Impaza and Sildenafil: Comparison of Clinical Effectiveness in Patients with Erectile Dysfunction

V. I. Petrov, A. S. Vekel'yan, A. V. Martyushev*, S. A. Sergeeva*, I. V. Smolenov, and O. I. Epstein*

A blind, placebo-controlled, randomized trial showed clinical effectiveness of the preparation Impaza containing antibodies to endothelial NO synthase in ultralow doses. Impaza surpassed placebo, but was less potent than sildenafil in the ability to improve erectile function and other parameters characterizing sexual activity of men. Safety of Impaza was greater than that of other test preparations.

Key Words: *controlled trial; erectile dysfunction; sildenafil; ultralow doses; antibodies to endothelial NO synthase*

Erectile dysfunction (ED) is a chronic disease associated with the inability to reach and/or maintain an erection sufficient for satisfaction of sexual activity. The incidence of ED among men of various ages is 10%. Published data show that 52% men at the age of 40-70 suffer from this disease [2]. The development of ED is related to the effects of various factors, including psychogenic agents and circulatory disturbances in vascular diseases. ED impairs the quality of life, self-evaluation, and relationship with a sexual partner [3].

Recent observations indicate that ED is a curable disease [4]. There are various medicinal preparations for the therapy of ED. However, the efficiency of these drugs was evaluated in a small number of descriptive studies. Sildenafil citrate (Viagra) is most potent preparation for the therapy of patients with ED. Its clinical efficiency and safety were revealed in controlled trials [4].

Preclinical [1] and clinical observations indicate that a new preparation Impaza containing antibodies to endothelial NO synthase in ultralow doses (C12+ C13+C200) and synthesized at the "Materia Medica Holding" Research-and-Production Company may recover erectile functions. However, the effectiveness and safety of Impaza were not compared with those of sildenafil and placebo.

Here we compared clinical effectiveness and safety of Impaza, sildenafil, and placebo in patients with ED. Besides this, we evaluated the value of Impaza during treatment of these patients.

Volgograd Medical Academy; *"Materia Medica Holding" Research-and-Production Company, Moscow

MATERIALS AND METHODS

A blind, placebo-controlled, randomized trial was performed on 2 parallel groups of 90 ambulatory patients (20-70 years) with ED. The patients were examined for 12 week. The severity of ED corresponded to 10-24 points by the scale of International Index of Erectile Function (IIEF). The development of ED was associated with psychogenic and vascular factors in 77.7 and 21% patients, respectively. The average age corresponding to onset of ED was 43.5±1.1. The symptoms of ED persisted for 4.1±0.5 years (0.5-13 years) before the start of examination.

The patients suffering from chronic alcoholism, drug addiction, sexually transmitted diseases, decompensated disorders that could affect the results of a trial, and hypersensitivity to test preparations, unable to respond adequately to the IIEF questionnaire, and involved in other clinical studies over the previous month were excluded from observations.

The patients were divided into 3 similar groups by block randomization. Group 1 patients received Impaza (1 tablet up to dissolution in the mouth) 2 and 1 h before sexual intercourse. Group 2 patients received sildenafil (Viagra, Pfizer) in a dose of 25 mg 1 h before sexual intercourse. Group 3 patients received placebo that was similar to Impaza, but did not contain the active substance (1 tablet, 2 and 1 h before sexual intercourse). Test preparations were given 2-3 times a week.

Clinical effectiveness was determined by the IIEF questionnaire (erectile function, satisfaction with sexual intercourse, orgasm, sexual desire, and general satisfaction), subjective evaluation by patients, and

0007-4888/03/supp-0150$25.00

opinion of physicians 4 and 12 weeks after the start of therapy.

An increase in the parameter "erectile function" more than by 50 (≥ 25 points), 30-50, and 10-30% was considered as the excellent, good, and satisfactory effect, respectively. Test preparations had no effect when this parameter underwent variations ±10%. A decrease in the parameter more than by 10% reflected the adverse effect.

The development and type of undesirable changes were determined by the standard open question. Tolerability of preparations was evaluated by a 4-point visual scale (1 point, bad; 4 points, excellent).

RESULTS

Integrative parameters characterizing sexual activity of patients were improved after 4-week therapy with Impaza (Fig. 1). Increasing the period of treatment was not followed by the reduction of its clinical efficiency. The average value of "erectile function" reached 77.8% of maximum. Other parameters increased less significantly compared to the first 4 weeks of therapy.

Sildenafil also improved IIEF parameters (Fig. 1). Most parameters characterizing sexual activity of patients increased by 40-70%.

Some parameters of IIEF tended to increase in the placebo group (Fig. 1). Significant differences were revealed only in the parameter "sufficient erection". Parameters "erectile function" and "orgasm" decreased to the initial level by the 12th week of observations.

The effectiveness of Impaza was subjectively evaluated as excellent, good, satisfactory, and unsatisfactory in 7 (23.3%), 19 (63.4%), 3 (10%), and 1 patients (3.3%), respectively. Lengthening of treatment to 12 weeks did not change the subjective evaluation of clinical effectiveness.

The results of sildenafil therapy were considered as excellent, good, and satisfactory in 14 (46.7%), 7 (23.3%), and 6 patients (20%), respectively. Three patients (10%) were excluded from observations due to the development of undesirable reactions.

In the placebo group the results of therapy were considered as excellent, good, satisfactory, and unsatisfactory in 3 (10%), 6 (20%), 12 (40%), and 9 patients (30%), respectively. After lengthening of observations to 12 weeks only 4 patients (13.3%) evaluated the results of therapy as excellent and good.

According to evaluation of physicians, treatment with sildenafil and Impaza was most effective (excellent, 73.3 and 46.7%, respectively; good, 10 and 26.7%, respectively; and satisfactory, 3.3 and 20%, respectively). Placebo therapy for 4 weeks produced no effect in 56.6% patients.

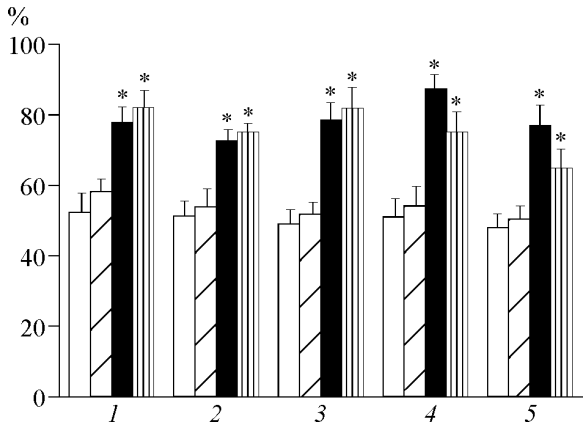

Fig. 1. Main parameters characterizing sexual activity of men with erectile dysfunction receiving placebo (12 weeks, slant shading), Impaza (12 weeks, dark bars), and sildenafil (4 weeks, vertical shading): erectile function (*1*), sexual satisfaction (*2*), orgasm (*3*), libido (*4*), and general satisfaction (*5*). Light bars: initial level. **p*<0.05 compared to placebo.

The therapy was well tolerable. Only 1 patient receiving Impaza suffered from headache, which appeared 3 h after the first treatment (by the end of sexual intercourse). The patient reasoned that further therapy is not required and refused to take Impaza. It is unlikely that the development of undesirable reactions in this patient was related to treatment with Impaza.

Sildenafil caused headache, reddening of the skin of the face, and changes in the acuity of vision in 20, 6.6, and 6.6% patients, respectively. Three patients had to be withdrawn from the sildenafil group because of considerable side effects (hypertension, headache, and vomit with further hospitalization and intensive therapy; headache, tachycardia, and changes in the acuity of vision; and headache, abdominal pain, and diarrhea). The undesirable effects developed 1-6 h after the first treatment and required additional therapy. The relationship between sildenafil therapy and development of undesirable reactions seems to be possible. One patient from the placebo group suffered from dyspepsia.

These data show that Impaza surpasses placebo, but is less potent than sildenafil in the ability to improve erectile function and other parameters characterizing sexual activity of men. The effect of Impaza was not reduced in time (12 weeks). Safety of Impaza was greater than that of sildenafil. Therefore, Impaza holds much promise for the therapy of patients with ED.

REFERENCES

1. T. G. Borovskaya, O. P. Loskutova, O. I. Epstein, and M. S. Zak, *Byull. Eksp. Biol. Med.*, Appl. 3, 52-53 (2001).
2. A. E. Benet and A. Melman, *Urol. Clin. N. Am.*, **22**, 699-709 (1995).
3. H. A. Feldman, I. Goldstein, D. G. Hatzichristou, *et al.*, *J. Urol.*, **151**, 54-61 (1994).
4. *NIH Consensus Development Panel on Impotence*, *JAMA*, **270**, 83-90 (1993).