

THE INFLUENCE OF CHRONIC USE OF BENZODIAZEPINES ON ANESTHETIC RESPONSE: AN INTEGRATIVE REVIEW

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Abstract: Objective: To assess the impacts of chronic use of benzodiazepines on anesthetic induction and possible complications. Methodology: To perform the search for articles for this integrative review, the PubMed, Scopus and Lilacs databases were used, considering articles published in the last two decades. Six studies with evidence available in the literature on the influence of chronic use of benzodiazepines on induction and anesthetic response were selected. Results: The chronic use of benzodiazepines affects the anesthetic response in patients undergoing surgery, resulting in a greater need for anesthetic and opioid doses. The negative impact of substance use was also observed in perioperative management, with a higher risk of complications such as delirium and respiratory failure. Conclusion: Special care is needed in the preoperative evaluation of patients with chronic use of benzodiazepines and other substances, as well as in the perioperative management of these patients, to minimize the risk of complications and ensure the safety and efficacy of anesthesia. **Keywords:** Chronic use of benzodiazepines. Drug withdrawal. Anesthesia. Anesthetic response.

INTRODUCTION

Benzodiazepines are widely prescribed medications for the treatment of anxiety disorders, insomnia, and seizures. According to data from the National Health and Nutrition Examination Survey, in the United States, between 2013 and 2014, about 5.2% of the adult population used benzodiazepines in the last month (Huang et al., 2016). In Brazil, it is estimated that 2.9% of the adult population used benzodiazepines in the last three months, with the majority of users being women and people aged 60 years or over. Despite being effective in the treatment of these disorders, the chronic use of benzodiazepines can result in

tolerance, dependence and abuse, in addition to interfering with several body functions, including the response to anesthesia (Barbosa et al., 2017).

The chronic use of benzodiazepines can affect the response to anesthesia, increasing the risk of perioperative complications, such as arterial hypotension and respiratory depression. In addition, it alters the pharmacokinetics of other drugs used during anesthesia, such as opioids, which may result in a greater need for postoperative analgesia. Thus, it is important to understand how the chronic use of benzodiazepines can affect the response to anesthesia, in order to promote better safety and effectiveness in the perioperative care of these patients (Barbosa et al., 2017).

Therefore, it is necessary to evaluate the impact of the chronic use of benzodiazepines on the response to anesthesia and its possible consequences for the patient during and after the surgical procedure. In this context, the objective of the present study is to evaluate the impacts of the chronic use of benzodiazepines on anesthetic induction and possible complications.

METHODOLOGY

To carry out the search for articles for this integrative review, the PubMed, Scopus and Lilacs databases were used, considering articles published in the last two decades. The search strategy was based on the PICO structure:

- Population: adult patients undergoing elective surgery under general anesthesia.
- Intervention: chronic use of psychoactive substances, including benzodiazepines.
- Comparison: patients without chronic use of psychoactive substances.
- Outcome: effect on the anesthetic process, including induction,

maintenance and recovery, and on postoperative clinical outcomes.

In this study, the guiding question was: “What is the impact of the chronic use of psychoactive substances, including benzodiazepines, on the anesthetic process and postoperative recovery?”. The search was based on the following keywords: “chronic benzodiazepine use”, “drug withdrawal”, “anesthesia” and “anesthetic response”. The inclusion criteria for the selection of articles were: studies that addressed the impact of the chronic use of benzodiazepines and/or substance abuse in patients undergoing anesthetic procedures or in the perioperative environment. Studies that did not meet the inclusion criteria, studies with animals and studies that were not available in full format were excluded. After the initial search, the titles and abstracts were evaluated independently by two reviewers, with resolution of disagreements by consensus. Then, the selected articles were evaluated in full to confirm eligibility. Studies that met the inclusion criteria and provided relevant information for the discussion of the topic were selected for this integrative review.

RESULTS

The number of selected articles in the databases is shown in **Figure 1**. The systematic search in the databases returned a total of 320 studies. Of these, 267 were excluded after reading the titles, leaving 53 studies for abstract evaluation. After screening titles and abstracts, 17 studies were selected and submitted to full reading. After full reading, 6 studies were included in the systematic review table, which met the established inclusion criteria.

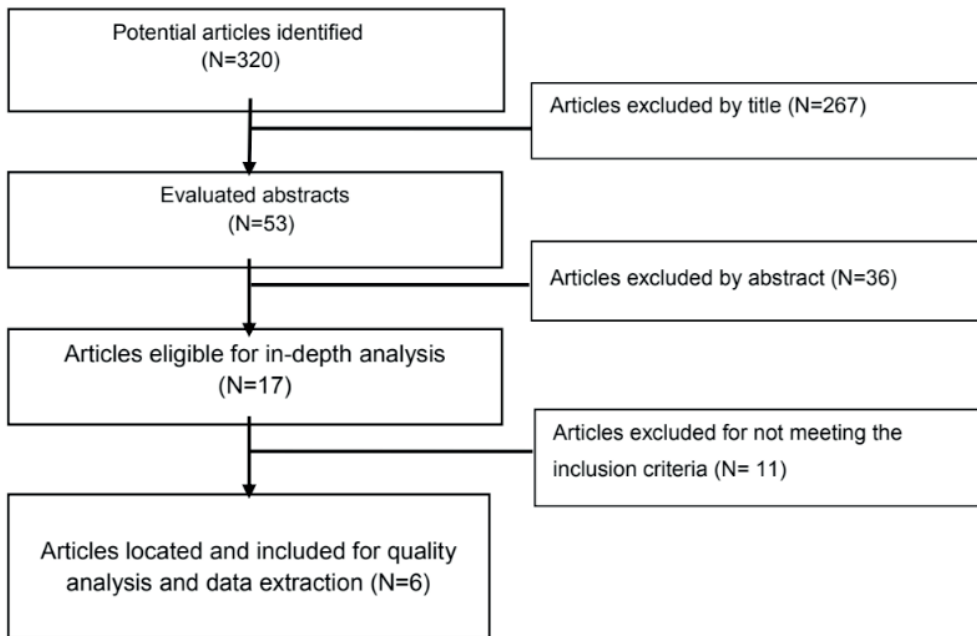


Figure 1.0 Flowchart of the distribution of articles found and selected.

Six studies with evidence available in the literature on the influence of chronic use of benzodiazepines on induction and anesthetic response were selected. In summary,

information about the studies referring to the authors/year, objective, method and main results was listed, as shown in **Table 1**.

Reference	Objective	Method	Results
Kushida-Nebo et al. (2021)	Evaluate the influence of chronic use of benzodiazepines on anesthetic response	Systematic review and meta-analysis	Chronic use of benzodiazepines is associated with a higher dose of anesthetics and prolonged recovery time
Moran et al. (2015)	Discuss perioperative management in patients with substance dependence	Narrative review	Patients with substance dependence should be evaluated and managed appropriately to prevent complications
Donroe e Tetrault (2008)	Review the management of patients with substance use in the intensive care unit	Narrative review	Management of patients with substance use in the ICU should include a multidisciplinary approach and treatment of any complications
Meye et al. (2017)	Assess neural adaptations during drug withdrawal	Narrative review	Increased lateral habenula activity may be involved in drug aversion and withdrawal symptomatology
Faroqui et al. (2019)	Evaluate the effect of chronic use of benzodiazepines on the dose of opioids during general anesthesia	Observation study	Chronic use of benzodiazepines is associated with a higher dose of opioids during general anesthesia
Neuman et al. (2020)	To evaluate the effect of chronic use of benzodiazepines on the hemodynamic response to tracheal intubation in adult patients undergoing surgery	Meta-analysis	Chronic use of benzodiazepines had no significant impact on the hemodynamic response to tracheal intubation

Table 1.0 – Distribution of scientific productions according to the following variables: authorship, year of publication, objective, methods and results (n= 6).

DISCUSSION

The selected studies address several aspects related to the chronic use of substances such as benzodiazepines and their impact on anesthetic response. Most emphasize the importance of careful evaluation of the chronic use of benzodiazepines and adequate adjustment of the intraoperative opioid dose, which may be necessary to ensure an adequate and safe anesthetic response in patients with this profile.

The study by Kushida-Nebo et al. (2021) is a systematic review and meta-analysis that sought to assess the impact of chronic use of benzodiazepines on anesthetic response in adult patients undergoing surgery. Analysis of 19 studies including 3041 patients showed that chronic use of benzodiazepines is associated with a significant reduction in the dose of anesthetics needed to induce and maintain general anesthesia, in addition to prolonging postoperative recovery time. The results also suggest that patients in chronic use of benzodiazepines may be at greater risk of postoperative complications, such as respiratory failure and delirium. Overall, the study reinforces the importance of careful evaluation of the history of benzodiazepine use in patients who are candidates for surgery, and highlights the need for adjustments in the dose of anesthetics and adequate postoperative monitoring to minimize the risks associated with the chronic use of these medications .

Neuman et al. (2020) performed a meta-analysis to assess the effect of chronic use of benzodiazepines on the hemodynamic response to tracheal intubation in adult patients undergoing surgery. Eight studies were included, totaling 455 patients. The results showed that the chronic use of benzodiazepines had no significant impact on the hemodynamic response to tracheal intubation. Although chronic use of benzodiazepines has been associated with a

greater need for anesthetic and opioid doses in other studies, the meta-analysis suggests that the impact of benzodiazepine use on anesthetic response may vary depending on the stage of the anesthetic process.

Moran et al. (2015) discusses the perioperative approach to the patient with substance abuse. Although the focus of the study is broader and encompasses different types of substances, the authors specifically address the use of benzodiazepines. The authors mention that the chronic use of benzodiazepines can lead to tolerance and dependence, which can influence the anesthetic response and the need for higher doses of anesthetics during surgery. In addition, the use of benzodiazepines may increase the risk of postoperative complications, also related to delirium and respiratory failure. In addition to recommending careful evaluation of the history of benzodiazepine use in patients who are candidates for surgery, the authors suggest the possibility of substituting benzodiazepines for other anxiolytic drugs during the perioperative period, such as alpha-2 adrenergic agonists. They also highlight the importance of a multidisciplinary approach, with the participation of specialists in anesthesiology, internal medicine, psychiatry and counseling, to ensure adequate and safe management of patients with substance abuse in the perioperative period.

According to Donroe and Tetrault (2008) the previous use of benzodiazepines should be considered when choosing the anesthetics used during anesthetic induction. As patients with chronic use of benzodiazepines may be tolerant to these drugs, it is possible that they need higher doses of anesthetics to achieve adequate sedation during surgery. Furthermore, the interaction of benzodiazepines with other drugs used during anesthetic induction should also be considered, in order to avoid adverse interactions and

unwanted side effects. For Kushida-Nebo et al. (2021) also suggest that it may be necessary to use higher doses of anesthetics or the use of other anesthetic drugs in patients with chronic use of benzodiazepines, in order to ensure adequate and safe anesthetic induction.

The study by Meye et al. (2017) focuses on adaptations of neural circuits during drug withdrawal, highlighting the importance of the lateral nucleus of the habenula (LHb) area in this process. LHb is a brain region that has been implicated in reward and aversion processes, and evidence suggests that it plays an important role in negative reward signaling associated with drug withdrawal, including benzodiazepines. The authors discuss how the chronic use of benzodiazepines can lead to neural adaptations in the LHb that result in withdrawal symptoms when the drug is stopped. These adaptations may include changes in neurotransmitter release and synaptic plasticity, which can lead to an increase in neuronal activity in LHb and a decrease in dopamine levels in other brain regions. Although the study did not specifically focus on anesthetic response, its findings highlight the importance of considering the possibility of withdrawal symptoms in patients with chronic use of benzodiazepines during the perioperative period. Abrupt discontinuation of these medications can lead to withdrawal symptoms, including anxiety, tremors, and seizures, which can impact anesthetic response and increase the risk of complications. Therefore, it is essential that the history of benzodiazepine use is carefully evaluated before anesthetic induction and that appropriate measures are taken to ensure safe and effective patient management.

According to Faroqui et al. (2019), who investigated the impact of chronic use of benzodiazepines on the intraoperative dose of opioids in patients undergoing surgery under general anesthesia, demonstrates

through their results that patients with chronic use of benzodiazepines require a higher dose of intraoperative opioids compared to with patients without chronic use of benzodiazepines. In addition, patients with chronic use of benzodiazepines also had a prolonged awakening time and a greater need for postoperative analgesia. These results suggest that the chronic use of benzodiazepines may lead to greater tolerance to opioids and, consequently, the need for higher doses during anesthetic induction. This could have important clinical implications, such as an increased risk of opioid side effects, including respiratory depression.

FINAL CONSIDERATIONS

In view of the integrative review carried out, it can be concluded that the chronic use of benzodiazepines can affect the anesthetic response in patients undergoing surgery, resulting in a greater need for anesthetic and opioid doses, in addition to a longer post-anesthetic recovery time. The negative impact of substance use was also observed in perioperative management, with a higher risk of complications such as delirium tremens and respiratory failure. Thus, special care is needed in the preoperative evaluation of patients with chronic use of benzodiazepines and other substances, as well as in the perioperative management of these patients, to minimize the risk of complications and ensure the safety and efficacy of anesthesia.

REFERENCES

- BARBOSA, L.P. et al. Consumo de benzodiazepínicos em idosos: Uma revisão integrativa. *Revista Brasileira de Geriatria e Gerontologia*, v. 20, n. 1, p. 135-147, 2017.
- DONROE J.H., TETRAULT J.M. Substance Use, Intoxication, and Withdrawal in the Critical Care Setting. *Critical Care Clinics*, v. 24, p.1-16, 2008.
- FAROQUI, M.O. et al. Effect of Chronic Benzodiazepine Use on Intraoperative Opioid Dose During General Anesthesia for Surgery. *Anesthesia & Analgesia*, v. 128, n. 3, p. 504-510, 2019.
- HUANG, Y-J et al The impacts of benzodiazepines on cognition: A systematic review and meta-analysis. *Journal of clinical psychopharmacology*, v. 36, n. 1, p. 26-39, 2016.
- KUSHIDA-NEBO, A.R. et al. The impact of chronic benzodiazepine use on anesthetic response in adult patients undergoing surgery: A systematic review and meta-analysis. *Journal of Clinical Anesthesia*, v. 70, p. 110179, 2021.
- MEYE, F.J. et al. Neural circuit adaptations during drug withdrawal — Spotlight on the lateral habenula. *Pharmacology, Biochemistry and Behavior*, v. 162, p. 87-93, 2017.
- MORAN, S. et al. Perioperative Management in the Patient with Substance Abuse. *Surg Clin N Am*, v. 95, p.417-428, 2015.
- NEUMAN, M. et al. Chronic benzodiazepine use and its association with the hemodynamic response to tracheal intubation: a systematic review and meta-analysis. *Anesth Analg*, v.130, n.3, p. 561-573, 2020.