

Considerations for the use of a loading dose of diazepam for the treatment of benzodiazepine dependence

Consideraciones respecto al uso de dosis de carga de diazepam para el tratamiento de la dependencia a benzodiazepinas

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Dear Editor,
After reading with interest and attention the recent letter to the editor published in this journal, "Diazepam loading: ¿Can a strategy for preventing alcohol withdrawal be used to treat benzodiazepine use disorder?" (Oliveras et al., 2018), we would like to make some considerations in this regard.

Currently, the extrapolation of this therapeutic tool used for the detoxification of alcohol dependence to its use in benzodiazepine dependence lacks scientific support, unlike other strategies that have shown favorable results in successive reviews, such as the gradual and slow reduction, previous replacement by a long half-life benzodiazepine (Voshaar, Couvée, Van Balkom, Mulder, & Zitman, 2006), the addition of psychological interventions such as cognitive behavioral therapy (Parr, Kavanagh, Cahill, Mitchell, & Young, 2009), and the recent evidence of the use of pregabalin and gabapentin (Sabioni, Bertram, & Le Foll, 2015) as supportive pharmacological treatment.

It should not be ignored that presentation of the withdrawal syndrome is heterogeneous. Previous use of high doses and long-term treatment are related to an increased incidence of the withdrawal syndrome, although there is no clear association with its intensity (Schweizer & Rickels, 1998). The duration and evolution of possible symptoms are also variable, as reflected in a prospective study (Vikander, Koechling, Borg, Tönn, & Hiltunen, 2010) where up to four patterns of evolution were observed for different

groups of symptoms over a period of 50 weeks, some of which, if they presented (symptoms related to anxiety and reactive depression and perceptible disorders), still persisted after the end of the study.

Some factors also negatively influence the process, such as the form of administration (too fast or too slow dose reduction), the presence of medical pathologies, poisons, life stressors, previous neurotic personality, and poor social support, among others (Dupont, 1990). Therefore, this inter-individual variability provides an added difficulty in the search for a generalizable standardized treatment based on the use of a loading dose with a long half-life benzodiazepine like diazepam when the gradual decrease of the drug is not performed in accordance with the tolerance of the symptoms presented by the patient, but instead depends exclusively on its pharmacokinetic properties.

On the other hand, the use of diazepam for a single loading dose may not be suitable to ensure the control of symptoms in a large group of patients because its pharmacokinetic parameters, such as the half-life, vary considerably (up to 30 times) depending on factors such as age, sex, liver function, co-administration of other drugs, even in relatively homogeneous populations (Greenblatt, Harmatz, Friedman, Locniskar, & Shader, 1989).

Moreover, the data collected in Spain reflect the high prevalence of benzodiazepines in the population over 75 years, as this age group receives a higher rate of prescriptions (Bejarano-Romero et al., 2008) and thus, there is a

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higher inherent risk for benzodiazepine abuse and dependence. In this population, where pluripathology and polypharmacy are characteristic, overdosing with diazepam would be counterproductive, given the increased vulnerability to the emergence of secondary effects, both paradoxical and expected due to sedation, favoring an increase in hospital stay (Kim et al., 2017).

We wish to highlight the commendable innovative strategy proposed, although, ultimately, despite the patient's favorable evolution described in the submitted case, there are some aspects to consider that would cast doubt on the application of this technique to achieve a favorable NNT (number [of patients] needed to treat), and studies are needed that support its effectiveness and safety.

Conflict of interest

The authors claim there is no conflict of interest.

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