P.6.044 The treatment of algesic disorders in opiate-addicted patients by the use of endogenous peptides

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Previous clinical research revealed high effectiveness of exogenous neuropeptides (cholecystokines, ceruletid) in the treatment of opiate withdrawal syndrome (OWS) in addicted patients. Later, S.K. Sudakov in the animal model of opiate addiction has achieved elimination of algesic symptoms by means of injection of aprotinine which inhibits proteolysis at the stage of formation of various peptides including functionally active ones. Our purpose is to estimate clinical effectiveness of the protease inhibitor aprotinine in the treatment of OWS in heroin-addicted patients. The study was carried out in 109 in-patients (48 males, 61 females) aged from 17 to 34 years, with disease duration from 6 months to 9 years. All patients were randomly divided into two groups, comparable by gender, age and disease duration. Every patient was ascribed to standardised treatment for elimination of OWS. Additionally, all patients of the 1st group were given a single intravenous infusion of aprotinine at a dosage of 30.000 antitripsine units diluted in 400 ml of 0.9% saline solution. The treatment started as soon as the signs of OWS appeared. Patients' condition was estimated by a 4-point scale, on the first day every hour, then daily for 5 days. Algesic conditions, autonomic symptoms, depression and drug craving were scored separately. All the data were tested statistically. The obtained results indicate significantly higher effectiveness of aprotinine treatment of OWS. Algesic and autonomic symptoms were found to be most susceptible to the therapeutic action of aprotinine. Less distinctive were intergroup differences in the dynamics of depressive symptoms. As regards drug craving, the advantages of aprotinine were not always significant. The different reactions of patients to aprotinine made it possible to distinguish among them three subgroups that differ by the structure of OWS. In the 1st subgroup, where algesic and autonomic symptoms prevailed, the effect was fast and full. In the 2nd subgroup, where depressive-dysphoric symptoms prevailed, the effect was minimal. In the 3rd subgroup algesic, autonomic and depressive-dysphoric disorders occurred in combination, and the therapeutic effect of aprotinine was intermediate.

Conclusion: taking into account the diametrical opposition of the symptoms of OWS to the direct pharmacologic action of opiates it is reasonable to suggest that the revealed variants of OWS reflect fundamental differences in patients' reactions to a drug. This was confirmed by genetic studies.

P.6.045 Pyrogenal in the treatment of sleep disorders in heroin-addicted patients

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In everyday clinical practice the problem of overcoming therapeutically resistant sleep disorders in heroin-addicted patients represents great difficulties. These disorders differ from usual neurotic sleeplessness by their especially unbearable character and because of these patients' unfortunate desire to take immediate measures, i.e., to administer again and again additional sleeping pills or injections; patients break hospital regime, insist on untimely discharge. Under such pressure doctors are often forced to prescribe excessive amounts of sedatives and other drugs which can produce states of intoxication and deteriorate the patient's condition. It is well known that therapeutic resistance of some pathologic states is often connected with a patient's low immune status. One effective way to raise the immune powers is pyrotherapy by means of pyrogenal injections. The purpose of our study is to determine the possibility to overcome the resistance of sleep disorders in heroin-addicted patients by the use of pyrogenal. The study was carried out in 16 female heroin-addicted patients aged from 18 to 31 years (mean age 24.1±2.1 years), with disease duration from 1 to 10 years (mean 6.1±0.6 years). All the data were statistically tested. All patients were in a post-withdrawal period; in 10 of them dissomnic disturbances were part of drug craving syndrome, in the other 6 they were combined with depression and resembled derealization conditions (the absence of the feeling of sleep). As a control served 10 analogous patients with comparable parameters. The patients of the basic group were given pyrogenal i.m. at doses of 50 to 150 μg. The doses and number of injections were dependent on the presence, degree and duration of temperature reactions of patients. Maximal duration of the course of pyrotherapy was 15 days. The control group of patients for the treatment of sleeplessness were given combinations of sedatives, neuroleptics and antidepressants. The results of pyrotherapy in the basic group was full normalization of sleep in 10 patients. An objective improvement, yet accompanied by the absence of the feeling of sleep, which required the prescription of placebo, occurred in 3 patients. No positive effect occurred in 3 patients, who were characterized by the absence of

temperature reactions to pyrogenal. Only one injection of pyrogenal was sufficient for two patients, three injections were required for 6 patients. In 2 patients the positive effect was reached after 4 injections. No complications were observed during the treatment course. In the control group during 15 days only partial therapeutic effect was reached in 4 patients.

Conclusion: Pyrotherapy by means of pyrogenal is an effective instrument for the treatment of prolonged dissomnic and probably depressive disturbances in heroin-addicted patients in the post-withdrawal period.

P.6.046 On the use of intravenous drop-by-drop infusion of neuroleptics with the purpose to retain heroin-addicted patients in treatment programme

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In the practice of heroin dependence treatment the situation often arises that after the elimination of acute manifestations of opiate withdrawal syndrome on the 7-9th day of stay in the clinic, patients refuse further treatment. As a rule, this is connected with an exacerbation of drug craving. In such situation the use of traditional treatment approaches is not very effective. For the estimation of the effect of intravenous infusion of neuroleptic to suppress drug craving and to retain patients in the treatment programme 52 patients were examined. All of them tried to cease their treatment course but agreed to stay for receiving "new procedure". The disease duration in these patients was from 1.5 to 9 years (mean duration 3.21±1.13 years). The tolerance of drug varied from 0.5 g to 3.0 g of heroin per day. All patients examined received basic therapy (tablets of haloperidol 4.5–6.0 mg per day, tablets of Tizercini 50–75 mg per day). They were divided randomly into two groups. The patients of the first group (29 persons) received intravenous infusions of a solution of sodium chloride 0.9% 400.0, containing haloperidol 10 mg, and relanium 10 mg. The second group (24 persons) were given the same doses of haloperidol and relanium by means of intramuscular injection. The comparison of these groups was based on the criterion of retention of patients in the treatment programme. During the course of therapy the patients of the first group, even after the initial infusion, displayed general improvement, reduction of anxiety, irritation, and tension, alleviation of mood, and normalization of sleep. At the same time their behavior was put in order. There were no complications and allergic reactions connected with preparations. Most patients (25 persons) changed their decision to refuse further treatment and remained in the clinic. Three patients continued to refuse and broke the course of therapy. Dysphoric disturbance accompanied by grumbling and irritability remained in almost half of the patients of the second group (11 persons); these patients continued to insist on discharging, and 8 of them left the clinic. 13 patients of the second group had extrapyramidal disturbances of different degrees, which aggravated negative disposition to treatment. So, in the first group 89.3 % of patients continued to be treated, whereas in the second group only 66.7% did ($p < 0.05$). Intravenous infusion of neuroleptics gives an opportunity to resolve more effectively the problem of suppression of drug craving and of retaining patients in the medical treatment program.

P.6.047 Non-steroidal anti-inflammatory drugs in the treatment of opiate withdrawal syndrome

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Non-steroidal anti-inflammatory drugs have good analgesic properties; as compared with opiate analgesic preparations they do not cause habituation, are easily tolerated by the patients, when used by short courses they practically cause no complications. Therefore we carried out a clinical study of one of the representatives of these drugs – ketanov (ketorolaki tromethaminum – Ranbaxy Laboratories Limited).

The purpose of the research was to estimate the influence of ketanov on pain disorders in opiate withdrawal syndrome (OWS), and also on transitory pain disorders in post-withdrawal state of heroin addiction comparing to tramadol (antagonist-agonist of opiate receptors).

Materials and methods: 56 male opiate dependent patients (age of 18 to 35, mean – 22.8±2.6) were included in an open comparative clinical study. Diagnostics of pivotal syndromes of dependence were carried out on the basis of ICD-10 criteria. All patients had full clinical pattern of heroin dependence, the duration of the disease varied from 0.5 to 6 years; daily doses of drug used were from 0.5 to 3.0 g of heroin. The degree of OWS severity was qualified as moderate in 39 and as severe in 17 patients. The treatment of OWS was complex, including anticonvulsants, α-2 adrenoreceptors agonists (clonidin), antipsychotics, sedatives. The basic group of patients were also given ketanov (90–120 mg); the control group patients – tramadol (400–800 mg).