Designer benzodiazepines: A new challenge

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Designer benzodiazepines: a new challenge

In the February 2015 issue of *World Psychiatry*, Schifano et al (1) gave an overview of novel psychoactive substances and their potentially harmful effects. They highlighted that in the last couple of years the number of drugs offered via Internet shops has increased dramatically and that benzodiazepines are often used to treat intoxications with these drugs in the clinical setting.

We would like to point out that designer benzodiazepines have become a rapidly growing class of drugs of abuse in their own right in the last two years. We believe that mental health professionals should be aware of this new development.

The first designer benzodiazepines available online were diclazepam, flubromazepam and pyrazolam (2-4). Recently, five others became readily available (i.e., clonazolam, deschloroetizolam, flubromazolam, nifoxipam and meclonazepam), none of which has been approved for medicinal use in any country. Nearly all of these compounds have been synthesized as drug candidates by pharmaceutical companies and their syntheses, as well as basic animal testing data, are described in the literature along with many more potential successors (5). Typical formulations are tablets, capsules or blotters in various doses. Furthermore, the drugs are also offered as pure powders with prices as low as 5-10 US cents per dose.

Immunochemical tests applied in clinical settings and drug rehabilitation detect most of the designer benzodiazepines with sufficient sensitivity. However, the mass spectrometric methods needed for confirmation do not regularly cover the latest designer benzodiazepines, due to lack of reference materials. Practitioners should be aware of this limitation and carefully assess seemingly "false-positive" results.

Due to their high potency, compounds like clonazolam or flubromazolam can cause strong sedation and amnesia at oral doses as low as 0.5 mg. Such low doses are extremely difficult to measure for users handling bulk materials, and tablets often vary greatly in the content of the active ingredient. This can lead to unintended overdosing, and could also be of concern in drug facilitated crimes (6).

Designer benzodiazepines are often taken as "self-medication" by users of stimulant and hallucinogenic drugs, leading to "upper downer cycles" (7) and risk of severe addiction in people frequenting the party scene. Persons with anxiety disorders also tend to self-medicate on these drugs if a medical prescription cannot be obtained (8). The high availability of these drugs via online vendors and the low price may facilitate development of addiction in this population.

Many "classical" benzodiazepines are listed in Schedule 4 of the 1971 United Nations Convention. They are also in Schedule IV of the U.S. Controlled Substances Act, but it is unclear if designer benzodiazepines are covered by the Controlled Substances Analogue Enforcement Act, 1986. Similar legal problems exist in most other countries in the world, making it difficult to reduce availability of these dangerous new drugs.

Bjoern Moosmann[1,2], Leslie A. King[3], Volker Auwärter[1]

[1]Institute of Forensic Medicine, Forensic Toxicology, Medical Center - University of Freiburg, Germany; [2]Hermann Staudinger Graduate School, University of Freiburg, Germany; [3]Basingstoke, UK

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