

Synthetic Opioids, (re)Emerging Problem in Europe and North America

Magdalena Sustkova

Department of Pharmacology, Third Faculty of Medicine, Charles University, Czech Republic

I would like to draw the reader's attention to group of synthetic opioids, which have been increasingly appearing or re-emerging during the last few years on the black drug markets in many European countries, the USA, Canada and elsewhere. Newly encouraged interest in synthetic opioids has been observed for last 6-7 years and recently has grown intensively. Increasing number of European countries (Germany, Bulgaria, Slovakia, Czech Republic etc.) have reported abuse of fentanyl (Janssen, 1962), which so far has been rather limited to Estonia (Fentanyl in Europe, 2012; Mouteney, 2015), fentanyl-related intoxications and deaths have markedly increased recently (to hundreds) in the USA (NIDA, 2015) and Canada (CCNDU Bulletin, 2014). Also the spectrum of different structures of synthetic opioids on the black market has significantly risen and many of these substances are already associated with serious or fatal overdoses (EMCDDA, 2009-12; European Drug Report, 2013-15).

All these derivatives of different structures act on central opioid receptors (μ and/or κ and/or δ) and induce opioid-like effects. Synthetic opioids, mainly the group of fentanyl analogues, are mostly highly effective substances, which, beside euphoria and other complex effects, induce deep sedation and respiratory depression at doses of micrograms per kilogram of body weight and possess extremely high risk of overdose and their use is also mainly associated with higher risk of addiction in comparison to heroin. These substances, predominantly used parenterally/intravenously, smoked, inhaled, snorted, can occur on the market individually or in various mixtures with other substances, frequently they are sold as "heroin" or are mixed with heroin as unknown admixtures and can cause unexpected serious or even fatal complications. Common analytical methods used for heroin/morphine-like derivative detections, such as immunoassays, are not reliable for detection of most new synthetic opioids/fentanyl analogues. This further complicates therapeutic decision-making during overdose treatment. However, also synthetic opioid overdoses require opioid receptor antagonists, e.g. naloxone (EMCDDA, 2009-12; European Drug Report, 2013-15; Rang, Ritter, Flower & Henderson, 2015).

The synthesis of selected synthetic opioids/fentanyl analogues is not very complicated (Valdez, Leif & Mayer, 2014) four fentanyl derivatives (fentanyl, alfentanil, sufentanil, remifentanil) are commonly used in human medicine, and considering the above mentioned potent effectiveness, one-dose-prices of synthetic opioids on the black market are very favorable in comparison to heroin. Heroin has had rather unreliable availability and quality recently (Fentanyl in Europe, 2012).

Altogether 15 different synthetic opioids have been reported to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA, 2009-12; European Drug Report, 2013-15) since June 2009: seven fentanyl analogues: (iso)butyryl-F-fentanyl-N-benzyl; butyryl-alfa-methylfentanyl; carfentanil; ocfentanil (=A-3217); 4-fluoro-butyrylfentanyl (=4F-BF); acetylfentanyl (=A-3217); n-butyrylfentanyl; three aminocyclohexanes: tramadol; ODT; AH-7921; one morphinan: butorphanol; four other structures:

W-15MT-45; 1-cyclohexyl-4-(1,2-diphenylethyl)piperazine (=MT-45); W-18; U-47700. Thus, these substances have recently occurred in one or more EU countries and have been associated (alone or in mixtures) with serious intoxications, overdoses or even deaths, e.g. 15 deaths were associated with AH-7921 in Europe (2012–2014); acetylfentanyl was implicated in 2 deaths in the United Kingdom (2014, 2015), however in the USA more than 40 fatal acetylfentanyl-related overdoses were reported (Stogner, 2014) (2013-2014); ocfentanyl was associated with 2 deaths in Belgium (2015); etc. (EMCDDA, 2009-12; European Drug Report, 2013-15). The serious consequences of synthetic opioids are obvious, although drugs are often (ab)used in mixtures with other psychoactive substances and interpretation of the toxicological reports is sometimes ambiguous.

As it has been mentioned above, many of the synthetic opioids, mainly fentanyl and its analogues, have been known or (ab)used already since 1970s -1980s on the black markets as "designer drugs", predominantly in the USA, e.g. alfa-methyl-fentanyl ("White China") caused a lot of deaths in California in late 1970s (Henderson, 1988).

In the Czech Republic first two deaths associated with fentanyl were reported in 2010 (mixture with paracetamol and caffeine). Further about 6 deaths are linked with recently predominant peculiar mode of use, when the drug users are injecting infusions of extracted fentanyl transdermal patches, which are used in management of chronic severe pain. About 200 users have recently been estimated (in the north and west Czech Republic), who gain original preparations (e.g. from unused preparations after cancer patients) or collect used fentanyl patches from trash cans of individual patients or sanatoriums. Thus, medical waste disposal must be always carefully controlled (European Drug Report, 2013-15).

As conclusion, the expanding (re)emergence of synthetic opioids on the black markets in Europe, North America and elsewhere should be reminded and relevant health-care facilities should be properly informed about possible increased incidence of opioid-like intoxications and the medical staff should be appropriately educated. Also the opioid preparation waste must be always carefully controlled and disposed.

About Author

The author, Magdalena Sustkova-Fiserova, PharmDr PhD, is a teacher and researcher at the Department of Pharmacology, Third Faculty of Medicine, Charles University in Prague, Czech Republic and a National EWS correspondent for the EMCDDA; Supported by Project PRVOUK P34.

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*Correspondence regarding this article should be directed to: magdalena.sustkova@lf3.cuni.cz

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