads to ED.

**DISCUSSION**

As healthy men age, their circulating testosterone concentrations fall by 1 to 2% per year on average and this begins as early as the third decade of life. The decline in the bioavailable testosterone levels,
Figure 2. Results from completed SF-36 questionnaires for all patients.

Table 3. Results of the completed SF-36 before and after treatment

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Testosterone gel (n = 19)</th>
<th>Alpha-lipoic acid (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>80.26 ± 2.72</td>
<td>81.58 ± 2.54</td>
</tr>
<tr>
<td>Role limitations due to physical health</td>
<td>39.47 ± 7.72</td>
<td>51.32 ± 7.27*</td>
</tr>
<tr>
<td>Role limitations due to emotional problems</td>
<td>73.68 ± 6.54</td>
<td>71.93 ± 6.38</td>
</tr>
<tr>
<td>Vitality</td>
<td>61.58 ± 2.57</td>
<td>62.10 ± 2.54</td>
</tr>
<tr>
<td>Emotional well being</td>
<td>81.68 ± 2.06</td>
<td>81.47 ± 2.03</td>
</tr>
<tr>
<td>Social functioning</td>
<td>57.24 ± 2.92</td>
<td>57.89 ± 2.9</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>42.42 ± 2.31</td>
<td>42.11 ± 0.08</td>
</tr>
<tr>
<td>General health perception</td>
<td>41.68 ± 1.65</td>
<td>42.83 ± 1.52</td>
</tr>
<tr>
<td>Physical health</td>
<td>43.32 ± 2.00</td>
<td>53.88 ± 2.02**</td>
</tr>
<tr>
<td>Mental health</td>
<td>55.23 ± 1.72</td>
<td>55.54 ± 1.73</td>
</tr>
<tr>
<td>Total score</td>
<td>51.32 ± 1.63</td>
<td>57.61 ± 1.78**</td>
</tr>
</tbody>
</table>

* p < 0.05; ** p < 0.01 intragroup significance.

As age increases, it is normally expected to be greater than the decrease in total testosterone due to the age-related increase of SHBG, which is inconsistent with what we found in our patients. Testosterone is directly involved in physiological processes such as self-esteem, sense of well-being, motivation, cognition and memory, muscle mass and strength, while sexual function is an integral part of the satisfaction with life. Testosterone affects nearly every organ in the body. There is growing evidence that levels...
of total testosterone and SHBG are lower in men with metabolic syndrome and/or T2DM than these in healthy controls. Moreover, some researchers argue that these two hormones levels may serve as early markers for vascular and metabolic disorders. The idea of this study was by using small doses of testosterone in non-hypogonadal men to assess its effect on the metabolic control of diabetes and ED as possible early manifestation of T2DM.

The glycemic control improvement, the lowering of the cholesterol levels and the reduction of the body weight have confirmed that testosterone levels and the components of metabolic syndrome (mainly of insulin resistance) are correlated. These results are due, at least in part, to the improved physical and emotional well being of patients. It must be noted that sexual desire was significantly increased as a result of the treatment with testosterone. All this contributes to the significant improvement of patients’ sexual function.

Our results suggest that regulation of the hypothalamic-pituitary-gonadal axis has been balanced at a lower level of total testosterone. This balance is upset after the transdermal testosterone therapy starts (testosterone increases a little but LH falls below the reference limit) and is not restored over the three-month treatment. It follows that proper assessment of gonadal function and hence an evaluation for a replacement therapy should not be made on the basis of just a single measurement of testosterone and the gonadotropins.

Erection depends to a large extent on the release of nitric oxide (NO) by vascular endothelial cells. Insulin resistance (IR) is a metabolic aberration that causes endothelial dysfunction; it is characterised by reducing the NO synthesis and release. Antioxidants such as alpha-lipoic acid prevent tissue and organ involvement by neutralizing the free radicals and reducing the oxidative stress. Alpha-lipoic acid is involved in the maintenance of normal blood sugar level, it also facilitates the glucose uptake in the tissues, improves insulin sensitivity and endothelial function, improves the lipid profile and reduces body weight. All this is confirmed by our results. Treatment with alpha lipoic acid led to improvement of patients’ self-assessment of their physical condition and health and a significant improvement of sexual function. And while treatment with testosterone has a stronger aphrodisiac effect, the effect of alpha-lipoic acid is more pronounced in improving the orgasmic function.

In the present study, the sexual problems in most of the cases have the character of a secondary sexual disorder, because the symptoms in each case have been developing slowly, gradually over months or even years after a period of normal sexual functioning. It is exactly the stigma or embarrassment of having such a sexual problem and, hence, the apparent neglecting of the problem that deteriorates the quality of life of these patients and delays the administration of a relevant therapy. Diagnosing ED in the patients we studied was a result of a careful, deliberate inquiring about it on the part of the research team rather than as consequence of patients’ complaints. We attribute the refusal of 12 diabetic patients to complete the study mainly to nonspecific symptoms and quite delicate character of the questions.

The beneficial effect on erectile function as a result of the two applied therapies needs some further explanation. First, based on the criteria for patients’ selection, we usually included in the study patients with “mild” and “mild to moderate dysfunction” (84.45% in total). For most of them it was the first time they openly admitted having such a problem. Although ED in these patients was mainly caused by a chronic somatic disease, we might have obtained even better results if treatment had been administered in conjunction with a psychiatrist or a psychologist. Secondly, the patients that were recruited for the study were usually with relatively satisfactorily controlled T2DM. The more direct and frequent doctor-patient communication has been demonstrated to affect beneficially the maintenance of good glycemic control and improves the quality of life of these patients. Thirdly, the satisfaction a man gets from the sexual act does not correspond to the severity of ED, there is an obvious discrepancy between the objective assessment of the severity of ED and the self-assessment made by an individual. Generally, patients tend to perceive their disorder as more serious than they are in fact, which is consistent with the findings of other authors.

In spite of the contradictory nature of the evidence about the role of testosterone for ED when there is concomitant insulin resistance, determination of the serum levels of testosterone, gonadotropins and SHBG should be obligatorily included in the cluster of laboratory tests. This may become the first stage of the algorithm for exploration of hypogonadism or of the overall hormonal status of the patient. The results of our study suggest that transdermal testosterone can be used in the treatment of ED in patients with T2DM but only after a detailed evaluation of the indications for prescribing and
compliance with the side action of the preparation.

Treatment with alpha-lipoic acid in endocrinology is prescribed most often for the treatment of diabetic neuropathy and usually after the onset of the first symptoms – which are most commonly subjective. Our data showed that timely initiation of treatment with alpha-lipoic acid leads to improvement in erectile function and health-related quality of life in patients with T2DM, even without subjective and/or clinical symptoms of late degenerative syndrome. We did not register any side effects due to the therapy applied in both groups.

Erectile function of patients should have a priority in the activity of both general practitioners and specialists. ED should be considered not only as an element of quality of life, but also as a potential predictor of serious vascular and metabolic risk. This requires that erectile dysfunction should be actively searched when taking the history of the disease and, if present, be followed by clinical and laboratory screening in cardiovascular and metabolic aspect. The test for erectile dysfunction is now freely available in many Bulgarian websites and can be performed independently and anonymously. This makes it possible to make a timely diagnosis of ED and administer the proper treatment, and also to conduct prophylaxis and possibly prevent some vascular and/or metabolic disorders therefore improving the quality of life of diabetics.

CONCLUSIONS

The causes of erectile dysfunction are complex: they include more neurological and vascular factors than hormonal disorders. Transdermal testosterone and alpha-lipoic acid have a tangible beneficial effect on erectile dysfunction and on metabolic disorders in T2DM and can be used to treat such patients.

REFERENCES

ЭФФЕКТ ПРИМЕНЕНИЯ ТРАНСДЕРМАЛЬНОГО ТЕСТОСТЕРОНА ИЛИ АЛЬФА-ЛИПОЕВОЙ КИСЛОТЫ НА ЭРЕКТИЛЬНУЮ ДИСФУНКЦИЮ И КАЧЕСТВО ЖИЗНИ ПАЦИЕНТОВ СО САХАРНЫМ ДИАБЕТОМ ТИПА 2

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РЕЗЮМЕ

ВВЕДЕНИЕ: Эректильная дисфункция (ЭД) представляет собой неспособность получить или задержать эрекцию, достаточную для осуществления успешного полового акта. ЭД проявляется в 28–75% мужчин с диабетом, причем этот процент нарастает с возрастом и с продолжительностью диабета.

ЦЕЛЬ: Настоящее исследование ставит себе цель исследовать эректильную функцию и качество жизни пациентов со сахарным диабетом типа 2 после применения трансдермального тестостерона или альфа-липоевой кислоты.

МАТЕРИАЛ И МЕТОДЫ: Проведено рандомизированное, проспективное, открытое обсервационное клиническое исследование эффекта 12-недельного применения трансдермального тестостерона или альфа-липоевой кислоты на эректильную функцию и качество жизни у 45 мужчин с Т2Д и ЭД. Прослежены: вес тела, ВМІ, альбумин, липиды, HbA1С, тестостерон, SHBG, LH, FSH и микроальбуминурия; заполнены вопросы IIEF и SF-36 для оценки ЭД и качества жизни до и после 12-недельного лечения альфа-липоевой кислотой (600 мг парентерально в течение 7 дней, вслед за которым 600 мг перорально) или трансдермальным тестостероном (50 мг в день).

РЕЗУЛЬТАТЫ: Лечение тестостероном привело к значимой редукции ВМІ (p < 0,01), к повышению уровня тестостерона (p < 0,01), появлению SHBG (p < 0,05), улучшению гликемического контроля и липидного профиля (общий холестерол p < 0,05, HDL-холестерол p < 0,05, триглицериды p < 0,05). В группе больных альфа-липоевой кислотой значимо снижается ВМІ (p < 0,01), HbA1С (p < 0,01), общих холестерол (p < 0,01), HDL-холестерол (p < 0,01) и триглицериды (p < 0,01). Наблюдается значимое улучшение показателей ЭД и в обеих группах. Наличие улучшения самооценки относительно физического состояния (p = 0,001), ограничений в результате ухудшения физического состояния (p < 0,001) и общего восприятия состояния здоровья (p = 0,021).

ВЫВОДЫ: Трансдермальный тестостерон и альфа-липоевая кислота имеют сходно благоприятный эффект как на эректильную дисфункцию, так и на нарушения метаболизма при Т2Д и имеют место в целостном лечении пациентов.