OPIOIDS OF FENTANYL SERIES IN THE ROLE OF NON-LETHAL CHEMICAL WEAPONS AND THE ISSUE OF THEIR IDENTIFICATION

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The article deals with the possible use of the synthetic opoid fentanyl and its derivatives as so-called non-lethal chemical weapons in military and non-military operations or terrorist acts. It contains information about the synthetic opoid fentanyl and its derivatives, the possibilities of identifying opiates of the fentanyl series and the evaluation of the possibilities of using psychotropic drugs in the form of non-lethal chemical weapons.

***Key words**: non-lethal weapons, legislative measures, fentanyl, identification of fentalogs, decontamination.*

1. INTRODUCTION

When it comes to the use of military force - especially in peacekeeping operations -, emphasis is placed on minimizing human and material losses. Since the end of the 20th century, there have been discussions about the concept of a new separate category of chemical weapons, the so-called non-lethal chemical weapons, capable of temporarily neutralizing enemy force without serious health consequences. Some opioid substances are classified as non-lethal chemical weapons, belonging in the group named calmatives. In the NATO Policy for Non-Lethal Weapons, approved by the NATO Council in 1999, NATO defines non-lethal weapons as substances "which are expressly designed and developed to incapacitate or eliminate persons with a low probability of death; achieving a minimum adverse effect on the environment".

The Chemical Weapons Convention (CWC) characterizes toxic substances as any chemical that is harmful when used under

conditions in which it is temporarily incapacitating or lethal. Some toxic substances, which have been considered for use as incapacitating chemicals, are even more toxic than chemicals developed for lethal purposes in the sense that their extremely small amounts are sufficient to produce an effect (Patočka: 2004).

States that have ratified the Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on Their Destruction (Paris, 1993) may use these chemicals for "non-prohibited purposes", which includes their maintenance for the purpose of maintaining public order, including the national suppression of unrest. An example is the use of two fentanyl derivatives, remifentanil and carfentanil, in a counterterrorism operation at the Dubrovka Theater in Moscow in 2002 (Riches: 2012).

The affected individual is not able to influence the reflex actions caused by these substances by his will, which leads to a reduction in the ability of this individual to continue the planned activity. Implementing an intervention using an incapacitating substance is considered a breakthrough in tactical solutions to problematic situations. Each State Party shall take the necessary measures to ensure that toxic chemicals and their precursors are developed, manufactured or otherwise acquired, stored, transferred or used in its territory or in any other place under its jurisdiction or control only for purposes not prohibited by this Convention. The handling of addictive substances is currently regulated by legislative frameworks for the handling of addictive substances, which are adopted individually by the governments of individual states (Středa, Kobliha, Halámek: 2001). The first international treaty on drug control is the International Convention on Opium, signed in The Hague on 23 January 1912 during the first international conference on opium, which was preceded by a conference of representatives of 13 states in 1909 in China. This International Convention on Opium was replaced in 1961 by the Single Convention on Narcotic Drugs. As of February 2018, the Single Convention already has 186 contracting parties (International_Opium_Convention).

In the broader context, the following pharmacological groups can also be included among the groups of substances that can be used, for example, to control street riots: emetic-inducing substances (emetics), sedatives and hypnotics, serotonin antagonists, substances influencing thermoregulation,

substances with hypotensive effect, nausea-inducing substances and muscle relaxants (Žďárová - Karasová and Žďára: 2018). Although the qualitative and pharmacokinetic characteristics of this group of substances are described as rapid, effective and reliable, it appears that not all of their representatives always have a sufficiently high safety ratio between effective and lethal dose and their duration of action is in some cases too long. From the group of psychotropic drugs, ie substances affecting the central nervous system, only quinuclidine-3-yl-diphenyl(hydroxy)acetate with a long elimination effect was included in the armament of some armies for over 50 years (until 1990) (Kobliha, Středa: 2015).

2. SYNTHETIC OPIOID FENTANYL

An opioid called fentanyl deserves attention in this area - a substance with qualitatively similar properties of morphine, but with effects about 80-100 times more pronounced, but in comparison with morphine with a shorter onset time and faster disappearance. The substance was synthesized on the basis of a change in the structure of the drug pethidine in the late 1960s in the Belgian company Janssen and, thanks to its functional parameters, was used in healthcare primarily as an intravenous anesthetic in surgery and to relieve severe pain in patients. Fentanyl is suitable for intravenous, transdermal, intranasal, oromucosal applications, and due to this it was

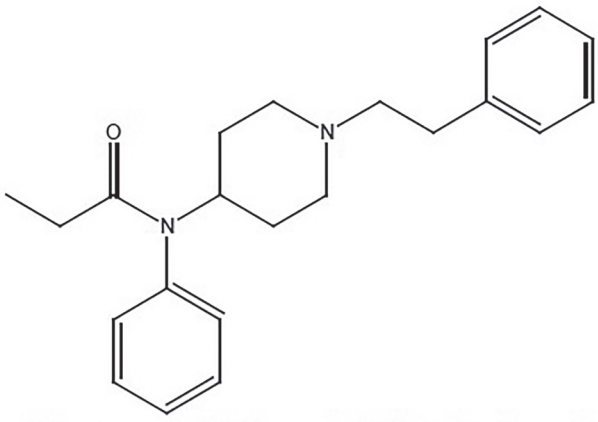

Fig. 1. Structure of fentanyl (*N*-fenyl-*N*-[1-(2-fenylethyl)piperidin-4-yl] propanamid)

soon used all over the world, together with its numerous analogues.

Over the years, hundreds of fentanyl derivatives with different effects have been synthesized, for example alfentanil, acryloylfentanyl, α-methylfentanyl, α-methylthiofentanyl, β-hydroxyfentanyl, β-hydroxy-3-methylfentanyl, carfentanil, remifentanil, sufentanil, thiofentanyl, 3-methylfentanyl, ocfentanil, cyclopropylfentanyl, 3-fluorofentanyl, 3-furanylfentanyl, methoxyacetylfentanyl, valerylfentanyl, lofentanil and others.

Some analogues such as sufentanil or carfentanil are used in veterinary medicine. Carfentanil is still the strongest known opiate among the fentanyl analogues and is used as a tranquilizer of large animals, however it is not officially allowed in human medicine (Hess: 2018). The basic structure of fentanyl can be easily changed with various substituents. Generally, fentanyl derivatives are called „fentalogs".

However, synthetic opioids also have negative effects on the human body, namely nausea, constipation, miosis, and euphoria. The danger of higher dosing lies in the risk of rigidity of the lung muscles - therefore, respiratory arrest may occur (Lüllmann: 2004).

Fentanyl is one of the most abused drugs among drug addicts. Recent estimates suggest that the number of fentanyl overdose deaths has reached a tragic number of victims in recent years, mainly in the United States, at over 70,000 (Niles: 2020).

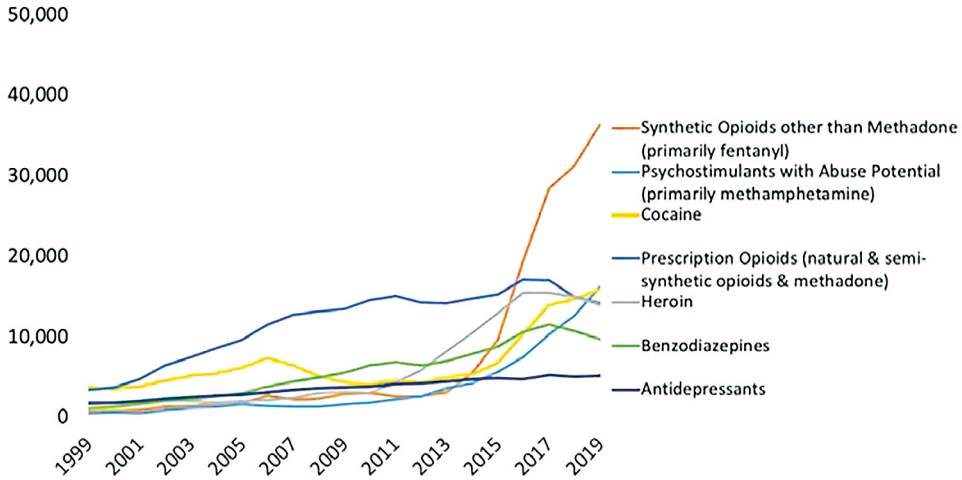

Fig. 2. Record an increase in the number of victims of synthetic opioid overdose

3. POSSIBILITIES OF IDENTIFICATION OF OPIOIDS OF FENTANYL SERIES

Due to the exceptionally high efficacy of some fentalogs and the dangers associated with it, there is a growing need for rapid identification of these substances by a variety of methods. The simplest methods for detecting the presence of fentalogs include rapid orientation immunochemical tests such as nal von minden GmBH tests with a stated cut-off value of 200 ng/mL, BTNX Inc. Ontario, Canada or PocketLab Fentanyl, which declares cut-off values of 10 ng/mL (Krieger: 2018).

Another relatively simple way to detect the presence of fentalogs is by thin layer chromatography (TLC). This decades-proven reliable separation technique is one of the inexpensive methods with minimal operator requirements and maintaining maximum reproducibility of results (Moravcová: 2014).

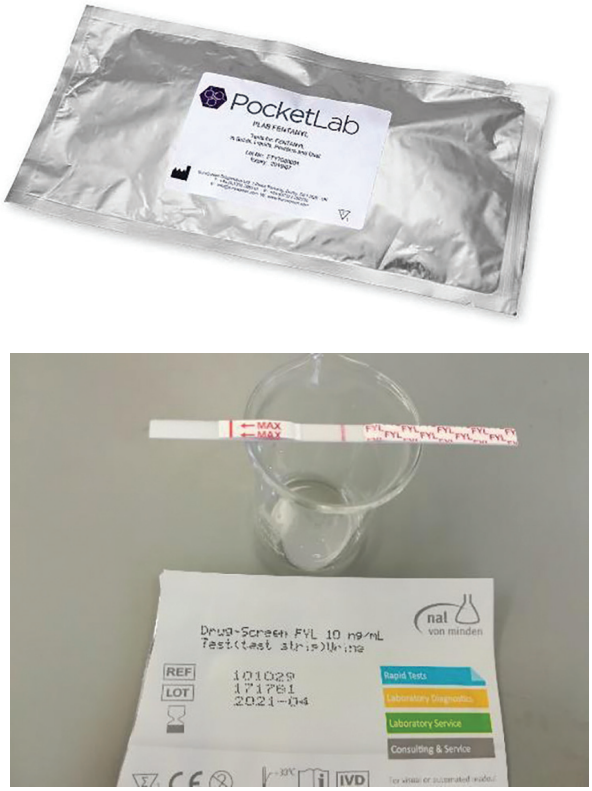

Fig. 3. Rapid orientation immunochemical tests

Being one of the simple and relatively cheap techniques designed mainly for quantitative analysis in difficult „field“ conditions, extraction spectrophotometry in the visible range of radiation can be utilized, using spectrometers of the Helios-Unicam series or Specord 40, Specord 200 and other types of these instruments (Jelínková: 2014).

Whether in terms of prevention or forensic research, analyses of not only drugs, but also other substances such as explosives and chemical warfare agents, are performed by sophisticated methods using liquid (HPLC) and gas chromatography (GC) combined with mass spectrometers with high scanning speed and programmable temperature. In the field of mass spectrometry, various types of ionization processes can be used: electron, chemical, electrospray, thermospray, accelerated atom or ion ionization and others (UNODC: 2017, Kahl: 2018).

The methods excel in high sensitivity and measurement speed, but the disadvantage is the lack of reference standards or the low profile of comparative samples in spectral libraries, especially in clinical or forensic laboratories (Marchei: 2018). In some experiments, coupled techniques with two LC-MS / MS mass spectrometers are preferably used to qualitatively identify fentalogs (Kraig: 2018). In recent years, companies have been offering mass detectors (TOF) with the highest mass resolution in the world (Pragolab: 2020).

Handheld spectrometers, such as the FT-IR True Defender, are used as a technique complementary to the First Defender Raman spectrometer for fast, yet accurate analysis in demanding conditions. The devices are resistant to impact and thermal shocks, they are waterproof and dustproof. Even in difficult conditions, users are able to perform fast and effective decontamination. Most types of this instrumental technique are intended for the immediate identification of test substances.

The MIL-STD 810G military standard is matched by the MIRA DS handheld Raman spectrometer, with a library of thousands of chemical data and HazMasterG3 applications that expressly assess the potential risks associated with hazardous substance analysis. The light, highly durable device weighing 0.7 kg can be used for work in critical conditions (Metrohm, 2021)

Fig. 4. Raman spectrometer MIRA DS

4. EVALUATION OF THE POSSIBILITIES OF USING PSYCHOTROPIC DRUGS AS NON-LETHAL CHEMICAL WEAPONS

The use of opioids within the group of so-called non-lethal chemical weapons cannot be underestimated. It is a group of weapons, the effect of which is aimed at the incapacity of personal, while eliminating material damage to the surrounding infrastructure and the environment. The danger of these incapacitants lies primarily in the amount that is used and in the concentration. Not only can people be disabled, but people can also be killed. This assumption can be demonstrated by the use of opioids in Dubrovka. These relatively readily available opioids could be misused in the event of a terrorist attack, posing an acute danger, especially in confined spaces. To eliminate the side effects of these „non-lethal weapons", it is necessary to address the possibilities of their rapid and accurate detection and identification, effective respiratory protection and the possible need for decontamination.

The synthetic opioid fentanyl and its derivatives have occupied an important place in the discussion since the second half of the last century in terms of their possible use in the so-called „humane" management of public order. However, a problem with the use of these highly effective chemicals

is the qualified determination of their desired concentration so as to achieve the desired effect. Associated with this is the issue of ensuring effective protection for the intervening components in the sense of eliminating unwanted exposure to the action of the contaminant and thus their decommissioning. In addition to the above uses of fentanyl and its analogs, alarming cases of overdose with these opiates in drug addicts are also known. Due to the growing number of cases of overdose with these substances, the negative effects on the health of both individuals and society as a whole on a global scale are being addressed.

The use of psychotropic drugs for any purpose must be approached with the utmost caution. For example, a fentanyl derivative, lofentanil, is much more toxic than nerve agents. It induces anesthesia at a dose of 0.025 micrograms per kilogram body weight, which is one hundred times less than the expected lethal dose of VX (Patočka: 2003). The toxicity value of substances is characterized by their therapeutic index, which is the ratio between the amount of therapeutic substance causing dangerous toxic effects and the amount causing the desired therapeutic effect. In other words: the ratio of the lethal dose for 50% of the population and the effective dose for 50% of the population. According to some experts, a chemical with a sufficiently high, „safe“, therapeutic index is not currently known (Klotz: 2003).

5. CONCLUSIONS

In its principles, the CWC unequivocally declares the exclusion of the deliberate use of chemical weapons and thus complements the commitments made in the 1925 Geneva Protocol. From the exact point of view, there is practically no strict division of chemicals into deadly and non-deadly. Any use of chemical weapons, even if they are said to be „non-lethal“, raises legitimate concerns about their possible misuse and carries with it the risk of possible adverse effects on the population, mainly related to the current lack of information on their pharmacological properties, adverse effects, decontamination and detection capabilities.

It is therefore meaningful to focus the attention of the professional public on adequate research of this group of chemical substances, especially in the field of their rapid detection using simple orientation tests or detection devices and sophisticated identification using adequate laboratory equipment.

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