Prophylactics of Erectile Dysfunction in Patients with Metabolic Syndrome

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For prophylactics of erectile dysfunction in patients with metabolic syndrome, all unfavorable life-style factors should be excluded and all metabolic disturbances should be corrected. This will reduce the severity and stabilize the course of metabolic syndrome. Administration of special drugs is required for prevention of erection disturbances.

Key Words: *erectile dysfunction; metabolic syndrome; endothelial function; asymmetrical dimethylarginine*

Metabolic syndrome (MS) combines the most important vascular risk factors and is one of the most common cause of erectile dysfunction (ED) [6,10,12]. Moreover, some investigators demonstrated a direct correlation between the incidence and severity of ED and the degree of MS [13]. Taking into account the fact that aggravation of ED negatively affects the efficiency of therapy, prevention of severe forms of erectile disorders, in particular, in patients with MS, is an urgent problem.

Among methods of prophylactics of vascular complications in patients with MS the main role is allocated to correction of life-style factors and body weight reduction [1,4,5]. The increase in the level of physical activity, even started in mature age, to a great extent helps to maintain erectile function in patients with MS [9,14]. Correction of other components of MS, including arterial hypertension and dyslipidemia, can require administration of drugs. However, drugs used for this therapy can negatively affect the erectile function, which dictates the need in selective approach in drug choice [5,7].

New highly efficient preparation for the treatment of ED, *e.g.* impaza, a preparation developed in Russia, can be used as the prophylactic means in patients with risk factors [1]. The mechanism underlying the effect of impaza is related to activation of endothelial NO-synthase playing an important role in the development of erection.

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MATERIALS AND METHODS

The study included 152 patients with MS (mean age 47.80±12.2 years) with normal erectile function at the time of examination. In all patients, complex clinical examination was performed. It included routine (history taking, examination, complete blood count and biochemical blood test) and special methods aimed at diagnostics of ED and MS. Erectile function was evaluated using International Index of Erectile function (IIEF) questionnaire. MS was diagnosed by criteria of National Cholesterol Education Program. The presence of at least 3 of 5 proposed criteria was considered as MS: abdominal obesity (waist circumference >102 cm or body mass index >28.8 kg/m^2), hypertriglyceridemia (>1.7 mmol/liter), low HDL level (<1 mmol/liter), arterial hypertension (>130/85 mm Hg), increased fasting blood glucose level (>6.1 mmol/liter).

For evaluation of endothelial function, postcompression tests on the brachial and cavernous arteries was carried out and the content of asymmetrical dimethylarginine was measured by IEA (ADMA ElisaKit) The concentration of asymmetrical dimethylarginine >0.573, 0.062-0.0572, and <0.062 μM corresponded to high, moderate, and the absence of ED

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risk, respectively. Plasma level of free testosterone was measured by IEA (DRG TechSystems)

The data were processed statistically using Student *t* test and χ^2 test.

Taking into account the fact that enrolled patients had many risk factors, they can develop ED in the future. Therefore dynamic observation over these patients was performed and prophylactic capacities of various methods used for correction of MS and ED were evaluated.

The patients were divided into 3 comparable groups: group 1 (n=51) no correction of MS before the start of the study; group 2 (n=50) correction of MS; group 3 (n=51) correction of MS and administration of impaza for prophylactics of ED. The duration of observation was 12 months; parameters of MS (anthropometry and biochemical blood tests) and erectile function were evaluated every 6 months.

The groups did not differ by concomitant diseases (Table 1). By the start of the study, 74.5% patients in group 1, 72% in group 2, and 70.6% in group 3 regularly received hypotensive therapy, 19.6, 16, and 17.6% patients, respectively, received hypoglycemic therapy, and 3.8, 4, and 2%, respectively received lipid-lowering drugs.

In group 2, correction of all metabolic disturbances was performed. Dietary recommendations and dosed physical exercise were used for weight loss. Blood glucose level in 8 patients with diabetes mellitus was corrected with sugar-lowering drugs; insulin therapy was applied in 2 patients. All 38 patients with insulin resistance received metformin (500 mg/day) was prescribed for improving tissue sensitivity to insulin. In patients with dyslipidemia (n=45), the level of lipids was corrected with a diet (according to recommendations of European cholesterol program). Sustanon-250 (preparation of testosterone esters) in individual doses was prescribed to 3 patients, in whom decreased levels of free and total testosterone were associated with reduced libido.

Group 3 patients, along with correction of metabolic syndrome received preparation for specific therapy of ED. Correction of life-style factors and metabolic disorders was carried out using the same measures as in group 2. The quality and character of therapy for correction of MS were the same in groups 2 and 3. Impaza (1 sublingual tablet daily), a preparation developed in Russia, was given daily for drug prophylactics of ED.

RESULTS

Body weight decreased in patients of groups 2 and 3 after a course of therapy. No significant decrease in body weight and waist circumference was noted in group 1, where no special measures aimed at correction of excess body weight was used.

The number of patients with type 2 diabetes mellitus in group 1 increased by 2 times over 12 months, while in groups 2 and 3 this parameter remained unchanged. The number of patients with insulin resistance and hyperinsulinemia significantly decreased in group 2 and especially in group 3 against the background of treatment aimed at improving tissue sensitivity to insulin, while in group 1 this parameter even increased.

Special diet and statin treatment improved the parameters of lipid metabolism in groups 2 and 3. The level of total cholesterol, triglycerides, and atherogenicity index in these groups decreased to the same extent, while HDL level increased and approached the normal. An opposite dynamics was observed in group 1 patients: the level of atherogenic lipids increased, while the concentration of HDL decreased.

The initial mean increase in the diameter of cavernous artery (%) in all groups was similar in all groups and corresponded to normal. However, after treatment these parameters considerably decreased in group 2 and especially in group 1 and remained unchanged in group 3. The degree of postcompression increase in brachial artery diameter in group 1 patients also significantly decreased, while in groups 2 and 3 this parameter increased (Table 2).

In groups 2 and 3, the number of patients with the level of asymmetrical dimethylarginine corresponding to high risk decreased by almost 3 times, while in group 1 this parameter little changed (Table 2).

Correction of metabolic disturbances in patients of groups 2 and 3 was accompanied by an increase in

TABLE 1. Incidence of Concomitant Diseases in Patients with MS and ED

Parameter	Group 1	Group 2	Group 3
Smokers, %	43.14	50	47.33
Patients with excess body weight, %	100	100	100
Patients with arterial hypertension, %	86.27	88	88.23
Patients with type 2 diabetes mellitus, %	19.60	20	21.56
Patients with dyslipidemia, %	80.39	90	88.23

TABLE 2. Changes in the Studied Parameters of MS against the Background of Different Variants of Therapy for ED (*M*±*m*)

Parameter	Group 1		Group 2		Group 3	
	before treatment	after treatment	before treatment	after treatment	before treatment	after treatment
Erectile function, IIEF score	26.76±0.91	23.05±3.23^{+}	27.04±0.99	25.42±2.47^{+*}	26.92±1.02	26.74±2.12*
Mean level of total testosterone, pg/ml	8.46±2.10	7.94±1.82^{+}	8.46±1.71	9.47±1.52^{+*}	8.58±2.04	9.84±1.88^{+*}
Patients with high-risk level of asymmetrical dimethylarginine, %	98.04	96.07^{+}	100	32^{+*}	100	31.37^{+*}
Mean increase in cavernous artery diameter, %	50.65±2.50	40.58±8.35	51.00±2.59	41.10±6.28*	50.25±2.86	50.76±5.82*
Patients with endothelial dysfunction of cavernous arteries, %	35.29	82.35^{+}	28	42^{+*}	41.17	23.52^{+*o}
Mean postcompression increase in brachial artery diameter, %	10.27±2.67	6.66±2.25^{+}	10.32±2.97	12.44±2.87^{+*}	9.25±3.30	12.21±3.40^{+*}
Patients with endothelial dysfunction of brachial artery, %	92.15	98.03^{+}	92	72^{+*}	94.11	68.62^{+*}

Note. *p<0.05 compared to: $^{+}$values before treatment, *group 1, ^{o}group 2.

total and free testosterone levels (Table 2). However, no significant differences between these groups were found. In group 1 patients, the level of sex steroids decreased.

The mean parameters of erectile function (IIEF score) in all groups initially surpassed 26, which corresponded to normal. After 12 months, in patients of groups 1 and 2, IIEF score significantly decreased, while in group 3 this parameter remained unchanged (Table 2). Group 1 patients had more pronounced changes in IIEF score and were less satisfied by the quality of intercourses.

Erectile disturbances were most often observed in group 1. More than half of these patients (52.94%) noted impairment of both spontaneous and adequate erections. In patients of groups 2 and 3, ED was less frequently observed (16 and 5.88%, respectively). The number of patients with moderate ED was maximum in group 1. All patients with ED were over 50 years.

Prophylactics is the major method of combating MS and ED. Pioneer studies showed that elimination of risk factors in individuals predisposed to MS reduces the incidence and severity of ED and other vascular complications, including type 2 diabetes mellitus [2,8,11]. Dynamic observation showed that the degree of compensation of metabolic and vascular disorders depends on performed therapy. Since not all patients in group 1 received adequate complex therapy, the main component of metabolic syndrome progressed over the observation period and led to a considerable increase in the number of patients with type 2 diabetes mellitus, insulin resistance, and compensatory hyperinsulinemia The absence of rational therapy promoted the development of more severe shifts in lipid profile, in particular, to elevation of triglyceride content, which, in turn, aggravated the existing vascular disturbances. In group 1, the number of patients with clinical and biochemical signs of endothelial dysfunction sharply increased. These changes probably led to the development of ED in more than half of patients.

High efficiency of pathogenetic therapy in groups 2 and 3 suggests that metabolic disturbances should be corrected in all patients with MS. In these groups, body mass index, waist circumference, and levels of systolic and diastolic blood pressure decreased to the same extent, parameters of lipid profile also improved. However, in group 2 (but not in group 3) the number of patients with endothelial dysfunction of the cavernous arteries significantly increased, which led to the development of ED in 8 (16%) cases. Evaluation of the diameter of cavernous arteries revealed improvement of endothelial function in cavernous bodies in group 3 patients. This was also seen from decreased number of patients with endothelial dysfunction of cavernous arteries. This fact attests to favorable effect of impaza on endothelial function of the cavernous arteries. Along with complex therapy, long-term prophylactic treatment with impaza considerably reduced the risk of ED development in patients with MS (5.88%). Moreover, the effect of impaza is related to stimulation of endothelial NO-synthase, which actively participates in the regulation of endothelial function. Other advantages of this preparation are its low price, absolute safety, and good tolerability.

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