EXPERIMENTAL METHODS FOR CLINICAL PRACTICE

Therapy of Peptic Ulcer with Semax Peptide

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 134, No. 7, pp. 83-84, July, 2002
Original article submitted April 17, 2002

Experiments used is combination with traditional preparations (omeprasole, de-nol, and solcoseril), Semax peptide (Met-Glu-His-Phe-Pro-Gly-Pro) possessing nootropic and neuroprotective activity significantly promoted ulcer healing in patients with refractory peptic ulcers. On day 14 of treatment ulcer healing was observed in 89.5% patients receiving intranasal Semax (1% solution, 2-4 drops 3 times a day for 10 days) *vs.* 30.8% in the control group. Clinical studies of antiulcer activity of Semax in different combinations with usual antiulcer drugs are needed.

Key Words: *Semax; peptic ulcer; cicatrization period; clinical study*

Semax, a synthetic analog of ACTH (4-7) with C-terminal Pro-Gly-Pro sequence (MEHFPGP) possessing no hormonal activity, is now used as a highly effective nootropic and neuroprotective agent [1,8].

Animal experiments and clinical studies demonstrated antihypoxic effects of Semax, which improved cerebral circulation, stimulated attention and operative memory, induced regeneration of damaged nerves, *etc.* [1,5,7,8].

Semax is used in the treatment of patients with ischemic stroke [6], organic damage to the brain (Huntington's chorea), and some cerebrovascular diseases. It is used for the correction of posttraumatic dysfunctions of the brain and mnestic functions after anesthesia and for the treatment of asthenotherapeutic disorders [6].

Semax was used for the treatment of the optic nerve [7].

Animal experiments demonstrated a positive effect of Semax on homeostasis in the gastric mucosa (GM) [3]. Intraperitoneal injection of Semax protected rat GM from damage caused by ethanol and water-immersion immobilization stress. Pronounced antiulcer activity was demonstrated on rats with ulcers induced by indomethacin [4].

Semax improves GM resistance to damaging factors and accelerates healing of acetate-induced ulcers [3], which are close to human gastric ulcers by their dynamics and histomorphological characteristics. Moreover, Semax accelerates recovery of the pancreas after acute pancreatitis [5].

The protective and therapeutic effects of Semax observed in animal experiments are comparable with those of glyproline Pro-Gly-Pro [2]. The antiulcer effect of Semax manifests at far lower doses (50 μg/kg) than that of Pro-Gly-Pro (1 mg/kg), *i.e.* this effect is most likely produced by the full-length peptide, but not a product of its proteolysis (Pro-Gly-Pro) [3].

A possible mechanism of antiulcer effect of Semax is a modulation of blood supply to GM. Semax improves blood rheology, possesses anticoagulant and fibrinolytic activities, and decreases platelet aggregation *in vivo* [9]. It also decreases vascular permeability and improves microcirculation in rats with acute pancreatitis [5]. Semax prevented indomethacin-induced reduction of blood flow in rat stomach, without modulating the basal blood flow [4]. This mechanism can

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0007-4888/02/1341-073$27.00

underlie the antiulcer effect of Semax in rats with ulcers induced by indomethacin and by other methods.

Hence, there are good grounds for clinical studies of the possible antiulcer effects of Semax. This paper presents the results of the first clinical study.

MATERIALS AND METHODS

We examined 32 patients aged 59-81 years (mean age 69.0±1.2 years) with refractory (at least 30 days) peptic ulcers. Ulcers (0.5-1.2 cm in diameter, mean 0.8± 0.2 were located in the antrum, body, and cardia and in subcardial compartments. Chronic peptic ulcers were diagnosed in all patients on the basis of morphological examination.

Semax was synthesized at the Laboratory of Regulatory Peptides, Institute of Molecular Genetics, Russian Academy of Sciences (Moscow). The patients were divided into 2 groups matched for sex, age, duration of peptic ulcer, location of ulcers, and concomitant diseases. The main group (n=19) received Semax intranasally (1% solution, 2-4 drops in both nostrils 3 times a day for 10 days) in addition to the basic therapy (omeprasole in a dose of 20 mg twice a day, denol in a dose of 120 mg 3 times a day, and solcoseril 2.0 intramuscularly). Controls (n=13) received basic therapy without Semax.

The data were processed statistically using Student's t test.

RESULTS

By day 14 of treatment ulcers healed in 89.5% patients of the main group (median period of healing 12.1 days) *vs.* 30.8% patients in the control group ($p<0.05$; median duration of ulcer healing 16.7 days). By day 21 ulcers healed in all patients in both groups.

Hence, Semax notably accelerated ulcer healing. The effect of Semax was realized against the background of traditional therapy for peptic ulcer producing primarily local effects, therefore we hypothesized a central mechanism of its effect. This is in line with the known neurotropic acivity of Semax. Presumably, Semax can replace some elements of the traditional therapeutic complex.

This problem requires further clinical studies, but even now Semax can be recommended as a drug accelerating ulcer healing and as an additive to traditional treatment.

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