

Study on the clinical value of alprostadil combined with α -lipoic acid in treatment of type 2 diabetes mellitus patients with erectile dysfunction

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Abstract. – OBJECTIVE: We investigated the clinical value of alprostadil combined with the α -lipoic acid in treating type 2 diabetes mellitus with erectile dysfunction (DMED).

PATIENTS AND METHODS: We selected a total of 76 cases of patients who were admitted to endocrinology department of our hospital from June 2014 to June 2015 and diagnosed as DMED, and the average age was (46.7 ± 7.2) years old, average course of diabetes mellitus was (6.2 ± 2.8) years and average body mass index was (25.4 ± 1.3) kg/m². 40 cases were randomly divided in the observation group while 36 cases were divided in the control group. They received blood glucose control therapy. The patients in the observation group received 60 mg alprostadil hydrochloride and 600 mg α -lipoic acid added into 250 mL normal saline, intravenous drip once per day for 2 weeks. The patients in the control group took tadalafil 5 mg orally, once per night for 2 weeks as a course of treatment. There were no cases of loss.

RESULTS: The effective rate of treatment in observation group is significantly higher than that in the control group (95.0% vs. 80.5%, $p < 0.05$). The score of IIEF-5, EHGS and the FMD value of brachial artery of the observation group after the operation were significantly higher than that of the control group ($p < 0.05$). The adverse reaction rate in the observation group was lower than that in the control group (7.5% vs. 13.9%, $p < 0.05$).

CONCLUSIONS: Alprostadil combined with α -lipoic acid can improve DMED patients' vascular endothelial function and erection hardness to treat erectile dysfunction with less adverse effects and better safety.

Key Words:

Alprostadil, α -lipoic acid, Type 2 diabetes mellitus, Erectile dysfunction.

Introduction

Erectile dysfunction (ED) is one of the common complications of type 2 diabetes mellitus in

males and according to reports, nearly 35%-75% of diabetes mellitus patients present with ED symptoms¹. Several researches suggest that nerve and vessel lesions caused by oxidative stress play an important role in the onset of diabetes mellitus with erectile dysfunction (DMED)². There is a lack of specific therapeutics for the treatment of DMED. Phosphodiesterase type 5 inhibitors (PED-5) is a promising drug which can treat the disease; however, it exhibits mild and moderate adverse effects such as headaches, facial flushing and transient visual impairment among others. It is not suitable for some DM patients due to its complication of cardiac and cerebral vascular diseases^{3,4}. We investigated whether the vasoactive agent alprostadil and antioxidant α -lipoic acid can treat DMED and achieve a better therapeutic effect.

Patients and Methods

Patients

A total of 76 cases of patients who were admitted to the Endocrinology Department in our hospital from June 2014 to June 2015 and diagnosed as DMED were selected continuously. Patients were between the ages of 37-65 years old, an average of (46.7 ± 7.2) years old, they had been on a course of drugs for diabetes mellitus for 3-10 years, with an average of (6.2 ± 2.8) years, and their body mass index (BMI) was between 23-28 kg/m², with an average of (25.4 ± 1.3) kg/m². Inclusion criteria: (1) The diagnosis of diabetes accorded with WHO standard in 1999; (2) The diagnosis and grading of ED were based on International Index of erectile function (IIEF-5), which the score 5-7 is severe, 8-11 is moderate, 12-21 is mild and ≥ 22 is without ED. Exclusion criteria: (1) ED was caused by sec-

ondary factors as congenital deformity of genital organ, dysplasia, reproductive system infection, operation, etc. (2) Patients who had a history of allergy or contraindication to the investigational drugs. Patients were randomly divided as 40 cases were put into the observation group and 36 cases in the control group. According to the comparison of age, course of diabetes and body mass index between both groups, the difference shows no statistical significance ($p > 0.05$).

Therapeutic Method

After the first diagnosis, all the patients stopped all other erectile dysfunction drugs to take hypoglycemic agents and (or) insulin as treatment, and they were guided dietetic contraindication and disease knowledge. Through the treatment, abnormal blood pressure and the blood lipid of some patients was controlled within normal limits. Blood sugar control standard is that fasting blood-glucose (FPG) is 4.4-6.1 mmol/L; two hours' postprandial blood glucose (2hPG) 4.4-8.0 mmol/L, controlled within normal limits. On the basis, the control group was taking Tadalafil (Lilly del Caribe Inc., approval numbers: H20120472) orally 5 mg, once per night for 2 weeks as a course of treatment. The observation group was receiving alprostadil injection hydrochloride (Beijing Tide Pharmaceutical Co., LTD, national medicine permission number: 10980023), adding a normal saline of 10 ml to 10 μ g injection hydrochloride, with a slow intravenous injection, alpha thioctic acid injection (Jiangsu Shenlong Pharmaceutical Company, national medicine permission number: 20059737) 600 mg added into normal saline 250 mL, intravenous drip once per day for 2 weeks as a course of treatment. We suggested that patients in both groups engage in sexual activity 3-5 times per month during courses of treatment.

Evaluation Index of Curative Effect

Evaluation of erectile function parameters:

1. A week after the course of treatment, we guide patients to fill in the IIEF-5 questionnaire to analyze the variation of the scale score and total score before and after the treatment.
2. Self-test erection hardness score (EHGS). We required patients to truly grade according to subjective feeling to erection hardness: I class (penis hyperemia without erection), II class (slight erection but failing to insert), III class (enough hard to insert but not strong and

durable), IV class (full erection, returning to normal).

3. We adopted the high-frequency color Doppler ultrasonography to measure brachial artery flow-mediated dilation (FMD), and assessed the changes of vascular endothelial function before and after the treatment. FMD value = change value of brachial artery diameter/basic inner diameter \times 100%.

Evaluation of Curative Effect

The treatment is effective judged by the improvement of the score of IIEF-5 and the erectile function by self-diagnosis. Also, a lack of adverse effects during the period of treatment also leads to efficacy.

Statistical Analysis

Statistical software SPSS19.0 (SPSS Inc., Chicago, IL, USA) has been used. The quantitative data are shown by the mean \pm standard deviation. The inter-group comparison is tested by the t -test. The qualitative data is shown by the number of cases or the percentage. The inter-group comparison is tested the by the χ^2 -test. $p < 0.05$ indicates statistical significance.

Results

The Comparison of Clinical Effects Between Both Groups

There were no cases of loss in the study as all patients were completely treated and followed-up. The treatment efficiency of the observation group was 95.0% (38/40) as 2 cases had no improvement in their erection. The treatment efficiency of the control group was 80.5% (28/36). There were significant differences of the treatment efficiency in both groups (= 4.918, $p < 0.05$).

The Comparison of Score of IIEF-5, EHGS and FMD value of Brachial Artery

A score of IIEF-5, EHGS and FMD value of the brachial artery in both groups were significantly different before the treatment, while all kinds of scores were improved after the treatment. Conversely, the scores of IIEF-5, EHGS and the FMD value of the brachial artery of the observation group are higher than that of the control group (Table I) ($p < 0.05$).

Table I. The comparison of score of IIEF-5, EHGS and FMD value of brachial artery of patients in both groups ($\bar{x} \pm s$).

Groups	Before the treatment			After the treatment		
	IIEF-5 score	EHGS score	FMD (%)	IIEF-5 score	EHGS score	FMD (%)
Observation group (n=40)	10.6 ± 4.4	2.0 ± 0.6	8.0 ± 0.8	16.9 ± 4.1	2.8 ± 0.9	9.2 ± 1.7
Control group (n=36)	10.1 ± 3.6	2.1 ± 0.5	7.9 ± 0.6	12.6 ± 3.5	2.3 ± 0.7	8.1 ± 1.0
<i>t</i>	0.538	0.728	0.611	2.829	2.681	3.089
<i>p</i>	0.491	0.121	0.943	0.037	0.041	0.025

The Comparison of Adverse Effect of Patients in Both Groups

The occurrence rate of adverse effects of the observation group was significantly lower than that of the control group (Table II) ($p < 0.05$).

Discussion

The pathology of DMED is complex and its specific pathogenesis is not completely clarified; thus, we cannot make the quantitative evaluation of the effect of most drugs. Phosphodiesterase type 5 inhibitors (PED-5) is currently the main drug, which can treat erectile dysfunction in the clinic, and has an improved effect on varied etiology ED patients with the effective rate of 79%-84%⁵. In this study, the control group taking Tadalafil 5 mg orally per night to treat ED also achieved significant effect with the effective rate of 80.5% in total; the score of IIEF-5 and the erectile function by self-diagnosed improved as well, which is in substantial agreement with the conclusion of studies at home and abroad⁶.

Vessels and blood supply are vital in penile erection mechanism, therefore, erectile dysfunction also belongs to a kind of vascular phenomenon, of which penile blood sinus endothelial system can control the diastole of smooth muscle, and NO release from nNOS under sexual stimulus can expand vessels, affecting the change of blood supply and shearing force of blood flow. After entering cavernous bodies, NO adjusted by K^+ on cytomembrane and Ca^{2+} channel can make

smooth muscle completely diastole, increasing blood flow of the artery of the penis so that the penis erects^{7,8}. That means vascular endothelial cells are essential to erectile function. In studies related to ED in past years^{9,10}, it has been found that nerve reflex conduction dysfunction caused by diabetic autonomic neuropathy and penile arterial lumen blocked by atherosclerosis may lead to penis perfusion deficiency, cavernous bodies lack of blood and oxygen and other factors, thus most ED patients have damaged endothelial function.

According to the conclusions of the study about NOS etiology, we combined alprostadil with α -lipoic acid to treat DMED. We concluded that the effective rate of the study was up to 95.0%, which is significantly higher than control group and less adverse effects with only 1 case of hypotension¹¹. Speculating the mechanism may be that as a new generation of broad spectrum cardiovascular and cerebral vascular active drug, alprostadil is so strong and stable that it can restrain activation of kinase Rho to make smooth muscle cells diastolic and vessels expanded, to attain the effects of relieving vasospasm and improving the blood circulation of ischemic tissue¹². Meanwhile, α -lipoic acid, the antioxidant can eliminate free radicals, chelated metal ions, etc., to improve the state of ischemia and hypoxia of nervous tissue, which has some effect on protecting vascular endothelial function as well as upgrading microcirculation¹³. The combination of both applied in a comprehensive way can help the penis blood sinus endothelial func-

Table II. The comparison of occurrence rate of adverse effect of patients in both groups.

Groups	Blurred vision	Headache	Gastrointestinal discomfort	Hypotension	Occurrence rate of adverse effect (%)	χ^2	<i>p</i>
Observation group (n=40)	0	1	1	1	7.5	3.547	0.023
Control group (n=36)	1	3	2	0	13.9		

tion and erection mechanism of DMED patients from different mechanisms. For ED patients, the decrease of FMD is the early sign of the damage of the endothelial function. Thus, the purpose of applying brachial artery ultrasound is to evaluate the improvement of the endothelial function of the penile artery and sexual function¹⁴. The results of this study show that, after receiving medicine, FMD values of the brachial artery of patients in both groups are better, and they are more significant in the observation group. Enough hardness of erection is the key basis of having a perfect sexual life about the sexual satisfactory degree and the social psychological function of ED patients¹⁵. According to the EHGS scale, we observed that the hardness by self-diagnosis before the treatment is unsatisfied with an average of 2.0-2.1, while after treatment, the hardness of patients in observation group is ameliorated significantly.

Conclusions

All the results showed that alprostadil and α -lipoic acid could help the endothelial function and the erection hardness of ED patients with a significant effect. Above all, alprostadil, the vasoactive agent combined with the antioxidant α -lipoic acid, could effectively help the endothelial function and the erection hardness of DMED patients to attain the aim to treat erectile dysfunction with lesser adverse reaction and more safety. Therefore, the clinical choice is preferable.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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