

## RISKS RELATED TO DIAZEPINE DEPENDENCE AND WITHDRAWAL MANAGEMENT LITERATURE REVIEW

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**Abstract: Introduction:** The chronic use of diazepam medication is increasing and, in addition, without a prescription or adequate medical prescription. It leads to changes in the GABA receptor, reducing its affinity for its neurotransmitter and decreasing GABAergic activity. This is manifested in the form of tolerance to the drug (MOSFIAK, 2020). **Objective:** To review the risks related to diazepam dependence and management of its withdrawal. **Result:** Unfortunately, there is still no robust evidence that any medication can be used to aid withdrawal from diazepam after prolonged use, although some research and reviews have been carried out in this regard (MOSFIAK, 2020). **Conclusion:** The chronic use of diazepam medication is increasing and, in addition, without a prescription or adequate medical prescription. It leads to changes in the GABA receptor, reducing its affinity for its neurotransmitter and decreasing GABAergic activity. This is manifested in the form of tolerance to the drug (MOSFIAK, 2020).

**Keywords:** Diazepam dependence; Chemical dependence; Addiction treatment.

## INTRODUCTION

The chronic use of diazepam medication is increasing and, moreover, without a prescription or adequate medical prescription. It leads to changes in the GABA receptor, reducing its affinity for its neurotransmitter and decreasing GABAergic activity. This is manifested in the form of tolerance to the drug (MOSFIAK, 2020).

In the absence or reduction of diazepam, the reduction in GABA receptor activity leads to less inhibition of excitatory neurotransmitters (ANICET, 2022).

Physical dependence, falls, memory changes, dementia, tolerance, functional impairment, daytime sedation, changes in sleep architecture, motor vehicle accidents and possible drug interactions are some of the

side effects expected from the chronic use of diazepam (ALMEIDA, 2017).

The risks are greater in the elderly, given the metabolic and renal excretion changes. This population also tends to be more sensitive to psychomotor effects (increasing the risk of falls, which is already a cause for concern in this age group) and cognitive effects, in addition to being at greater risk for drug interactions and more vulnerable to adverse effects due to their hemoconcentration (less water in the body) (MOSFIAK, 2020).

Symptoms usually last a few days or weeks (some references mention 2 weeks, while others say it can last up to 6-8 weeks). The onset of symptoms varies according to the half-life of the medication taken (ANICET, 2022).

Since some of these symptoms may be associated with the reason why the medication was prescribed, the doctor and the patient may mistakenly believe that this justifies its continued use (ALMEIDA, 2017).

Withdrawal symptoms are more likely to be observed after an abrupt reduction in the usual dose of the medication or even sudden discontinuation of its use. The higher the doses taken, the more severe the symptoms (ANICET, 2022).

In medications with a long half-life, withdrawal symptoms can be felt after up to a few weeks of discontinuation. However, in those with a short half-life, they can appear in 24-48 hours (ANICET, 2022).

Regarding the diagnostic criteria for diazepam dependence, present in the DSM-5, the patient must present at least two of the following symptoms hours or days after the reduction or discontinuation of an anxiolytic, sedative or hypnotic medication that had been used for a long time: Seizures (grand mal type); Increased autonomic activity (tachycardia and sweating); Anxiety; Tremors in the upper limbs; Agitation; Insomnia;

Illusions or hallucinations; Nausea/vomiting (ALMEIDA, 2017)

It is always worth noting that, when there is abuse (capable of causing benzodiazepine intoxication), Flumazenil is the best option. It undoes benzodiazepine modulation in the brain, reducing sedation (ALMEIDA, 2017).

Unfortunately, there is still no robust evidence that any medication can be used to aid in the withdrawal of diazepam after prolonged use, although some research and reviews have been carried out in this regard (MOSFIAK, 2020).

For men aged  $\geq 65$  years (taking the medication despite its duration, its prescription as a first line in the elderly should be avoided), and for women between 18-64 years old who have been using it for more than 4 weeks: Explain the risks, benefits, withdrawal plan, symptoms and duration; Recommend withdrawal; Perform slow and gradual withdrawal; Inform that reduction strategies combined with psychotherapy may be more effective than reduction alone; Withdraw approximately 25% of the dose every 2 weeks and, at the end, withdraw more slowly (decrease 12.5% instead of 25% or alternate days with and without the medication) and advise on sleep therapy; Monitor, every 1 or 2 weeks, the duration of gradual withdrawal. During this, the following are expected: improvement in cognition, alertness, daytime sedation and reduction in falls and attention to withdrawal symptoms (see clinical picture); Use non-pharmacological approaches in the treatment of insomnia and psychotherapy, if necessary (ANICET, 2022).

## MATERIAL AND METHODS

The search was conducted in the PubMed database and was limited to articles published between 2017 and 2024 that met the criteria of being literature reviews and case reports.

Then, the keywords in the titles of the articles were analyzed and those whose theme best fit our objective were selected.

Three articles were selected for full reading.

## DISCUSSION

Unfortunately, there is still no robust evidence that any medication can be used to assist in the withdrawal of diazepam after prolonged use, although some research and reviews have been carried out in this regard (MOSFIAK, 2020).

## CONCLUSION

The chronic use of diazepam medication is increasing and, moreover, without a doctor's prescription or adequate medical prescription. It leads to changes in the GABA receptor, reducing its affinity for its neurotransmitter and decreasing GABAergic activity. This is manifested in the form of tolerance to the drug (MOSFIAK, 2020).

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