Patterns of chronic benzodiazepine use in the elderly

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Abstract

Background: In several countries, prevalence studies demonstrate that chronic use of BZD in the elderly population is very high. This scenario has reached pandemic proportions for decades and is an important public health problem. Objectives: To examine the independent association between chronic benzodiazepine use in depression, anxiety and bipolar disorder, as well as other clinical and sociodemographic factors. Methods: This cross-sectional study was developed from a population-based survey and conducted from March, 2011 to December, 2012 using a random sample of 550 elderly people who were enrolled in the Family Health Strategy in Porto Alegre, Brazil. Data was collected from identifying epidemiological and health data (sociodemographic, self-perception health, self-reported diseases, smoking, alcohol and pharmacotherapeutic evaluation) and from the diagnoses of mood and anxiety disorders. Results: Elderly patients diagnosed with depression, anxiety, concomitant depression/anxiety and bipolar disorders, and those who were using antidepressants have a higher risk of benzodiazepine use. Individuals who self-reported drinking alcohol had a lower risk of benzodiazepine use. Discussion: Benzodiazepines are often used by the elderly for long periods, which has a direct impact on the treatment of mood and anxiety disorders and on vulnerable groups such as the elderly, who may be unnecessarily taking these drugs.

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Introduction

Benzodiazepines (BZD) comprise a subgroup of psychotropic drugs that act selectively to allosterically modulate gamma-aminobutyric acid subtype A (GABAA) receptor and mediate inhibitory synaptic transmission throughout the central nervous system1. They are commonly recommended for a variety of conditions such as anxiety, depression, somatic complaints, insomnia, alcohol withdrawal, delirium and violence and aggressive behavior in psychoses and disorders induced by neuroleptics2-4. The therapeutic indication for this group of drugs should be short term and for specific conditions such as those mentioned above.

Elderly people are more likely to use BZD2, but they feel less secure and have questionable clinical indications for taking BZD such as nonspecific emotional suffering3 or a chronic insomnia complaint. In several countries, prevalence studies demonstrate that chronic use of BZD in the elderly population is high, ranging from 3.9% to 35.9%6-8. This scenario has reached pandemic proportions for decades and is an important public health problem, because chronic use of this drug results in an increase in morbidity factors related to the risk of falls, intoxication and worsening of depressive symptoms and cognition9,10.

Depressive10,11 and anxiety disorders are frequent in the elderly, constituting an important source of emotional suffering and consequently the increased use of this pharmacological class8-13. Newer treatment consensus recommendations for depressive and anxiety disorders do not suggest BZDs as a first-line therapeutic14,15. The risk/benefit ratio increases when treating these disorders in the elderly, making the indication for BZD even more unfavorable. This is because of pharmacokinetic and pharmacodynamic changes that occur with aging, which may lead to an increased sensitivity of these individuals to the effects of BZD.

Thus, this study aims to examine the independent association between chronic BZD use in depression, anxiety and bipolar disorders, as well as other clinical and sociodemographic factors in a sample of elderly people who are enrolled in the Family Health Strategy (FHS).

Methods

Study design

This cross-sectional study was developed from the population-based survey entitled “The multidimensional study of the elderly in the family health strategy in Porto Alegre, Brazil (EMI-SUS)”16. The EMI-SUS was conducted from March, 2011 to December, 2012 and enrolled a random sample of elderly people who were participating in the FHS in Porto Alegre (RS/Brazil). Inclusion criteria were age ≥ 60 years and records registered in the FHS.

Data collection

The data collection procedure included identifying epidemiological and health data (sociodemographic, self-perception health, self-reported diseases, smoking, alcohol and pharmacotherapeutic evaluation) that were collected by community health agents at the homes of the elderly and during specialized psychiatric evaluation, which was carried out by professionals trained at the Hospital São Lucas of Pontificia Universidade Católica do Rio Grande do Sul.

The mood disorder (major depression/dysthymia, bipolar) and anxiety diagnosis was made by psychiatrists using the DSM-IV criteria, and following the mental health evaluation protocol of the study17. The validated Brazilian version of the Mini-International Neuropsychiatric Interview (MINI) was used for evaluating psychiatric diagnoses18, and the psychometric properties of the instrument were considered satisfactory to excellent, with a good accuracy for anxiety and mood disorders in primary health care in Brazil19.

For pharmacotherapeutic evaluation, the participants were asked to specify all drugs used. In the interview conducted by the
community health agent, this information was confirmed from prescriptions, drug packaging and medical records at the FHS. Drugs were coded according to the Anatomical Therapeutic Chemical (ATC) classification system recommended by the World Health Organization. In this study, psychotropic medications included were BZD (N05BA, N03AE01), antidepressants (N06A, N06CA01), antiepileptic (N03A), antipsychotics (N05A) and other psychotropic drugs (N04AA02, N04BA01, N05BB01, N06BA07, N06BC01).

Sample size

The sample size of the study was calculated using a 0.05 significance level. Considering a target population of 22,000 elderly people enrolled by ESF in Porto Alegre, a minimum sample size of 491 elderly people was chosen, considering a 3.5% acceptable error for an expected prevalence of 20.0%.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (IBM SPSS Inc. Chicago, Illinois, version 17). The variables were described by the frequency, mean and standard deviation. Associations between categorical variables were tested using Pearson’s chi-square test. In specific cases, the chi-square test for linear tendency (ordinal variables with few categories) was used. To control for confounding variables and independence of variables, multivariate analysis was performed through Poisson regression.

Ethical considerations

This study was approved by the Ethical Research Committee of the Pontifícia Universidade Católica do Rio Grande do Sul (number 10/04967) and Porto Alegre Municipal Department of Health (registration 499/process 001.021434.10.7). All participants were informed of the objectives and research methods and they signed an informed consent form, according to the Guidelines and Norms Regulating Research of Resolution 196/96 of the National Health Council of the Ministry of Health.

Results

The 550 individuals included in the study were between 60 and 103 years of age (mean age, 68.6 ± 7.2 years), and comprised mostly females (63.1%). Most of these elderly people were married (37.8%), had incomplete primary education (69.1%), a little more than half of the individuals (55.0%) received less than one minimum wage (250 US dollars) and little more than half of the families (55.5%) received less than three minimum wages.

The prevalence of BZD use was 7.3%. This prevalence is compared with sociodemographic variables in Table 1. Those who had been widowed were found to use more BZD (10.8%) while single people used less BZD (1.1%; \( P = 0.044 \)). There were no statistically significant differences in the other sociodemographic variables.

Elders diagnosed with mood disorders represented 38.2% of the total population studied, with depression responsible for 28.8% and anxiety 20.2%. Elderly people without a diagnosis of mood disorder used less BZD (1.1%; \( P = 0.003 \)) and anxiety (10.5%) used BZD more often. Those who self-reported that they drank alcohol had a lower risk of using BZD. Individuals who self-reported that they drank alcohol had a lower risk of BZD use.

Discussion

Large-scale BZD use has been widely accepted worldwide, because these drugs have been considered to be effective as anxiolytics and they are safer than the drugs that were previously available, such as barbiturates. The benefit of a lower toxicity and less potential to develop a chemical dependency contributed to the widespread BZD use over the past decades; this transformed a “benefit” into an important public health problem, especially in the elderly who are typically the main consumers this type of drug.

The prevalence of BZD use (7.3%) is considered high. Brunoni et al. presented data from six universities located in different Brazilian regions (São Paulo, Rio de Janeiro, Salvador, Porto Alegre, Belo Horizonte and Vitória), where they detected a BZD use prevalence of 3.9% (in those 35 to 75 years of age), and older people were the most likely to use BZD (OR 3.48). The prevalence was even higher (21.7%) in an elderly community sample of residents of the city of Bambuí, Minas Gerais, Brazil. Prevalence rates in other countries ranged from 16% in Australia to 31% in Finland and 36% in Canada. These results are particularly important because there are guidelines that classify the BZD use as inappropriate, particularly because of side effects in the elderly.

Table 1. Benzodiazepine (BZD) use compared with sociodemographic variables

| Sociodemographic variables | BZD use | \( P \) |
|----------------------------|---------|------|
| Gender                     |         |      |
| Female                     | 317 (91.4) | 30 (8.6) | 0.105† |
| Male                       | 193 (95.1) | 10 (4.9)  |      |
| Age (years)                |         |      |
| 60-69                      | 315 (52.6) | 25 (7.4)  | 0.875‡ |
| 70-79                      | 152 (92.7) | 12 (7.3)  |      |
| 80 or more                 | 43 (93.5) | 3 (6.5)   |      |
| Race                       |         |      |
| White                      | 320 (91.2) | 31 (8.8)  | 0.270‡ |
| Black                      | 96 (97.0) | 3 (3.0)   |      |
| Brown                      | 71 (93.4) | 5 (6.6)   |      |
| Other                      | 15 (93.8) | 1 (6.3)   |      |
| Marital status             |         |      |
| Married                    | 190 (92.7) | 15 (7.3)  | 0.044† |
| Widowed                    | 141 (89.2) | 17 (10.8) |      |
| Divorced                   | 83 (93.3) | 6 (6.7)   |      |
| Single                     | 90 (98.9) | 1 (1.1)   |      |
| Education (years)          |         |      |
| 0                          | 79 (95.2) | 4 (4.8)   | 0.299† |
| 1-7                        | 341 (91.4) | 32 (8.6)  |      |
| 8 or more                  | 80 (95.2) | 4 (4.8)   |      |
| Individual income (minimum wage) |         |      |
| <1                         | 302 (91.8) | 27 (8.2)  | 0.215‡ |
| 1 or more                  | 179 (94.7) | 10 (5.3)  |      |
| Total                      | 510 (92.7) | 40 (7.3)  |      |

† Pearson chi-square test; superscript numbers show results of residual analyses.
‡ Chi-square test for linear tendency.
Table 2. Benzodiazepines (BZD) use compared with clinical and health variables

| Clinical and health variables       | BZD |   | P  |
|-----------------------------------|-----|---|----|
|                                   | No n (%) | Yes n (%) |   |
| Mood or Anxiety disorder          |         |         |    |
| No                                | 307 (97.8) | 7 (2.2) | <0.001† |
| Depression                        | 87 (84.5) | 16 (15.5) |   |
| Anxiety                           | 34 (89.5) | 4 (10.5) |   |
| Depression and Anxiety            | 45 (88.5) | 7 (13.5) |   |
| Bipolarity                        | 27 (84.4) | 5 (15.6) |   |
| Self-perceived health              |         |         |    |
| Great/Good                        | 183 (94.8) | 10 (5.2) | 0.003† |
| Regular                           | 279 (93.6) | 19 (6.4) |   |
| Poor/Very poor                    | 41 (78.8) | 11 (21.2) |   |
| Smoker                            |         |         |    |
| No                                | 214 (93.4) | 15 (6.6) | 0.161† |
| Yes                               | 183 (93.8) | 12 (6.2) |   |
| Ex-smoker                         | 98 (88.3) | 13 (11.7) |   |
| Alcohol use                       |         |         |    |
| No                                | 327 (90.8) | 33 (9.2) | 0.001† |
| Yes                               | 150 (98.7) | 2 (1.3) |   |
| Drug use                          |         |         |    |
| 0                                 | 74 (100.0) | 0 (0.0) | <0.001† |
| 1-2                               | 111 (95.7) | 5 (4.3) |   |
| 3-4                               | 127 (93.4) | 9 (6.6) |   |
| 5 or more                         | 196 (88.3) | 26 (11.7) |   |
| Pharmacological classes           |         |         |    |
| Antidepressants                   |         |         |    |
| No                                | 458 (96.8) | 15 (3.2) | <0.001† |
| Yes                               | 52 (67.5) | 25 (32.5) |   |
| Antipsychotics                    |         |         |    |
| No                                | 498 (93.6) | 34 (6.4) | <0.001† |
| Yes                               | 12 (66.7) | 6 (33.3) |   |
| Antiepileptics                    |         |         |    |
| No                                | 501 (93.1) | 37 (6.9) | 0.017‡ |
| Yes                               | 9 (75.0) | 3 (25.0) |   |
| Others psychotropics              |         |         |    |
| No                                | 494 (92.9) | 38 (7.1) | 0.524‡ |
| Yes                               | 16 (88.9) | 2 (11.1) |   |

† Pearson chi-square test; superscript numbers show results of residual analyses.
‡ Chi-square test for linear tendency.

Table 3. Final model of multivariate analysis using Poisson regression

| Variable                  | PR   | CI 95%      | P    |
|---------------------------|------|-------------|------|
| Mood or Anxiety disorder  |      |             |      |
| No                        | 1    |             |      |
| Depression                | 2.92 | 1.08-7.85   | 0.034|
| Anxiety                   | 7.06 | 2.44-20.44  | <0.001|
| Depression and Anxiety    | 3.51 | 1.32-9.37   | 0.012|
| Bipolarity                | 3.54 | 1.04-12.11  | 0.044|
| Antidepressants           |      |             |      |
| No                        | 1    |             |      |
| Yes                       | 8.60 | 4.14-17.89  | <0.001|
| Alcohol use               |      |             |      |
| No                        | 1    |             |      |
| Yes                       | 0.23 | 0.06-0.94   | 0.040|

PR: prevalence ratio; CI: confidence interval.
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Conflicts of interest and financial disclosure
None was declared.

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