Letter

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Recreational use of GHB and prescribed drugs: the challenge in forensic and clinical toxicology

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Abstract

The dual nature and the double use of γ-hydroxybutyric acid (GHB) are the fundamentals of its spread as recreational drug. Endogenously, GHB acts as inhibitory neurotransmitter while exogenously it is administered in the form of sodium oxybate to treat cataplexy and to menage alcohol withdrawal. Illicit GHB is extensively used along with prescribed drugs and drugs of abuse for its euphoric and anabolic effects. Since it has been used as incapacitating agent to perpetrate rapes and commit robberies, GHB represents a social and public health issues. The tight window of detectability in biological matrices and the difficultly to read symptoms of polydrug overdose represent the modern challenges in forensic and clinical toxicology. ***Clin Ter 2021; 172 (5):e423-424. doi: 10.7417/CT.2021.2351***

Key words: *GHB, overdose, polydrug use, prescribed drugs*

Dear Editor,

The double nature of γ-hydroxybutyrate (GHB) is the key to its success as a recreational drug. This small fatty acid naturally occurs in mammalian central nervous system (CNS) and it is considered both the precursor and the metabolite of γ-aminobutyric acid (GABA), the major inhibitory neurotransmitter. Exogenously, GHB has a narrow number of clinical applications, due to its several adverse effect. In July 2002, GHB salt, sodium oxybate (Xyrem®), was approved by the United States Food and Drug Administration (US FDA) for the treatment of cataplexy in narcoleptic patients and lately for treatment of excessive daytime sleepiness in patients suffering from narcolepsy. Whereas, in in Italy and Austria, the analogue Alcover® was approved for the management of alcohol withdrawal and detoxification in alcoholics. (1). At low doses GHB produces euphoria and relaxation with the same neurobiological mechanism of addictive drugs (2,3). At higher than physiological concentrations, GHB competes with GABA for the activation of $GABA_B$ producing nausea and vomiting, headache, vertigo, impaired speech, hallucinations, aggression, delirium, bradycardia, hypothermia, amnesia, respiratory depression, seizure or clonic movements and non-reactive coma (1,2).

Illicit GHB is produced in clandestine laboratories and sold inexpensively both in the street or on the Internet. To bypass international legislations, new analogs, namely γ-butyrolactone (GBL) and 1,4-butanediol, emerged from the illegal market, replacing GHB because cheaper and legally available. These substances are in vivo transformed in GHB and, as GHB, then rapidly eliminated (4). This short period of detection represents a challenge in forensic toxicology when it is requested to determine the single unintentional exposure. In these circumstances is therefore crucial a rapid and expeditious blood and urine collection (5). Another more reliable option is represented by hair analysis. For this purpose, it is necessary to wait a reasonable length of time for collecting hair (from a minimum of 7 days up to 1 month or more). The segmental analysis of hair into 5 mm segments and the calculation of a ratio between the targeted segment and the others result fundamental to detect single GHB exposure (6). According to the Guidelines for the Forensic Analysis of Drugs Facilitating Sexual Assault and Other Criminal Acts of the UNODC (7), the ratio should be at least 10. More recently Bertol et al proposed lower ratios than UNODC: 4.45:1 (95% CI 3.52–5.63) and 3.35:1 (95% CI 2.14–5.18) to detect a single GHB exposure after one and two months respectively (7,8). The situation is even more complicated in post-mortem cases, not only for endogenous GHB but also for the post-mortem production. Higher cut-offs in comparison to ante-mortem samples have been proposed: 10 μg/mL for urine and 30 μg/mL for whole blood, when no signs of advanced putrefaction are detectable (6,9). However, in applying these cut-off values it is fundamental to carefully evaluate the post-mortem interval as suggested by Busardò et al (9), which strongly influences the post-mortem production of this compound both in blood and urine specimens. Discriminating between endogenous and exogeneous GHB remains a very difficult task for forensic toxicologists. It requires an integrated approach by analysing multiple biological matrices, when available, for a correct interpretation of each case (6,8).

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Although several international restrictions came into force to stop its spread, GHB continues to be extensively abused for its body-performing and sexual-enhancement properties with polydrug and polypharmacy as the most common paths of consume. GHB and prescribed drugs are more and more related with accesses to emergency rooms and deaths, beside classic drugs of abuse. Some of these prescribed drugs, notably benzodiazepines, opioids/opiates and antiepileptics, possess high potential of abuse and promote additive effects that easily result in CNS depression in case of GHB co-intake. Prescribed drugs are diverted from the legal market or added as adulterants with the buyer unsuspecting of their presence in the product he purchased and unaware of possible risks that go with it (10). Unfortunately, health care practitioners are unaware of the scenario of polydrug use and the presence of classic drugs of abuse might mask typical symptoms of CNS depression leading to misdiagnoses or incorrect attribution of the cause of death. A strict prescription policy is therefore requested to reduce the availability of drugs, including sodium oxybate, for diversion from the illicit market.

Conflict of interest: The authors declare that there is no conflict of interest regarding this manuscript.

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