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Instituto de
Geriatria e Gerontologia

PAJAR
Pan American Journal of Aging Research
PAJAR, Porto Alegre, v. 11, p. 1-13, jan.-dez. 2023
ISSN-L: 2357-9641

http://dx.doi.org/10.15448/2357-9641.2023.1.45098

ARTIGO ORIGINAL

Is it possible to deprescribe benzodiazepine receptor agonists in older adults?

É possivel desprescrever medicamentos agonistas dos receptores benzodiazepínicos em idosos?

¿Es posible desprescribir los fármacos agonistas de los receptores benzodiacepínicos en los ancianos?

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Received on: Aug 30, 2023.
Approved on: Oct 31, 2023.
Published on: 04 dez 2023.

Deprescribing in older adults
Desprescrição em Idosos
Desprescripción en los ancianos

Abstract

Aim: to analyze the viability and related factors for deprescribing benzodiazepine receptor agonists (BZRA).
Methods: this is a longitudinal, prospective, interventional study performed with older adults assisted at a geriatric psychiatry outpatient clinic; these were divided into two groups: BZRA users and non-users. The instruments used in this study were a general questionnaire, the Geriatric Depression Scale (short form), the Geriatric Anxiety Inventory, and the Pittsburgh Sleep Quality Index.
Results: we evaluated 74 patients, 40 (54.1%) of which were BZRA users and 34 (45.9%) were non-users, with an average age of 71.3 ± 7.5 years. Patients who used BZRA had a higher dropout rate of the deprescription process 26 (65%). Seven patients completely stopped using BZRAs (17.5%) and five reduced their use (12.5%). The mean scores for depression and anxiety symptoms were lower at the final assessment. As to sleep quality, BZRA users presented higher baseline values and both groups presented reductions in scores at the end of the treatment.
Conclusion: deprescribing is viable and safe. However, there is resistance by both the patient and prescribers. The levels of anxiety, depression, and sleep quality improved after discontinuing BZRA.

Keywords: deprescriptions, receptors, GABA-A, aged.

Resumo

Objetivo: verificar a viabilidade e os fatores relacionados à desprescrição de agonistas de receptores de benzodiazepínicos (ARBZ).
Métodos: estudo longitudinal, prospectivo e intervencionista, realizado com idosos atendidos no ambulatório de psiquiatria geriátrica, os quais foram divididos em dois grupos: os usuários e os não usuários de ARBZ. Os instrumentos utilizados foram: Questionário geral, Escala Depressão Geriátrica Reduzida, Inventário de Ansiedade Geriátrica e Índice de Qualidade do Sono de Pittsburg.
Resultados: foram avaliados 74 pacientes, 40 (54,1%) usuários de ARBZ e 34 (45,9%) não usuários, com média de idade de 71,3±7,5 anos. Pacientes em uso de ARBZ apresentaram maior taxa de abandono ao processo de desprescrição 26 (65%). Sete pacientes cessaram o uso de ARBZ completamente (17,5%) e cinco reduziram (12,5%). Em relação aos sintomas depressivos e ansiosos, as médias dos escores foram menores na avaliação final. Em relação à qualidade do sono, os usuários de ARBZ apresentaram valores superiores na linha de base e, ao fim do tratamento, ambos os grupos apresentaram redução desses valores.
Conclusão: a desprescrição é viável e segura. No entanto, existe uma resistência tanto da parte do paciente como dos prescritores. Os níveis de ansiedade, de-

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pressão e qualidade do sono melhoram após a retirada dos medicamentos ARBZ.
Palavras-chave: desprescrições, receptores de GABA-A, idoso.

Resumen
Objetivos: verificar la viabilidad y los factores relacionados con la deprescripción de agonistas de los receptores benzodiacepínicos (ARBZ).
Métodos: se realizó un estudio longitudinal, prospectivo e intervencionista con ancianos que acudían a la consulta externa de psiquiatría geriátrica, divididos en dos grupos: usuarios y no usuarios de ARBZ. Los instrumentos utilizados fueron un cuestionario general, la Escala de Depresión Geriátrica Reducida, el Inventario de Ansiedad Geriátrica y el Índice de Calidad del Sueño de Pittsburg.
Resultados: se evaluaron 74 pacientes, 40 (54,1%) usuarios de ARBZ y 34 (45,9%) no usuarios, con una edad media de 71,3±7,5 años. Los pacientes que tomaban ARBZ presentaron la mayor tasa de abandonos del proceso de desprescripción con 26 (65%). Siete pacientes dejaron de tomar ARBZ por completo (17,5%) y cinco redujeron su consumo (12,5%). Con respecto a los síntomas depresivos y de ansiedad, las puntuaciones medias fueron más bajas en la evaluación final. Con respecto a la calidad del sueño, los usuarios de ARBZ mostraron valores más altos al inicio y al final del tratamiento ambos grupos mostraron una reducción de estos valores.
Conclusiones: la desprescripción es factible y segura. Sin embargo, existe resistencia tanto por parte de los pacientes como de los prescriptores. Los niveles de ansiedad, depresión y calidad del sueño mejoraron tras la retirada de la ARBZ.
Palabras clave: deprescripciones, receptores de GABA-A, anciano.

Introduction

Population aging has come to the spotlight worldwide, with projections of over 2 billion people being 60 years old or older in 2050[1]. As their years of life increase, older adults are more prone to chronic health conditions, which often result in multimorbidity;[2] treatment of these conditions requires many drugs, thus resulting in polypharmacy[3].

By definition, deprescribing is a supervised and systematic process that aims to identify, discontinue, or reduce medications that are no longer appropriate[3]. Many protocols evaluate medication safety in older adults, such as the Beers criteria[4], START/STOPP[5], FORTA (Fit for The Aged)[6], and the Brazilian Consensus on Potentially Inappropriate Medications for Older Adults[7]. These guidelines indicate which ones are considered potentially inappropriate medications (PIMs).

Many psychotropic medications are listed as PIMs, especially benzodiazepine receptor agonists (BZRA), which include benzodiazepines and Z-drugs. BZRA are widely prescribed due to their sedative-hypnotic properties, being frequently used for treating anxiety, insomnia, panic disorder, social anxiety disorder, obsessive-compulsive disorder, medication withdrawal, and adverse effects of antidepressants and antipsychotics. There are specific protocols that help and guide towards the best way to deprescribe this drug class, such as the BZRA Deprescribing Algorithm and Guidelines[8].

Recent studies show that one every five adults aged 65 years or older uses BZRA, 47% of which are long-term users[9]. Although they present good tolerability, these drugs have a poor benefit-risk ratio. Long-term use (for more than 4 weeks) is associated with adverse events and could cause cognitive impairment, falls, fractures, vertigo, and dizziness, in addition to prescription drug abuse and addiction[8].

Therefore, deprescribing BZRA becomes fundamental within policies that concern the treatment of older patients. Recent studies focus on the types of interventions and factors that influence BZRA deprescribing, with success rates that vary between 20% and 80%[4,5,8]. However, the routine implementation of such deprescribing strategies is limited, evidencing a knowledge gap on how to successfully deprescribe this drug class.

Improving our knowledge on factors involved in BZRA deprescribing becomes vital to increase success rates, indicating the best way for conducting the deprescribing process with higher adherence and effectiveness, especially in the older adult population. Therefore, the aim of this study is to identify factors involved in BZRA deprescribing, verifying adherence to the protocol steps, appearance of withdrawal symptoms, and dropout, as well as comparing levels of anxiety, depression, and sleep quality of users and non-users of this drug class.

Methods

Study design and ethical aspects

This is a longitudinal, prospective, interventional study of the older adult population assisted at the geriatric psychiatry outpatient clinic of a tertiary hospital in Porto Alegre, Brazil. Patient selection and follow-up took place from March 2020 to October 2021. The study was approved by the institution's Research Ethics Committee CAEE No. 89158218.5.0000.5336; Opinion Number 2.823.737.

Participants

All individuals aged 60 years or older assisted at the geriatric psychiatry outpatient clinic were invited to participate in the study. Older adults were divided into two groups: those who used BZRA (daily, for more than 4 weeks) and those who did not use these substances.

We only included individuals who accepted to participate in the study and after signing the informed consent form.

We excluded individuals who were not able to understand the questions of evaluation instruments used in the study (due to impaired cognitive or hearing capacity) and/or who refused to participate in the study. We also excluded those who used BZRA as part of anti-epileptic, alcohol abuse, or akathisia treatments.

Data collection

Data were collected at the first medical consultation through a semi-structured interview that used research instruments; it was performed by duly trained psychiatry residents under systematic supervision of the research group (psychiatrists and pharmacy professionals). All instruments were reapplied at the end of the treatment after clinical stabilization.

Figure 1 illustrates the studied groups, as well as the follow-up and outcome after intervention. The first group was formed by patients who used BZRA, and the second group comprised those who did not use BZRA. Both groups had the same type and frequency of medical consultations.

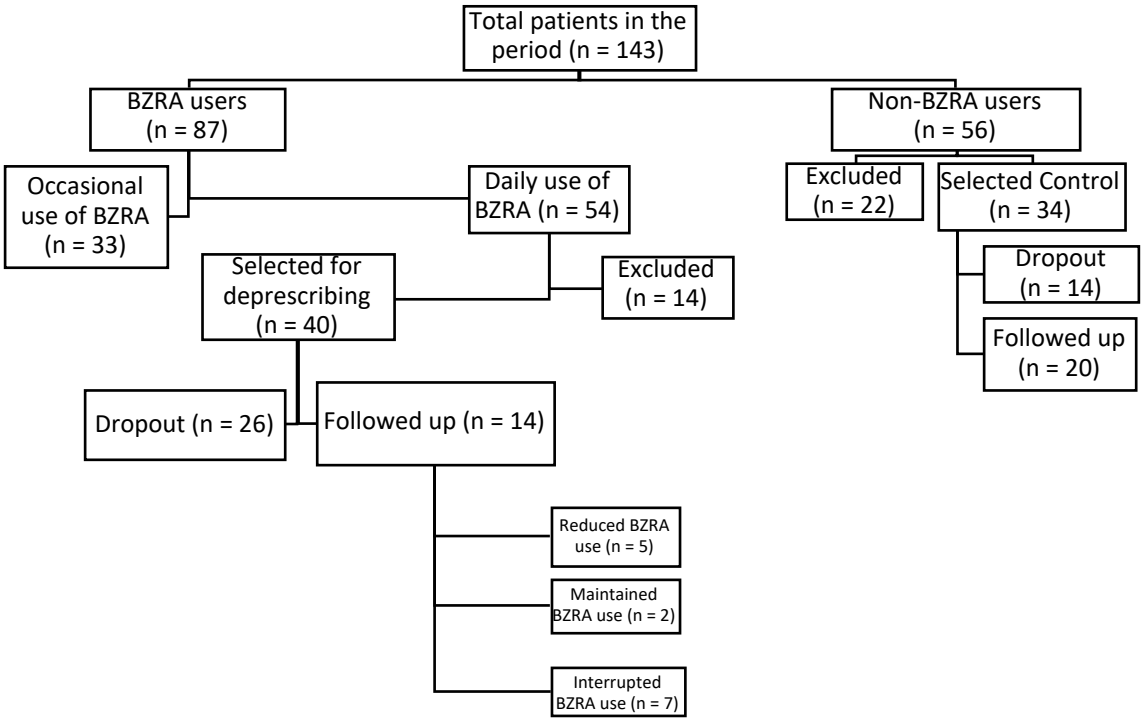

Figure 1. Patient selection and follow-up flowchart.

Instruments

General questionnaire

This instrument was elaborated by our research group and contemplates information on sociodemographic characteristics, such as age, sex, having a partner/roommate, education level, housing arrangement, retirement, assistance type, medications used, clinical comorbidities, psychiatric diagnosis, and sleep characteristics.

Depression symptoms

Depression symptoms were assessed through the Geriatric Depression Scale (GDS-15), short form. GDS-15 is one of the most widely used instruments for detecting depressive episodes in older adults. Out of its 15 items, 10 indicate the presence of symptoms when answered positively, whereas the others (questions 1, 5, 7, 11, 13) indicate depression when answered negatively. A cut-off of six points or more was used for defining the presence of depression symptoms. GDS-15 has 92% sensitivity and 89% specificity, and its validity and reliability have been supported both by clinical practice and research. In a validation study that compared the long and short forms of the GDS for assessing depression symptoms, both scales were successful in differentiating adults with depression from those without depression, with a high correlation ($r = 0.84$, $p < 0.001$)[10].

Anxiety symptoms

The Geriatric Anxiety Inventory (GAI) was developed as a brief instrument for assessing anxiety in the older adult population. The inventory comprises 20 dichotomous items considering the previous week. The authors of the original instrument determined values of 10/11 as cut-off points for indicating the presence of generalized anxiety. As for its psychometric parameters, the GAI presents a Cronbach's alpha of 0.91 for the normal older population and 0.93 for the geriatric population[11].

Sleep quality

The Pittsburgh Sleep Quality Index (PSQI) is a tool that assesses sleep quality and possible sleep disorders in the previous month. The main objectives of this scale are to evaluate sleep quality in a practical and standardized way, distinguishing between "good" and "poor" sleepers. It comprises 19 questions divided into seven groups that approach various aspects related to sleep quality. It has a 4-point scale varying from 0 to 3. Other five questions are directed to the bed partner or roommate of the evaluated individual and do not contribute to the total score. The final score ranges from 0 to 21. Its interpretation is divided as follows: a score of 0 to 4 is considered as good sleep; a score of 5 to 10 is considered as poor sleep, and scores of 11 or more indicate the presence of a sleep disorder. Therefore, higher indices indicate worse sleep quality. This instrument has a high degree of internal consistency, with a Cronbach's alpha of 0.83[12,13].

Intervention

The deprescribing process was performed according to the following stages:

(1) Patient evaluation and application of the research instruments.

(2) Patient stratification into groups: those using BRZA (for more than 4 weeks) and those who did not use BZRA.

(3) Psychoeducation of BZRA users on the harms of the long-term use of this drug class and presentation of a deprescribing plan.

(4) Shared decision-making for facilitating the deprescribing process.

(5) Guidance on sleep hygiene and behavioral measures for relieving baseline symptoms (anxiety and depression symptoms).

(6) Application of the deprescribing plan.

(7) Monitoring and recording. Patients were monitored at each follow-up visit.

The deprescribing plan[3] was elaborated based on an ensemble of guidelines extracted from the BZRA Deprescribing Algorithm and Guidelines[8], the Beers criteria[4], START/STOPP5, FORTA[6], and the Brazilian Consensus on Potentially Inappropriate Medications for Older Adults[7]. This plan consists in gradually reducing the BZRA dose by 25% at each follow-up visit; if this is not possible due to the lack of readily available doses, the dose should be reduced by 50% until complete discontinuation. In case of withdrawal symptoms or any discomfort, the patient should return to the last well-tolerated dose for a longer period (one month) and then continue tapering the dose. Before starting deprescribing, treatment of underlying psychiatric conditions was initiated and/or adjusted with pharmacological measures (antidepressants, mood stabilizers, antipsychotics, anticonvulsants, non-benzodiazepine sleep aids such as melatonin) and non-pharmacological measures (improvements in lifestyle with a healthy diet and physical activity, sleep hygiene, and psychotherapy). When necessary, other alternative drugs (mentioned above) were added to treatment as substitutes.

Statistical analysis

Data were stored in an Excel spreadsheet and analyzed with SPSS software, version 21.0. The normality of data distribution was verified with a Kolmogorov-Smirnov test. Descriptive, non-parametric data were presented as median values and interquartile ranges, parametric data were presented as means and standard deviations, and categorical variables were described by absolute and relative values. For comparing quantitative measures, we used Student's t and Mann-Whitney tests; for verifying the association between categorical measures, we used Pearson's chi-square and Fisher's exact tests.

The Generalized Estimating Equations model was used for verifying differences between the scale results of patients using BZRA or not and the behavior of both groups throughout time. Statistical significance was set at $p < 0.05$.

Results

We evaluated 74 patients with a mean age of 71.3 ± 7.5 years, mostly female (74.3%); most of them had a partner/roommate (54.2%), had 9 to 12 years of formal education (43.1%), lived with someone (spouse, family member, or caregiver) (84.9%), were retired (76.1%), received assistance via health insurance (79.7%), faced clinical comorbidity (87.8%) with a median of 3 concomitant comorbidities, and used clinical and psychiatric drugs (74.3%). No significant statistical association was observed between the studied sociodemographic variables and the groups (use of BZRA or not). BZRA users also used more psychiatric medications (median of 2 vs 1) ($p = 0.001$) and a higher number of drugs in total (median of 7 vs 6) ($p = 0.009$) (**Table 1**).

Table 1 – Characteristics of the total sample according to the use (or not) of BZRA by older adults assisted at a geriatric psychiatry outpatient clinic of a tertiary hospital between March 2020 and October 2021 (n = 74).

Characteristics	Total n (%)	BZRA use		P
		Yes n (%)	No n (%)	
Age in years (mean±SD)	71.3±7.5	72.6±7.8	69.9±7.0	0.124*
Sex				0.697‡
Female	55 (74.3)	29 (72.5)	26 (76.5)	
Male	19 (25.7)	11 (27.5)	8 (23.5)	
Has a partner/roommate				0.844‡
Yes	39 (54.2)	21 (55.3)	18 (52.9)	
No	33 (45.8)	17 (44.7)	16 (47.1)	

Characteristics	Total n (%)	BZRA use		P
		Yes n (%)	No n (%)	
Education (years of schooling)				0.192*
0-4	13 (18.1)	10 (26.3)	3 (8.8)	
5-8	14 (19.4)	7 (18.4)	7 (20.6)	
9-12	31 (43.1)	16 (42.1)	15 (44.1)	
≥13	14 (19.4)	5 (13.2)	9 (26.5)	
Living arrangement				0.936ǂ
With someone	62 (84.9)	33 (84.6)	29 (85.3)	
Alone	11 (15.1)	6 (15.4)	5 (14.7)	
Retired				0.632ǂ
Yes	54 (76.1)	29 (78.4)	25 (73.5)	
No	17 (23.9)	8 (21.6)	9 (26.5)	
Type of health assistance				0.272ǂ
Health insurance	59 (79.7)	30 (75.0)	29 (85.3)	
Private	15 (20.3)	10 (25.0)	5 (14.7)	
Presence of clinical comorbidity				0.999ǂ
Yes	65 (87.8)	35 (87.5)	30 (88.2)	
No	9 (12.2)	5 (12.5)	4 (11.8)	
Clinical comorbidities (median, IQR)	3.0 (1.0-4.0)	3.0 (1.0-4.0)	3.0 (1.0-4.0)	0.754§
Clinical drugs	9 (12.2)	1 (2.5)	8 (23.5)	£
Psychiatric drugs	10 (13.5)	5 (12.5)	5 (14.7)	£
Clinical and psychiatric drugs	55 (74.3)	34 (85)	21 (61.8)	£
Clinical drugs (median, IQR)	4.0 (2.0-6.0)	4.0 (2.0-7.0)	3.5 (1.8-5.0)	0.245ǂ
Psychiatric drugs (median, IQR)	2.0 (1.0-2.3)	2.0 (2.0-3.0)	1.0 (0.8-2.0)	0.001ǂ
Total drugs (median, IQR)	6.0 (3.8-8.0)	7.0 (4.0-9.0)	6.0 (3.0-6.5)	0.009ǂ
Total	74 (100%)	40 (54.1%)	34 (45.9%)	

p: *: Student's t-test; ǂ: Pearson's chi-square test; ǂ: Fisher's exact test; §: Mann-Whitney test. £: data did not allow significance analysis; IQR: interquartile range; SD: standard deviation. Missing data were: one for household living arrangement; two for marital status and education level; three for retired.

The most frequent diagnostic hypotheses attributed to patients who sought assistance were depressive disorders (29.7%), mixed anxiety and depressive disorder (25.7%), anxiety and/or panic disorders (17.6%), and bipolar affective disorder (14.9%). Insomnia as an isolate diagnosis was present only in one older adult (1.4%).

Around 40 (54.1%) individuals were BZRA users, among which Zolpidem (18.9%) and Clonazepam (17.6%) were the most frequently used drugs with a median duration of use of 12 months. Their prescription was most frequently made by a psychiatrist (30.0%) or internist (30.0%), and patients resorted to other physicians for new requests (82.5%) (**Table 2**).

Table 2 – Variables related to sleep and BZRA use in older adults assisted at a geriatric psychiatry outpatient clinic of a tertiary hospital between March 2020 and October 2021 (n = 74).

Variables	n (%)
BZRA use	
Yes	40 (54.1)
No	34 (45.9)
Type of BZRA	
Clonazepam	13 (17.6)
Diazepam	7 (9.5)
Alprazolam	3 (4.1)
Bromazepam	5 (6.8)
Lorazepam	2 (2.7)
Flurazepam	1 (1.4)
Non-benzodiazepines	
Zolpidem	14 (18.9)
Duration of use in months (median, IQR)	12.0 (5.0-90.0)
Who prescribed it?	
Psychiatrist	12 (30.0)
Internist	12 (30.0)
Cardiologist	9 (12.2)
Neurologist	4 (10.0)
Self-medication	3 (4.1)
Who renewed the prescription?	
Different physicians	33 (82.5)
Always the same physician	5 (12.5)
Self-medication	2 (5.0)

Individuals who used BZRA presented higher dropout rates (n = 26, 65%) when compared to those who did not use this drug class (n = 14, 41.1%) (p = 0.008). The highest dropout rate regarding the follow-up of BZRA users occurred after the first consultation (n = 13, 32.5%); these individuals did not return for a second follow-up visit.

Out of 14 patients who got to the end of the deprescribing process, 7 (17.5%) achieved complete discontinuation, 5 (12.5%) reduced their use of BZRA, and 2 (5%) continued using them (Figure 1). A median of 5.5 consultations were required for the deprescribing process. Only one patient presented withdrawal symptoms with tapering and none after total discontinuation.

Out of 27 patients who attended the second follow-up visit, 21 (77.8%) did not correctly adhere to the instructed prescription; at the third visit, out of 23 patients, 13 (56.2%) did not adhere to the prescription; at the fourth visit, out of 18 patients, 9 (50%) did not adhere to the prescription; at the fifth visit, out of 15 patients, 2 (15%) did not adhere to the prescription, and from the sixth visit onwards, only 1 patient (7.1%) did not adhere to the prescription (**Table 3**).

Table 3 – Variables related to medical follow-up visits and adherence to desprescription among older adults who used BZRA assisted at a geriatric psychiatry outpatient clinic of a tertiary hospital between March 2020 and October 2021 (n = 40).

Follow-up visit	Attendance n (%)	Adherence to desprescription	
		Yes n (%)	No n (%)
1	40 (100%)	-	-
2	27 (67.5%)	6 (22.2%)	21 (77.8%)
3	23 (57.5%)	10 (43.8%)	13 (56.2%)
4	18 (45.0%)	9 (50%)	9 (50%)
5	15 (37.5%)	13 (85%)	2 (15%)
6	14 (35%)	13 (92.9%)	1 (7.1%)
7	14 (35%)	14 (100%)	0

The mean scores of instruments assessing depression and anxiety symptoms were lower at the final assessment in relation to the baseline ($p < 0.001$), but with no statistical difference between groups. As to sleep quality, BZRA users presented higher baseline values ($p < 0.036$). Regarding their final assessment, both groups presented reduced scores when compared to the baseline ($p < 0.001$) (**Table 4**).

Table 4 – Results of the depression, anxiety, and sleep quality scales through time among older adults who used BZRA or not, assisted at a geriatric psychiatry outpatient clinic of a tertiary hospital between March 2020 and October 2021 (n = 74).

Variables	BZRA use		P		
	Yes (mean±SD)	No (mean±SD)	Groups	Time	Groups vs time
Depression			0.440	<0.001	0.025
Baseline	$7.8^{a.*}$±0.4	$6.6^{a.*}$±0.5			
Final assessment	$3.0^{b.*}$±0.5	$4.3^{b.*}$±0.7			
Anxiety			0.238	<0.001	<0.001
Baseline	$13.1^{a.*}$±0.8	$10.4^{a.*}$±1.0			
Final assessment	$3.5^{b.*}$±0.6	$6.3^{b.*}$±1.2			
Sleep quality			0.036	<0.001	0.835
Baseline	$11.0^{a.A.}$±0.7	$8.4^{a.B.}$±0.8			
Final assessment	$4.5^{b.}$±0.4	$3.5^{b.}$±0.5			

p: Generalized Estimating Equation with a Bonferroni post hoc test (different lower-case superscript letters indicate a significant statistical difference between groups; upper-case superscript letters indicate a statistical difference between the baseline and the final assessment; an asterisk indicates statistically different behavior of variables between groups through time).
SD: standard deviation.
Depression: Geriatric Depression Scale – GDS15; Anxiety: Geriatric Anxiety Inventory; sleep quality: Pittsburgh Sleep Quality Index.

When questioning patients about their ideal sleep pattern, they reported preferring to fall asleep at 22:00, to wake up at 08:00, sleeping for 9 hours, and most of them would rather not wake up during the night (59.5%) (**Table 5**).

Table 5 – Sleep-related variables in older adults assisted at a geriatric psychiatry outpatient clinic of a tertiary hospital between March 2020 and October 2021 (n = 74).

Variables	Total n (%)	BZRA use		P
		Yes n (%)	No n (%)	
Bedtime (mean±SD)	22.0±2.7	22.0±1.0	21.9±3.8	0.889[a]
Getting up time (mean±SD)	8.0±1.1	7.8±1.2	8.3±0.8	0.037[a]
Number of hours of sleep (mean±SD)	9.3±1.7	9.2±1.7	9.4±1.7	0.649[a]
Wakes up in the middle of the night				0.292[b]
No	44 (59.5%)	26 (65.0%)	18 (52.9%)	
Yes	30 (40.5%)	14 (35.0%)	16 (47.1%)	

p: a: Student's t-test; b: Pearson's chi-square test; SD: standard deviation.

Discussion

The present study proposed to describe the frequency with which older adults assisted at a geriatric psychiatry outpatient clinic had indications for BZRA deprescribing, as well as their characteristics; the appearance of withdrawal symptoms; their adherence to instructions given during deprescribing; dropout rates; levels of depression, anxiety, and sleep quality; along with their impression of an ideal sleep pattern compared to those who did not use this drug class.

More than half of the older adults assisted at our outpatient clinic used BZRA. The frequency of the use of these drugs among older adults is heterogeneous, varying from 10% to 42% in the general population and reaching up to 60% in hospitalized patients[9,14–17]. Their broad use observed in this study, even though we analyzed outpatient care, is probably due to a relationship with the psychiatric specialty and because our study was performed at a tertiary hospital. This way, the percentages observed in this study were higher and similar to values observed in hospitalized patients.

In the literature, data on who prescribes BZRA the most are inconsistent. Some studies indicate that internists, especially at primary care level, prescribe BZRA the most in absolute numbers because they care for a larger number of patients; other state that psychiatrists are the main prescribers[15,18,19]. The available data indicate a similarity between the main prescribers: both were present at the same rates. In 62.5% of BZRA prescriptions, the prescriber was another physician (not a psychiatrist). This way, it is reasonable to invest in the education of these professionals on the harms of long-term BZRA use or even on avoiding their use, as well as to promote the implementation of deprescribing strategies, thus ensuring higher safety and quality of life for older adults.

Important and striking data refer to the way older adults renew their BZRA prescriptions. Around 82.5% of prescription renewals were performed by different physicians, that is, treatment was not continued by the same professional. Changing the responsible physician can end up hindering the assessment of correct medication use. Although prescribing professionals acknowledge the risks, 50% of them continue renewing prescriptions, justifying their actions because they feel uncomfortable changing a medication prescribed by a colleague[20]. They also report issues such as lack of time and mental health resources[21]. This way, we observed that physicians who do not have an established doctor-patient relationship tend to maintain the prescription and make deprescribing more difficult.

Most of the older adults who used BZRA dropped out of outpatient follow-up, not returning for a second visit. The conduct at the first follow-up visit was to maintain the BZRA prescription

with no changes and add psychoeducation. The probable explanation for this high initial dropout rate may be related to the patient's fear of being denied the medication in the future. One of the limitations of this study was the absence of supportive psychotherapy treatment and/or psychoeducation strategies apart from the clinical consultation.

Some studies evaluated the openness of older adults to deprescribing BZRA. Results showed that most of them are available to talk about this theme, understand the need for deprescribing, and wish to participate in deprescribing strategies. However, when it comes to putting it into practice (actual drug tapering), they become resistant[22,23]. It is important to note that patients in these studies received psychoeducation on the theme (long-term use of BZRA) and then spontaneously reached out to the program for participating in deprescribing strategies. In the present study, on the other hand, older adults first sought assistance wishing to receive the medication and found a place that aimed to optimize prescriptions, having deprescribing among its strategies.

In 17.5% of the older adults who participated in this study, we were able to reach complete discontinuation of BZRA; when considering the older adults who reduced the use of these drugs, this rate increases to 30%. Nevertheless, these values are lower than those found in the literature, ranging from 20% to 80%[4,5,8,20,24–27]. It is important to highlight that not all studies were performed specifically with the older adult population. In this age group, the deprescribing process can be even more complex, and more strategies may be required for safe and effective deprescribing.

Another factor that may interfere with BZRA deprescribing is the possibility of their interruption causing withdrawal symptoms, leading to negative outcomes. This scenario can affect the conduct of the prescriber, who fears interrupting the use of this drug class[8]. Only one of the participants in this study presented withdrawal symptoms, being instructed to return to the last effective dose and continue using it for a longer period before moving forward with the tapering steps[5,8]; no interference was seen in the success rate. Therefore, the occurrence of withdrawal symptoms should not discourage deprescribing, on the contrary, proper patient monitoring is important throughout all stages of the process as well as interventions to minimize withdrawal symptoms, if necessary.

We observed that patients had difficulties adhering to the proposed drug regimen, especially at the second follow-up visit; this margin was continually reduced until the sixth visit. That is, the doctor-patient relationship was being strengthened, which together with clinical improvement made the older adults feel safer when following recommendations. Studies demonstrate that patients who trust their prescriber are more prone to adhering to recommendations, facilitating BZRA deprescribing[28].

The depression and anxiety scores at the beginning and end of treatment were similar in BZRA users and non-users, with higher levels at the beginning of the treatment and lower levels at the end. Therefore, we verified that the long-term use of this drug class for controlling depression and anxiety symptoms was ineffective and the clinical picture can be stabilized with other measures, whether pharmacological (such as the use of safer medications for older adults) or non-pharmacological.

According to the literature, the first-line pharmacological treatment of depression and anxiety symptoms involves antidepressants, especially serotonin reuptake inhibitors and norepinephrine reuptake inhibitors [29,30,31]. Sometimes, initial treatment requires BZRA for controlling isolated symptoms, insomnia, and anxiety crises until antidepressants reach their therapeutic threshold; no additional benefits are observed after this initial period[32]. Therefore, once clinical stabilization has been reached, BZRA deprescribing should be recommended.

When questioned about their ideal sleep pattern, the older adults reported preferring to fall asleep on average at 22:00, to wake up at 08:00, sleeping for 9 hours, and most of them would rather not wake up during the night. These data highlight their inaccurate belief on how ideal

sleep should be like at this stage of life, which contributes to dissatisfaction with their sleep schedule and to indiscriminate use of medications in order to try to reach this ideal imagined sleep pattern.

It is known that sleep changes with age, and complaints related with sleep alterations increase even in the absence of disorders, occurring in more than 50% of older adults[33]. Due to changes in the circadian rhythm, it is natural for older adults to have fragmented sleep (ie, including nocturnal awakenings) that lasts less than in young or middle-aged individuals, with a mean duration of 6-7.5 hours[34,35].

BZRA users presented higher scores at the sleep quality scales than non-users, and both groups reduced these scores at the end of the treatment, gaining control over the displayed symptoms. This way, once again data show that the use of this drug class is not necessarily effective for controlling sleep-related complaints and that investing in other strategies such as sleep hygiene and control of baseline pathologies could be more effective.

This study was performed between March 2020 and October 2021, which coincided with the COVID-19 pandemic. As older adults are a high-risk group for COVID-19, many of them feared leaving the house; on top of that, health authorities recommended social isolation. This situation may have contributed to the number of dropouts, as well as a higher difficulty in deprescribing BZRA due to increased uncertainty in face of the pandemic.

Conclusions

We conclude that BZRA deprescribing is viable in the older adult population with few adverse effects, as instructed by current guidelines. However, the success of complete discontinuation can vary according to the population and intervention employed, emphasizing that the crucial moment for successful BZRA deprescription with the elderly should be at the first consultation. Older adults should be considered the most important aspect in the focus of deprescribing strategies; the decision should be shared and involve the physician, the multidisciplinary team, the patient, and the family, otherwise non-adherence will affect the outcomes and maintain chronic problems related to inadequate use of BZRA. The levels of anxiety, depression, and sleep quality improved even after BZRA discontinuation, underscoring that the basis of treatment should happen with other drug classes such as antidepressants in addition to non-pharmacological measures, psychoeducation, and sleep hygiene.

Further research is required on BZRA deprescribing in older adults, as this group is highly susceptible to the adverse effects of these drugs, in order to understand the factors involved and help health professionals conduce the deprescribing process, optimizing success rates and especially associating with dynamic psychotherapy resources.

Acknowledgments

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001.

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Os textos deste artigo foram revisados pela SK Revisões Acadêmicas e submetidos para validação do(s) autor(es) antes da publicação.