

“Diazepam loading”: ¿Can a strategy for preventing alcohol withdrawal be used to treat benzodiazepine use disorder?

“Carga de diazepam”: ¿puede una estrategia para prevenir abstinencia al alcohol usarse con éxito para tratar la dependencia a benzodiazepinas?

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To the Editor,
Benzodiazepines (BZDs) are central nervous system (CNS) depressants which are widely used to treat insomnia and anxiety, despite having long-term adverse side effects. (Fortea González, Oriolo, Balcells Oliveró, Sánchez Del Valle & Castellvi, 2017). As with alcohol, continued use can lead to tolerance and dependence phenomena. Discontinuation in such cases can produce abstinence symptoms such as tremors, anxiety, seizures and, occasionally, death (Brett y Murnion, 2015).

Diazepam is a BZD used to treat and prevent alcohol withdrawal (Bird & Makela, 1994), as well as BZD withdrawal. Diazepam has a long elimination half-life (20-100 hours), as does its active liver metabolite, nordiazepam (36-200 hours) (Greenblatt, Shader, Divoll & Harmatz, 1981), which means that therapeutic concentrations can be present for prolonged periods even after short-term treatments (Muzyk, Leung, Nelson, Embury & Jones, 2013). It also has a highly lipophilic nature, making for rapid onset of action, with maximum concentration in the CNS being quickly reached.

Among the strategies for tackling alcohol withdrawal, the use of a BZD loading dose is considered valid (Lligoña, 2007; Wasilewski et al., 1996). The pharmacokinetic profile of diazepam allows a high initial loading dose to achieve an immediate and sustained treatment effect. Normally this load takes the form of 20 mg of diazepam doses orally every 2 hours until the patient is drowsy but reactive, producing

therapeutic concentrations of diazepam and nordiazepam for more than 72 hours.

Nevertheless, despite its pharmacological properties and its use for alcohol withdrawal, the loading strategy has not been reported in the literature for treating BZD withdrawal, except as an initial strategy in the case of acute withdrawal symptomatology followed by a gradual descending pattern (Sellers, 1988).

We describe the case of a 51-year-old woman with a history of long-term BZD use disorder, who was successfully detoxified after receiving a loading dose of diazepam without the subsequent administration of benzodiazepines.

Her toxicological history featured abuse of snorted cocaine and cannabis in the past. She habitually smoked tobacco and drank alcohol sporadically. Personality disorder stands out in her medical history, with predominantly histrionic and borderline characteristics (DSM-5), and self-harming behaviors.

BZD use was initiated by medical prescription for panic attacks and subsequently developed into a pattern of dependence. She had two hospital admissions for detoxification, where a tapering dose of clonazepam was applied, with subsequent relapse. Recently she had been taking 5 mg of lorazepam and 100 mg of diazepam daily.

The patient was taken to the emergency room after an estimated overdose of 200 mg of diazepam with the intention of committing suicide. The toxic urine screen was negative for opioids and ethanol. During the observation

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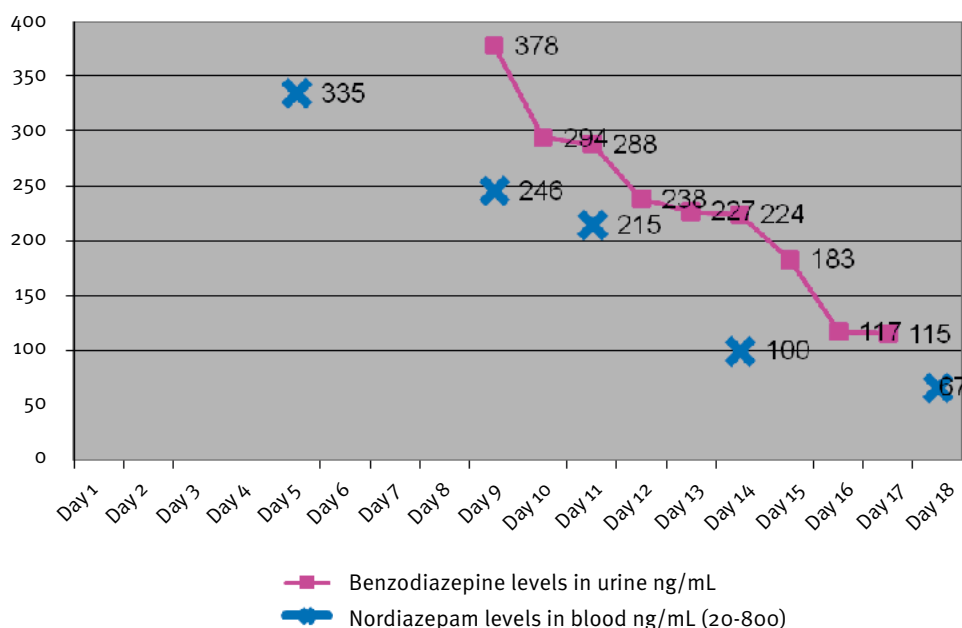


Figure 1. Monitoring of benzodiazepine levels in urine and nordiazepam in blood (the interval considered therapeutic by the laboratory is shown in brackets) during the time of admission. The presence of therapeutic levels of active metabolite in blood is noticeable over a prolonged period.

period she had respiratory depression, for which an intravenous perfusion of flumazenil was administered for 8 hours. Activated charcoal was not administered. She was subsequently admitted to the acute psychiatric unit.

Since flumazenil suppresses the effects of BZDs by inhibition but does not eliminate them from the organism, a diazepam loading strategy analogous to that used for alcohol detoxification was chosen to treat the patient’s BZDs withdrawal syndrome. The loading dose was considered to be the earlier intake of 200 mg of diazepam.

She experienced neither symptoms nor severe signs of BZD withdrawal such as delirium or seizures. No signs or symptoms of abstinence were found or reported spontaneously beyond mild anxiety that gradually subsided, nor was a rescue dose required. On the fourth day, monitoring of BZDs in blood and urine was initiated. She was discharged after 18 days and has remained abstinent for 24 weeks.

In our experience, and consistent with its use for alcohol withdrawal, diazepam loading may be a valid strategy on its own for the prevention and treatment of BZD abstinence. The half-life of diazepam and its metabolites (such as nordiazepam) makes it possible to maintain elevated serum levels of active substance, enabling progressive reduction over time (Figure 1) and thereby preventing abstinence symptoms from appearing. In this way the administration of new doses of BZDs is avoided and substance-seeking behavior is not reinforced, as would be

the case if BZDs were administered in split doses during several days.

Despite the patient’s own overdose being taken as a loading dose in our case, such doses could be administered in a supervised manner to avoid subsequent complications. Thus, although new studies are needed to assess the safety, loading dosage and efficacy in comparison with conventional strategies for treatment and prevention of BZD withdrawal, diazepam loading could be an effective alternative that could also minimize the relapse into use of BZDs.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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