



Fund “Nauka” Project № 23004 Resume – Competition-Based Session 2023:

“Antidote effect of intralipid 20% in acute intoxication with fentanyl”

Project leader: Prof. Petko Penkov Marinov, MD, PhD

Drug abuse has come increasingly into the focus of public health in recent decades. To date, fentanyl is one of the most current psychoactive substances, displacing heroin from the illicit drug market. Its addition to cannabinoids, cocaine, methamphetamine, ketamine, and/or methylenedioxymethamphetamine is also growing. Epidemiological data indicate that in 2021, as a result of fentanyl intoxications, more than 71238 deaths were recorded in the United States.

Unfortunately, over the last year, fentanyl intoxications in Varna have followed world trends. Evidence of the observed “explosion” of the opioid overdose are the documented three deaths at home between April and August in 2023. The fatal outcome is known to be due to a combination of factors – high lipophilicity of the molecule, distribution in brain tissue and occupying opioid receptors with suppression of multiple nerve impulses. In this regard, a number of clinical cases confirm that the proven antidote for opiate intoxications naloxone is insufficiently effective due to its lower lipophilicity.

In previous studies, the antidote effect of Intralipid 20% in acute intoxications with lipophilic xenobiotics has been proven. This motivates the purpose of the present project – to study the antidote effect of Intralipid 20% in acute intoxications with fentanyl in experimental animals. The study design provided observation of survival and behavior after treatment with a lethal or toxic dose of fentanyl, respectively, followed by injection of individual groups of animals with naloxone, intralipid 20%, or a combination of naloxone and intralipid 20%.

The expected positive results will have therapeutic and social implications given the epidemic of fentanyl overdose deaths.

The expected **results** have the potential to be applied in science and practice:

1. Rapid control of toxic symptoms and prevention of fatal cases is expected when toxic and lethal doses of fentanyl are administered to rats. This will demonstrate release of fentanyl-occupied receptors and a favorable course of intoxications. The effect will be long-lasting and will prevent re-exacerbation of symptoms, a commonly observed effect of naloxone administration (related to the enterohepatic circulation of opiates and the retention of fat-soluble fentanyl in brain tissue for a long period of time);
2. The positive effect of Intralipid 20% will reduce the dose of naloxone to an acceptable therapeutic value that does not lead to toxic effects;

3. The application in science, practice and economic efficiency of the method are indisputable given the low price of Intralipid 20%, its low toxicity and rare side effects;
4. The social significance of the epidemic of overdose deaths related to fentanyl and fentanyl analogs is undeniable;
5. Methods for quantification of fentanyl in the lipid and liquid phase of plasma will contribute to understanding the mechanism of action of Intralipid 20% as an antidote, as well as to determine optimal blood levels of Intralipid 20%.