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Consequences of prolonged use of benzodiazepines related to the increase in mental disorders: a literature review

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Abstract: The indiscriminate use of benzodiazepines in the world has been growing for years, mainly for long periods and, in cases, without justification. The aim of this research is to conduct a literary review on the consequences of excessive consumption of benzodiazepines, especially its dependence, characterizing a complementary literary review, concluded through other studies, with qualitative method. The articles gathered were searched from the SciELO, PUBMED and Google Scholar databases. Addressing a need for awareness of the time of use of the drug, because the longer the period, the more difficult to interrupt the treatment, as well as increase the chances of developing abstinence. Concluding that the lack of adequacy of mental health issues by primary care professionals, the division of care, overwork, resource limitations and little investment in training contribute to

the inadequate use of benzodiazepines.

Keywords: Benzodiazepines. Indiscriminate use. Prescription medications

1. Introduction

Adolescence is a phase of great changes for humans, The indiscriminate use of benzodiazepines (BDZ) in the world has been growing for years, mainly for long periods and, in cases, without justification. This class of psychotropic drugs is among the five best-selling controlled drugs in Brazil, with higher consumption in regions with higher population level and higher prevalence of physicians (FEGADOLLI *et al.*, 2019).

Benzodiazepines are characterized by their high dependence content, which is related to their pharmacokinetics, such as high lip solubility and biological half-life. The higher the lip solubility and the lower the half-life, the greater the potential for dependence. Lip solubility is what defines the rate of absorption, speed and extent of delivery of the drug. It is an important characteristic of BDZ, as it has good emission in tissues and ease in overcoming the hematoencephalic barrier (SCHALLEMBERGER *et al.*, 2016).

As for the development of psychological dependence in chronic benzodiazepine users, both the clinician and the patients have as an obstacle to perform protocols to restrict the use. Many patients are unaware of or show disinterest in the adverse effects and resistance to medication withdrawal (ALVIM *et al.*, 2017). In addition, in Brazil, medicines that require the presentation of medical prescriptions are easily purchased in the market (RAMOS *et al.*, 2020). The prescription of medicines in the elderly involves polypharmacy, drug interaction and inadequate medications. Benzodiazepines are a highlight, whose long-term use is common and grows among the elderly (ALVIM *et al.*, 2017).

There is a need for awareness about the indiscriminate use of BZDs, as they have a degree of dependence that can worsen the patient's quality of life. The longer the time of use, the more difficult it will be to stop treatment, and the chances of developing abstinence increase with prolonged use (BASTOS *et al.*, 2016).

Due to the overload of the public system, physicians are unable to provide quality care, without prioritizing dialogues that seek to understand the patient's need and often leaving him without explanation regarding treatment. Therefore, it is essential to the good conduct of the pharmacist at the time of dispensing the psychotropic drugs, making clear the therapeutic indication, correct daily dosage and the adverse effects caused by indiscriminate use (PEREIRA *et al.*, 2008).

The aim of this research is to conduct a literary review on the consequences of excessive consumption of benzodiazepines, especially its dependence.

2. Methodology

This is a qualitative article characterized as documentary

by providing a new interpretation of data obtained for other studies, allowing the researcher to choose the focal point for his research.

The articles gathered in the work were searched from the scientific electronic library online (SciELO), medical published – services of the U.S. National Library of Medicine (PUBMED) and Google Scholar databases. The descriptors used were "benzodiazepines", "indiscriminate use of benzodiazepines" and "misuse of prescription drugs". The selection criteria were: articles published in the following languages: Portuguese and English; full text available in the database; period from 2008 to 2021. The exclusion criteria were duplicate articles, opinions, theses and dissertations.

3. Results and Discussion

150 results were obtained during the research, of which the criteria were based, resulted in 12 relevant articles for the literature review that were demonstrated in Table 1. The analysis of the theme is fundamental, because it exposes the individualistic scenario of the performance of primary care professionals, apart from the recommendations so that benzodiazepines are not prescribed for more than four weeks. Inserting benzodiazepines into treatment, which would be a solution creates a contradiction with the possibility of an escape picture by both professionals and users (FEGADOLLI *et al.*, 2019).

Table 1. List of selected articles in the survey

Search title	Kind	Author and year	Goal
Use and abuse of benzodiazepines in primary health care: professional practices in Brazil and Cuba	Article	FEGADOLLI, C.; VARELA, N.M.D.; CARLINI.E.L.A. (2019)	The present study sought to understand care aspects present in the basis of the indiscriminate use of benzodiazepines.
Acute angular closure triggered by oral use benzodiazepines	Article	Matos. A.G.; CASTILLO. P.D.B.; GREAT-GRANDSON. J.A.L.; PAULA.J.S. (2021)	Glaucoma by acute closure of the iridocorneal angle is one of the adverse events with a higher risk of blindness, being described particularly in the elderly.
Increased use of benzodiazepines among older adults: Bambuí Project	Article	OLIVE TREE. A.L.M.L.; BIRTH. M.M.G.; COAST. E.C.; Firmo. J.O.A.; COAST. M.F.L.; FILHO.A.I.L. (2020)	The study aimed to investigate the trend of benzodiazepine use among older elderly (75 years or more) living in the community.
Evaluation of	Article	MR.	The aim of this study

dependence and anxiety in benzodiazepine users in a municipality in the interior of Rio Grande do Sul		SCHALLEMBERGER. J.B.; COLET.C.F. (2016)	was to verify the level of dependence and anxiety among users of these drugs in the public health system.
Information about benzodiazepines: what does the internet offer us?	Article	BRANCHES. T.B.; Bokehi. L.C.; OLIVE TREE. E.B.; Gomes. M.S.A.; Bokehi. J.R.; NEUTER. S.R. (2020)	This work looked at the quality of information published on the internet about 4 benzodiazepines widely used in Brazil: alprazolam, clonazepam and diazepam.
Prevalence and factors associated with the use of benzodiazepines in community elderly	Article	I SAW IT. M.M.; CROSS. D.T.; SCALLOP. M.T.; BASTOS. R.R.; LEITE.I.C.G. (2017)	assess the prevalence and factors associated with the use of benzodiazepines in elderly people in the community.
Use of psychotropic drugs among elderly residents in community: prevalence and associated factors	Article	ABI-ACKEL. M.M.; COAST. M.F.L.; COAST. E.C.; FILHO.A.I.L. (2017)	To investigate the prevalence and factors associated with the use of psychotropic drugs among the elderly.
Use of potentially inappropriate medicines by elderly at home	Article	LEE. L.M.; FLOWERS. T.P.; COAST. S.C.; REIS.A.M.M. (2016)	The objective was to evaluate the frequency of home use of potentially inappropriate medications by the elderly and to analyze the clinical significance.
The evolution of Pharmaceutical Care and the perspective for Brazil.	Article	PEAR TREE. R.L.P.; FREITAS.O. (2008)	Pharmaceutical Care, a recent practice of pharmaceutical activity, prioritizes guidance and pharmacotherapeutic follow-up and the direct relationship between the pharmacist and the drug user.
Use of benzodiazepines in the Municipal Health Service of Coronel Fabriciano, Minas Gerais.	Article	FIRMINO. K.F.; Abreu, abreu. M.H.N.G.; PERINIE.; MAGALHÃES.S.M.S. (2012)	In this study, the indications of benzodiazepines were evaluated in the Municipal Health Service of Coronel Fabriciano MG,

			verifying their compliance with what is recommended by the literature.
Side effects attributed to the undue and prolonged use of benzodiazepines.	Article	NUNES. B.S.; BASTOS.F.M. (2016)	The objective of this work was to highlight the side effects caused by the undue and prolonged use of benzodiazepines, based on a review of the literature and its pharmacokinetic and pharmacodynamic characteristics.
Non-pharmacological interventions in sleep and quality of life: a randomized pilot study	Article	SANTOS M.A, CONCEIÇÃO A.P, LUCENA R.E, FERRETTI-REBUSTINI R.E.L, CIOL M.A, HEITHKEMPER M.M, CRUZ D.A.L.M. (2017)	Estimate the effects of non-pharmacological interventions to improve the quality of sleep and life of patients with heart failure.

Source: Prepared by the author

The meetings between physicians and patients are decisive for the result of the degree of population medicalization, so it is quite common for benzodiazepine users to use the health problem to influence medical management, seeking to convince and obtain a prescription, because it is already a degree of dependence (FEGADOLLI *et al.*, 2019).

Generally, 80% of the first prescriptions are made by a general practitioner (FIRMINO *et al.*, 2012), however, professionals often do not feel comfortable dealing with mental illnesses and report difficulties (SCHALLEMBERGER *et al.*, 2016).

The lack of psychiatrists in primary care health centers may be one of the reasons for most visits being made by general practitioners. One of the obligations of primary care is the resolution of cases and small problems at the level of the health center and, only, when necessary, cases should be directed to specialized care (SCHALLEMBERGER *et al.*, 2016).

Devoid of precise methods for coping, the indiscriminate use of benzodiazepines is provoked without great perceptibility. For health systems, it is treated as something insignificant compared to other problems. However, although the system does not identify the focus of the problem, it is perceived by professionals alone (FEGADOLLI *et al.*, 2019).

Usually are occurrences of insomnia generated by depressive conditions that lead to the use of benzodiazepines, which through a hasty diagnosis, adopt benzodiazepines as an initial measure. Despite treating insomnia, the patient remains in a depressive condition and in the future requiring

higher doses of medications. Another important situation to be mentioned would be menopause, usually associated with depression, insomnia, mood change, where most clinicians usually associate with a depressive condition, not treating menopause and consequently not solving the problem (FEGADOLLI *et al.*, 2019).

Therefore, the restriction of the use of benzodiazepines has been assimilated to contradictions related to the safety of these drugs: by the association with the occurrence of adverse events. Currently in agreement with therapeutic indications, other drugs have been replacing BZD in the treatment of anxiety disorders, such as newer and safer antidepressants in geriatrics such as sertraline hydrochloride, and the association of non-pharmacological measures in the conduction of sleep disorders and insomnia symptoms (OLIVEIRA *et al.*, 2020). Therapies used include cognitive behavior, phototherapy, teaching sleep hygiene habits, and relaxation therapies.

In this complex scenario, although professionals recognize the possibility and need for changes in a set of efforts, the measures are considered as alternatives far from reality, little or no effective (FEGADOLLI *et al.*, 2019). The reason for the continuous use of benzodiazepines is reported as a fear of the return and intensification of symptoms, or the impairment of the performance of daily activities (ALVIN *et al.*, 2017).

Tolerance is the main notorious result of chronic benzodiazepine use. Characterized when a person has a reduced drug response, which occurs when the drug is used repeatedly and the body adapts to its constant presence. Frequent administration of the drug results in modification in the right dose-response curve, so that higher doses/concentrations of the drug are necessary to provide the same effect, thus increasing the risks of benzodiazepine users taking higher doses than those prescribed by their physicians (FEGADOLLI *et al.*, 2019).

Another important factor is the case where benzodiazepines are presented, by some authors, as the main drugs involved in exogenous intoxications in Brazil. It is justifiable to assume that the ease of access to information about these products on the internet without property may be factors that contribute to the irrational use of these products (RAMOS *et al.*, 2020).

Return visits to the doctor should be considered as a care, because a rational prescription should be systematic in frequent follow-up of the patient. However, in practice, it is found that patients return only to obtain a new prescription (ALVIN *et al.*, 2017).

Gradual discontinuation of use may be positive by reducing the dose. Cognitive behavioral therapy is indicated as efficient in the treatment of chronic insomnia, contributing to the reduction of benzodiazepine use in the elderly. Interferences in prescription, substitution, psychotherapies and pharmacotherapies may contribute to decreased dependence on benzodiazepines. Efforts should be made to educate and insure patients (ALVIN *et al.*, 2017).

4. Conclusions

The current world scenario contributes to the increase in the generation of benzodiazepine users seeking relief from symptoms that could be treated in another way and little or no effective control over use. Through the study based on the articles, we conclude that the indiscriminate consumption of benzodiazepines occurs due to failures in the system, both through the professionals and the system itself and through the lack of knowledge of the patients. Thus, a better approach on irrational use is necessary, in so that methods of awareness, integration and professional training on the subject are developed.

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