

Efficiency of Combined Therapy with Impaza and Type 5 Phosphodiesterase Inhibitors in Prophylactics of Posttraumatic Erectile Dysfunction

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The use of combined pharmacotherapy with impaza and type 5 phosphodiesterase inhibitors helps to prevent and/or considerably reduce the risk of posttraumatic erectile dysfunction in men with traumas and strictures of the urethra. This therapy is indicated at early terms after trauma of the urethra for prophylactics of erectile dysfunction.

Key Words: *erectile dysfunction; trauma of the urethra; urethral stricture; impaza*

Recovery of sexual function after trauma of the urethra (TU) is an important component of the quality of life in men. TU and subsequent reconstructive operations often lead to erectile dysfunction (ED).

Information about morphological changes in the cavernous bodies (CB) of the penis is required for better understanding of the mechanisms of ED development after TU. This factor can determine the choice of the time for the start and end of treatment and its duration.

Trauma triggers the synthesis of growth factors, fibrogenic cytokines, proteolytic enzymes, and other bioactive molecules by lymphocytes and monocytes, the initial stimuli for cell proliferation; by the end of the inflammation process, the functional tissue in the organ is replaced by the connective tissue, which considerably impairs its function.

Examination of previously untreated patients ($n=25$) after TU showed that the degree of CB fibrosis varies from moderate to severe and directly depends on the time after trauma. At early terms after TU (less than 3 months), sites of induration and sclerosis alternated with sites with normal structure (Fig. 1, *a*). Other morphological picture was observed in patients having TU more than 3 months ago. The walls of most

lacunes were presented by fibrous connective tissue, the lacunes were deformed without scalloped walls; no smooth muscle cells were seen (Fig. 1, *b*).

In patients having TU more than 6 months ago, sharply pronounced fibrosis of CB was observed (Fig. 1, *c*).

Cavernous tissue in these patients is often completely replaced with mature fibrous tissue with hyalinosis foci. Lacunes were not discernible, their lumen was sharply deformed; epithelium lining the lacunes was desquamated. The remaining endothelial cells had signs of cytoplasm swelling and reduction of organelles, lipid droplets were seen in the cytoplasm. The basal membrane was deformed and loosened in many cases; these changes were more pronounced on the endothelial side. Muscle tissue was absent. All these changes led to pronounced endothelial dysfunction.

Functionally and morphologically determined character of ED in men after TU strictly defines the time interval for the start of therapy aimed at minimizing the consequences of injury or preventing complications. According to data obtained in a morphological study, this period includes the first few weeks after TU, when irreversible fibroplastic processes in the cavernous body and penile vessels are initiated. On the basis of these data we concluded that this therapy should be started as soon as possible after TU and should affect the vascular bed of the cavernous tis-

sue, first of all, on endothelium. We chose impaza, a preparation containing ultralow doses of antibodies to endothelial NO synthase, and type 5 phosphodiesterase inhibitors.

MATERIALS AND METHODS

Twenty-seven patients with TU with preserved erectile function were examined and treated. A modern diagnostic algorithm was used during patient examination: history taking and collection of complains, filling IIEF questionnaire, general clinical laboratory tests, physical examination, biochemical analysis of the blood, hormone measurements, pharmacological diagnostic test, Doppler ultrasonography and complex neurophysiologic examination of the penis, and CB biopsy.

All patients underwent reparative plastic surgery for the first time, history of the disease did not exceed 4-5 months. Taking into account the results of our previous morphological study, this fact is of principal importance, because the proposed treatment protocol suggests that the prophylactics of posttraumatic vasculogenic ED is maximally efficient, if it is performed within first few months after TU.

The patients were divided into 2 groups: group 1 patients ($n=12$) were treated in a hospital before the proposed approach to the treatment was introduced into practice, while group 2 patients ($n=12$) received impaza and type 5 phosphodiesterase inhibitors according to a patented protocol (Patent of the Russian Federation No. 2308271) for 6 months.

The results of the therapy were evaluated using IIEF scale, dynamic Doppler ultrasonography, and morphological examination of CB.

RESULTS

In patients of group 2, the incidence of ED decreased to 13.3%, whereas in group 1 TU was associated with ED of different severity in all patients.

Three months after surgery, the maximum systolic blood flow rate in CB was below the normal in group 1 patients and corresponded to physiological norm in group 2 patients (Table 2). Parameters of end-diastolic blood flow rate were similar.

Index of peripheral resistance (RI) is an important parameter for ascertainment of the absence or presence of vasculogenic ED. In group 2, RI corresponded to physiological norm (it is accepted that vasculogenic ED cannot be proven, if $RI < 0.85$).

The internal diameter of cavernous arteries can also be a marker of the risk of vasculogenic ED after TU, because the intensity and quality of circulation in the cavernous body sharply decrease without prophylactic therapy, which leads to its fibrosis (Table 2).

Biopsy of CB was performed 8 months after TU and 3 months after surgery. Morphological study showed that in group 1 patients, the walls of the majority of caverns consisted of smooth muscle cells and were lined with endothelial cells; no signs of atrophy of smooth muscle fibers were observed. There were signs of focal mild fibrosis of the stroma with minor

TABLE 1. Sexual Disturbances in Men 6 Months after TU (IIEF Score, $M \pm m$)

IIEF domains	No. of questions	Maximum score	Mean score for the domain	
			group 1	group 2
Erectile function	1-5, 15	30	15.0 \pm 1.8	25.0 \pm 0.2
Orgasm	9, 10	10	4.0 \pm 1.4	8.0 \pm 1.0
Sexual desire	11, 12	10	5.5 \pm 1.4	7.9 \pm 1.2
Intercourse satisfaction	6, 7, 8	15	6.3 \pm 2.1	13.9 \pm 1.1
General sexual satisfaction	13, 14	10	6.1 \pm 0.8	9.0 \pm 0.8

TABLE 2. Parameters of Blood Flow in CB of the Penis 3 Months after Surgery on the Urethra ($M \pm m$)

Parameter	Group 1	Group 2
Maximum systolic blood flow rate, cm/sec	17.3 \pm 0.9	27.5 \pm 3.1
Maximum end-diastolic blood flow rate, cm/sec	3.1 \pm 0.2	3.30 \pm 0.25
Index of peripheral resistance (RI)	0.76 \pm 0.20	0.856 \pm 0.100
Inner diameter of cavernous arteries, mm	0.83 \pm 0.80	1.15 \pm 0.20

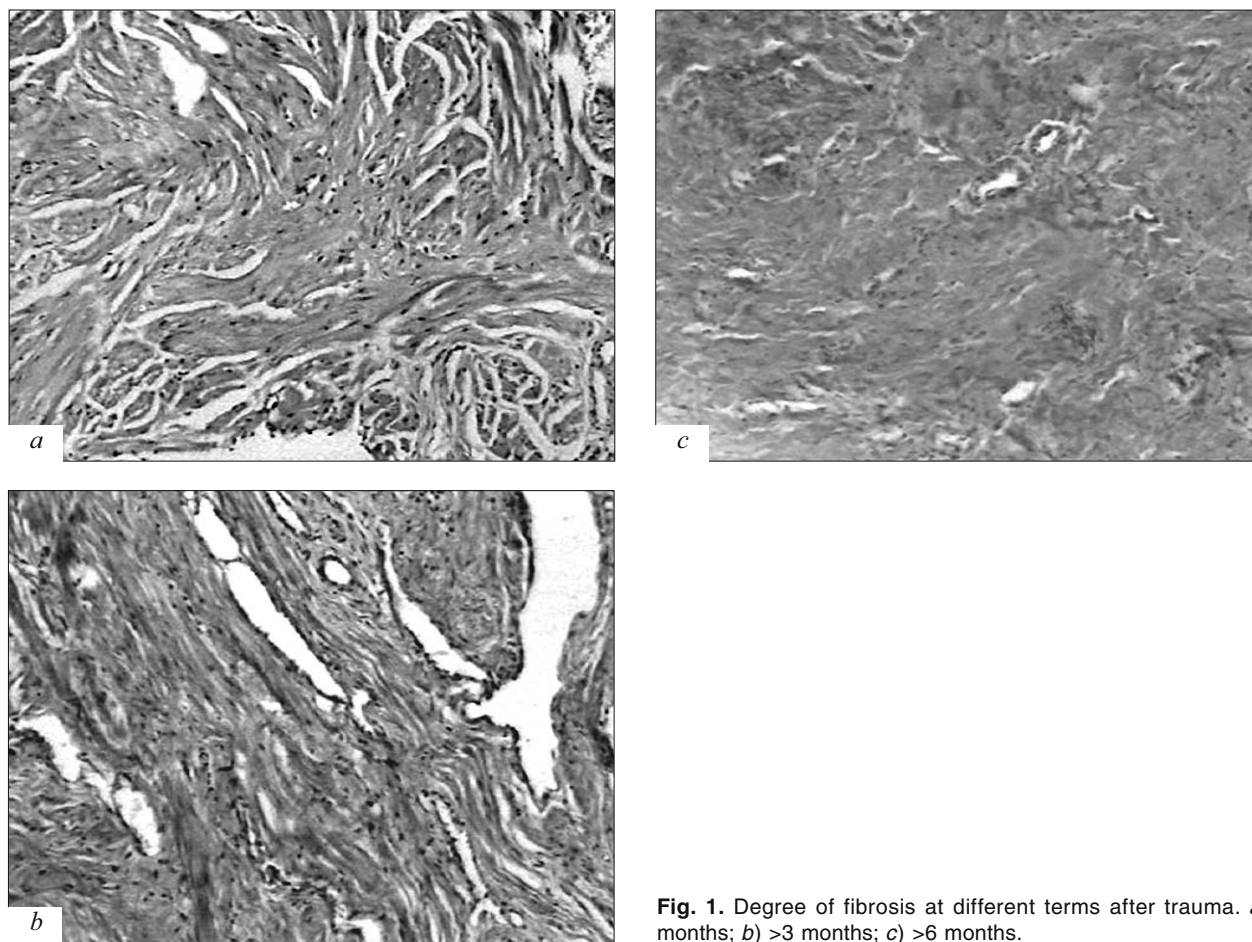


Fig. 1. Degree of fibrosis at different terms after trauma. a) <3 months; b) >3 months; c) >6 months.

deformation of the lumen in some caverns. The walls of caverns retained scalloped appearance and were not deformed, whereas in group 2 patients replacement of the cavernous tissue with mature fibrous connective tissue was observed.

Irreversible degenerative destructive changes in the cavernous tissue and tunica albuginea develop over 6 months after TU. These processes are the main cause of posttraumatic ED. Early (1 month after TU) administration of preparations modulating activity of endothelial NO synthase (impaza) and type 5 phosphodiesterase inhibitors (levitra) makes it possible to prevent or considerably reduce the risk of posttrau-

matic ED in men, which is confirmed by the results of morphological examination and ultrasonography.

REFERENCES

1. Kh. S. Ibishev, *Proceedings of the 3rd Russian Conference "Men Health"*. Moscow (2006), p. 198.
2. M. I. Kogan and Kh. S. Ibishev, *Ibid.*, pp. 164-165.
3. M. I. Kogan and Kh. S. Ibishev, *Progress in the Treatment of Upper Urinary Tract Diseases and Urethral Strictures* [in Russian], Ekaterinburg (2006), p. 410.
4. M. I. Kogan, Kh. S. Ibishev, and S. I. Sidorenko, *Proceedings of XI Russian Urologist Congress* [in Russian], Moscow (2007).