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Paradoxes of evidence in Russian addiction medicine

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BACKGROUND: For many years, clinical protocols for treatment of drug abuse patients and treatment standards in Russian Federation were not grounded on the principles of evidence-based medicine [1]. Recommendations for use of certain drugs were not accompanied by any indication of the level of credibility of the evidence supporting it. The appearance in 2014 of such indications in clinical recommendations can be considered a significant step forward for the science of addiction medicine [2].

OBJECTIVES: To compare Russian evidence and practice in addiction medicines with international standards.

METHODS: Situation and literature analysis.

RESULTS: The analysis shows that in the wording of recommendations on the use of medicines, some were subject of serious methodological errors. For some drugs globally there is high quality evidence supporting effects of certain drugs globally, but this is not recognized in Russia. As a result, Russian standards of clinical care for the treatment of dependency syndrome are radically different to the standards of therapy, presented in the WHO recommendations. This is due both to the disregard of the meta-analyses presented in the Cochrane reviews and also to the specific bioethical preferences in drug treatment in Russia.

According to the Cochrane review, drugs with proven efficacy are antagonists and agonists of opioid receptors (for opioid dependence) and antagonists of opioid receptors (for alcohol dependence). In Russian clinical protocols treatment of dependence syndrome with drug of proven efficacy include antipsychotics, antidepressants and anticonvulsants (the level of credibility of evidence A and B according to Russian scientists).

It is known that there is no convincing data on the effectiveness and safety of antipsychotics in the treatment of alcohol dependence syndrome [3]. 13 randomized trials with a double blind placebo-controlled design involving 1593 patients assessing effects of amisulpride, aripiprazole, flupentixolum dekonoat, olanzapine, quetiapine, tiapride showed that antipsychotics do not result in abstinence, do not reduce abuse and do not stop craving in alcoholic patients: *"Antipsychotics should not be used in patients with a primary diagnosis of dependence. Appointment of antipsychotics for the treatment of substance abuse disorders are contraindicated, since not only does it not improve the condition of patients, but it can even worsen the course of the disease, leading to a reduction in the duration and quality of the remission, and is fraught with serious side effects that threaten the health of patients."*

SSRI antidepressants indirectly improve the results of treatment of comorbid alcoholism in depressed patients, without affecting alcohol dependence *per se*. Also, there is currently no convincing evidence of the efficacy of anticonvulsants in the treatment of dependence syndrome, particularly alcohol.

Despite the fact that traditional psychotherapeutic interventions remain widespread in practice, and treatment of alcohol dependence syndrome showed high efficiency, there is no convincing evidence for long-term benefits as opposed to short-term benefits.

The Cochrane Review with data based on 146 scientific studies involving 21,404 patients confirmed the effectiveness of opioid receptor agonists in treatment of opioid dependence. This therapy showed a statistically significant reduction in the use of illegal drugs, HIV transmission and risky sexual behavior, and was significantly more effective compared to the conventional maintenance therapy with opioid receptor antagonists. In countries, where law prohibits prescribing and use of opioid agonists for opioid dependence treatment, the drugs of choice are antagonists.

A meta-analysis of thirteen randomized placebo-controlled trials of oral form of naltrexone (1158 subjects), did not show any advantages of this type of treatment both for management and prevention of relapse compared with placebo [4]. Special studies also showed no inclination to reduce the use of opiates in patients receiving naltrexone [5]. However, studies carried out in Russia, showed the best results for daily intake of naltrexone after detoxification, which increased the duration of remission [6]. It was noted that the effect is associated with higher levels of adherence and family support in the examined population.

An overview based on controlled clinical studies on the use of antipsychotic drugs (neuroleptics) in patients dependent on opioids revealed no evidence of effectiveness of this approach. It was concluded that the use of antipsychotics is justified only in the presence of co-morbid psychiatric problems in patients [7]. In a recent meta-analytic review on the use of atypical antipsychotics for off-label indications (off-label), there was a lack of data to support the effectiveness of their use in substance abuse [8, 9]. The effectiveness of anticonvulsants in the treatment of opioid dependence syndrome has not been proven.

In connection with the above puzzling fact, for Russian standards of treatment (clinical guidelines) the level of credibility of the effectiveness of antipsychotics and antidepressants in treatment of substance abuse is assessed as A or B. This paradox raises the question of the methodology for determining the level of credibility of evidence. It should be noted that Russian recommendations for inclusion of certain drugs and therapies are based on sufficient consensus of experts rather than on the results of meta-analyses [2].

CONCLUSIONS: This fact casts doubt on credibility and validity of scientific recommendations. Thus, one may say that Russian addiction medicine is not based on evidence, which is, in our view, erroneous and may impair the quality of care.

Keywords: Paradoxes, evidence-based medicine, addiction medicine

Conflict of interest statement: None.

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