Prescribing pattern of benzodiazepines in outpatients without a diagnosis of mental disorders - Retrospective study

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Abstract

Introduction: Benzodiazepines (BZD) are efficient drugs used to reduce anxiety, treat insomnia, or used as myorelaxants. BZDs are generally recommended for short-term use due to numerous side-effects and addiction.

Objective: To investigate the prescribing pattern in family medicine outpatient clinics, in patients without the diagnosis of a mental disorder, and the influence of socio-demographic characteristics on BZD use.

Method: A retrospective study of BZDs use, in a ten-year period (2009-2019), was conducted in patients treated in five family medicine teams of three primary health care centers in the Republic of Srpska. The study was carried out by reviewing electronic health records (EHRs) of patients above 18 years of age. The patients with the diagnosis of mental disorders were not recruited in the study. The study included 8560 EHRs, and 259 patients with the diagnosis of the mental disorders were excluded from the study.

Results: Out of a total of 8301 analyzed EHRs, in 1044 (12.58%) patients at least one prescription for BZDs was found in a ten-year period. Females used BZDs in a greater percentage (71.07%), persons older than 65 years (44.54%), patients with secondary school education (60.44%), patients with chronic diseases (88.60%), patients living in an urban environment (75.96%). The most prescribed BZD was bromazepam (80.17%).

Conclusion: The use of BZDs in our patients is quite considerable when compared to recommendations. The strategies to reduce BZD prescribing are necessary to reduce the chronic use of these drugs.

Keywords: family physician, anti-anxiety agents, prescriptions, long-term use

Obrazac propisivanja benzodiazepina ambulantnim pacijentima koji nemaju dijagnozu mentalnih bolesti - Retrospektivna studija

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Sažetak

Uvod. Benzodiazepini (BDZ) su efikasni lekovi koji se koriste za ublažavanje anksioznosti, lečenje insomnije, ili kao miorelaksanti. Preporučuju se, uglavnom, za kratkotrajnu upotrebu zbog njihovih neželjenih efekata i pojave zavisnosti.

Cilj rada. Istražiti Obrazac propisivanja benzodiazepina kod pacijenata koji se leče u ambulantama porodične medicine a koji nemaju dijagnozu mentalnog oboljenja, kao i uticaj sociodemografskih karakteristika na upotrebu BDZ.

Metod. Retrospektivna studija o upotrebi BDZ sprovedena je u desetogodišnjem periodu (2009-2019) kod pacijenata koje je lečilo pet timova porodične medicine, iz tri doma zdravlja u Republici Srpskoj. Studija je realizovana pregledanjem elektronskih kartonova (EZK) pacijenata starijih od 18 godina. Pacijenti s dijagnozama mentalnih bolesti nisu uključeni u studiju. Studijom je obuhvaćeno 8.560 EZK, ali 259 pacijenata s dijagnozama mentalnih oboljenja isključeno.

Rezultati. U desetogodišnjem periodu od ukupno 8.301 analiziranog EZK, kod 1.044 (12.58%) pacijenata pronđen je najmanje jedan recept za BDZ. Žene koriste BDZ u većem prosentu – 71.07%, stariji od 65 godina – 44.54%, pacijenti sa završenom srednjom školom – 60.44%, sa hroničnim bolestima – 88.60%, pacijenti koji žive u urbanim sredinama – 75.96%. Najpromoviraniji BDZ je bio bromazepam – 80.17%.

Zaključak. U poređenju s preporukama, upotreba BDZ kod naših pacijenata je mnogo veća. Neophodna su planiranja za smanjenje propisivanja BDZ kako bi se smanjila dugotrajna upotreba ovih lekova.

Ključne reči: porodični lekar, lekovi protiv anksioznosti, propisivanje, dugotrajna upotreba
Introduction

Benzodiazepines (BZDs) are efficient drugs, mostly prescribed to reduce anxiety, treat insomnia, cause myorelaxation, and prevent seizures. Clinical guidelines generally recommend short-term use of these drugs for up to 6 weeks. The recommendations for the short-term use limit are based on drug tolerance and addiction.

However, regardless of all recommendations, the prescribing pattern and use of BZDs worldwide is increasing. In the USA, BZDs prescription (primary for anxiety disorders and insomnia) has increased by 320% from 1996-2013. In the same period, the percentage of death outcomes related to BZDs overdose has increased by 500%-5. According to the report of The National Institute on Drug Abuse (NIDA) from 2004, 48 million people older than 12, use benzodiazepines in the USA, which is approximately 20% of the total population.

A wide-range study about the use of drugs conducted from 1996-2002, at the University of pharmacology, British Columbia (BC), Vancouver, Canada, reported that benzodiazepines are among the top prescribed drugs. Only during 2002, 84 million pills of benzodiazepines were prescribed. The same study showed 9.7% of the BC population (400.000 people) got at least one prescription for benzodiazepines during 2002.

The study conducted in Germany from 2009-2014 recruited 31 family physicians and showed that approximately 5% of patients who visited a family physician got at least one prescription for BZD. The results of the study showed that BZDs were routinely prescribed in family medicine. The study about benzodiazepine prescriptions in the Republic of Srpska (Bosnia and Herzegovina) from 2011-2018 revealed that 2.98% of all prescriptions were prescriptions for benzodiazepines. The study showed these drugs were prescribed to 10.63% of patients, and 23.81% of BZDs were prescribed for non-psychiatric diagnoses.

Many physicians often prescribe benzodiazepines for patients with depression, anxious reactions, cardiovascular and gastrointestinal diseases, tension headache, chest pain, or low back pain. It appears that BZDs not only diminish symptoms of anxiety but also diminish somatic difficulties of cardiovascular and gastrointestinal diseases, although the exact pathophysiological mechanism is not yet well understood.

The results of numerous studies revealed benzodiazepines are more often used by female patients than male patients, older patients (> 65 years), patients with chronic diseases, and patients living in urban areas.

In our country, a small number of studies on the topic of prevalence and use of benzodiazepines were conducted. The available data, we came across, reveal a high prevalence of benzodiazepine use in the patients in the Republic of Srpska. It is to be expected that patients with mental disorders use these drugs at a higher percentage. However, it is estimated

Uvod

Benzodiazepini (BZD) su efikasni lekovi koji se najčešće propisuju za smanjenje napetosti, lečenje nesancije, izazivaju miorelaksaciju i sprečavaju epileptične napade. Klinički vodiči generalno preporučuju kratkotrajnu upotrebu ovih lekova, a najduž je do 6 nedelja. Preporuke za kratkoročnu upotrebu su zasnovane na toleranciji i zavisnosti od ovih lekova.

Međutim, bez obzira na sve preporuke, Obrazac propisivanja i upotreba BZD širom sveta je u porastu. U Sjedinjenim Američkim Državama (SAD) propisivanje BZD primarno je za anksiozne poremećaje i nesancije, povećano je za 320% tokom 1996-2013. god. U istom periodu, procenat smrti koje se povezuju s predoziranjem benzodiazepinima povećan je za 500%-5. Prema izveštaju Nacionalnog instituta za zloupotrbu narkotika (NIDA) iz 2004. godine, 48 miliona ljudi starijih od 12 godina koristi BZD u SAD, što je približno 20% ukupne populacije.

Obimna studija o upotrebi lekova, sprovedena 1996. - 2002. god. na Univerzitetu za farmakologiju Britanske Kolumbije, Vankuver, Kanada, pokazala je da su BZD među najpropisivanjim lekovima. Samo tokom 2002. god. propisano je 84 miliona tableta BZD, odnosno 9,7% populacije (400.000) Britanske Kolumbije dobilo je bar jedan recept za BZD.

U studiji sprovedenoj u Nemačkoj 2009-2014. godine, učestvovao je 31 lekar porodične medicine. Pokazano je da je kod približno 5% pacijenata, koji su posetili svog porodičnog lekara, propisan najmanje jedan recept za BZD. Prema rezultatima ove studije, BZD se rutinski propisuju u ordinacijama porodične medicine. U Studiji o propisivanju BZD sprovedenoj u Republici Srpskoj (Bosna i Hercegovina) tokom 2011-2018. godine, 2,98% svih propisanih recepta BZD odnosilo se na 10,63% pacijenata, a 23,81% BZD na nepsihiatrijske dijagnoze.

Mnogi lekari često propisuju BZD pacijentima s depresijom, anksioznosću, kardiovaskularnim i gastrointestinalnim bolesima, tenzijom glavoboljom, bolom u grudima ili bolom u leđima. Izgleda da BZD ne smanjuju samo anksioskost, već i somatske tegobe uzrokovane kardiovaskularnim ili gastrointestinalnim bolesima mada tačan patofiziološki mehanizam još uvek nije poznat.

Rezultati brojnih studija otkrivaju da BZD češće koriste pacijentkinje, starije osobe (>65 godina), pacijenti s hroničnim bolesima i pacijenti koji žive u gradskim sredinama. U našoj zemlji je sproveden manji broj studija na temu pretežne upotrebe BZD. Dostupni podaci do kojih smo došli otkrivaju visoku upotrebu BZD kod pacijenata u Republici Srpskoj. Za očekivati je da pacijenti s mentalnim oboljenjima koriste ove lekove u većem procentu, međutim, uočeno je da i ih pacijenti bez dijagnoze mentalne bolesti koriste u znatnom broju.
that patients without the diagnosis of mental disorders use these drugs in a considerable number.

**Objective**

Our objective was to investigate the prescribing pattern of family physicians for BZDs in adults, without the diagnosis of mental disorders, and the influence of socio-demographic characteristics on BZD users (gender, age, level of education, marital status, residence – urban or rural).

**Method**

The research represents a retrospective study of benzodiazepines use in a ten-year period, (2009-2019). The study was conducted in five family medicine teams, from three primary health care centers in the Republic of Srpska: 3 family medicine teams from primary health care center Banjaluka, with the mainly urban population, and one team from primary care center Foca and Celinac, respectively, with the mainly rural population.

The study included all the adults over the age of 18, who were the patients of the five aforementioned family medicine teams. The study included a total of 8,560 patients. Out of this number 259 patients with mental disorders were excluded, so the remaining 8,301 patients were included in the study. For the final analysis, we used the data of the patients that had at least one prescription for benzodiazepines in a ten-year period. The data about prescribing patterns of family physicians and socio-demographic characteristics of patients were obtained from electronic health records (EHRs).

The data collection was performed by reviewing EHRs and a questionnaire was created for the purpose of this study to enter the data from the medical records. Regarding prescribing pattern of family physicians, the following data were analyzed: is the drug recommended by a family physician or prescribed following the recommendation of another specialist; the presence of chronic diseases (cardiovascular diseases, chronic pulmonary diseases, diabetes, musculoskeletal diseases, cancer); the class of used benzodiazepine (bromazepam, diazepam, alprazolam, other); the duration of therapy (<6 weeks, ≥6 weeks to 1 year, 2-5 years, 6-9 years, ≥10 years), and course of benzodiazepine therapy (continuous or “as required”).

Socio-demographic data used for the purpose of analysis were: age, gender, level of education, marital status, and residence.

For the purpose of the statistical analysis, in relation to age, patients were divided into four age groups: 18-30 years, 31-45 years, 46-64 years and ≥65 years. In relation to the educational level, patients were divided into four groups: patients without formal education, patients who graduated from primary and secondary school, and patients who graduated from a university. In relation to marital status, patients were divided into four groups: single, married, divorced, and widowed. In relation to residence, patients were divided into two groups: urban and rural.

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Istraživanje predstavlja retrospektivnu studiju deseto-godišnje upotrebe BZD (2009-2019). Studija se sprovedena u pet timova porodične medicine iz tri doma zdravlja u Republici Srpskoj: tri tima porodične medicine iz Doma zdravlja Banjaluka sa, uglavnom, urbanom populacijom i po jedan tim iz Domova zdravlja u Foću i Čelincu s pretežno ruralnom populacijom.

Studija je obuhvatila sve odrasle osobe preko 18 godina, koje su bile pacijenti pomenutih pet timova porodične medicine - ukupno 8.560 pacijenata. Od ovog broja isključeno je 259 pacijenata sa dijagnozama mentalnih bolesti, tako da je 8.301 pacijent uključen u studiju. Za konačnu analizu koristili smo podatke pacijenata kojima je bar jednom propisan BZD kod traju postmatrish deset godina. Podaci o propisivačkim obrisima porodičnih lekara i sociodemografskim karakteristikama pacijenata, dobijeni su iz elektronskih zdravstvenih kartona (EZK).

Prikupljanje podataka je izvedeno pregledanjem EZK, a osmišljen je i upitnik za potrebe ove studije kako bi se u njega uneli podaci iz zdravstvenih kartona. Što se tiče propisivačkog obrisca porodičnih lekara, analizirano je sledeće: da li je lek preporučen od strane porodičnog lekara ili je propisan po preporuci drugog specijaliste; prisustvo hronične bolesti (kardiovaskularne bolesti, hronične plućne bolesti, dijabetes, koštan-mišične bolesti, karcinomi); klasa upotrebljenih BZD (bromazepam, diazepam, alprazolam, drugi); dužina trajanja terapije (<6 nedelja, ≥6 nedelja do 1 godine, 2-5 godine, 6-9 godina, ≥10 godina) i način korišćenja BZD (kontinuirano ili ‘po potrebi’).

Sociodemografski podaci korišćeni za analizu jesu: godište, pol, nivo obrazovanja, bračni status i mesto stanovanja. Što se tiče propisivačkog obrisca porodičnih lekara, analizirano je sledeće: da li je lek preporučen od strane porodičnog lekara ili je propisan po preporuci drugog specijaliste; prisustvo hronične bolesti (kardiovaskularne bolesti, hronične plućne bolesti, dijabetes, koštan-mišične bolesti, karcinomi); klasa upotrebljenih BZD (bromazepam, diazepam, alprazolam, drugi); dužina trajanja terapije (<6 nedelja, ≥6 nedelja do 1 godine, 2-5 godine, 6-9 godina, ≥10 godina) i način korišćenja BZD (kontinuirano ili ‘po potrebi’).

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were divided into four groups: married, single, divorced, and widowed. In relation to residence, patients were divided into two groups: urban and rural. The patients from the city of Banjaluka were distributed in the group with urban residence, as the three family medicine teams mainly treat the population that lives in an urban area. The patients from Foča and Čelinac were distributed in the group with rural residence, as these two family medicine teams mainly treat the population that lives in a rural area.

This research was conducted according to the Helsinki Declaration about medical researches and the principles of good clinical practice. The approval for conducting the study was obtained from the Ethics Committee of the Primary Health Care Center Banjaluka.

Statistical analysis

The collected data were presented for at least 95% of the included patients. The categorical variables were presented as numbers and percentages and compared using the chi-square test. The continuous variables were expressed as the mean with standard deviation or median with interquartile range and compared with Student’s t-test or Mann-Whitney U test according to the data distribution and the number of groups. Kolmogorov-Smirnov test and visual assessment were used to estimate the normal distribution of continuous variables. Univariate, as well as multivariate binary logistic regression analysis, was used to identify independent predictors of ‘as needed’ treatment. All statistical analyses were performed using IBM SPSS Statistics, version 25.0 (New York, USA).

Results

Out of a total of 8301 analyzed medical records, in a 10-year period, 1044 patients (12.58%) used benzodiazepines.

Patients using benzodiazepine were most frequently females (71.07%), persons over 65 (44.54%), patients who lived in urban areas (75.96%), and patients with chronic diseases (88.60%). Married patients were the most frequent users, and in respect to education, those with secondary school (60.44%) used benzodiazepines the most (Table 1).

The largest number of benzodiazepine prescriptions was not recommended by family physicians, but other specialists (65.42%). The majority of patients were recommended to use the drugs, not as a continuous course of therapy, but ‘as needed’, 732 (70.11%). In relation to the duration of benzodiazepine therapy, the majority of patients used these drugs for 2-5 years, and a small number of patients, 169 (16.19%), used these drugs according to recommendations (<6 weeks). The most used benzodiazepines in our patients were bromazepam 837 (80.17%), diazepam 116 (11.11%), and alprazolam 61 (5.84%), while other benzodiazepines were used in a smaller percentage (Table 1).
Table 1. The characteristics of patients using benzodiazepines (n=1044)

| Variables/Variable                                      | N    | %       |
|--------------------------------------------------------|------|---------|
| **Gender/Pol**                                         |      |         |
| Female/Žene                                            | 742  | (71.07) |
| Male/Muškarci                                         | 302  | (28.93) |
| **Age (years)/Starost (godine)**                       |      |         |
| 18-30                                                  | 24   | (2.30)  |
| 31-45                                                  | 114  | (10.92) |
| 46-64                                                  | 441  | (42.24) |
| >65                                                    | 465  | (44.54) |
| **Recommended for use by/Preporučeni za upotrebu od strane** |  |         |
| Family physicians/ Porodičnog lekara                   | 361  | (34.58) |
| Other specialists /Drugih specijalista                 | 683  | (65.42) |
| **Education/Obrazovanje**                              |      |         |
| No education/Bez obrazovanja                           | 67   | (6.42)  |
| Primary school/Osnovna škola                           | 200  | (19.16) |
| Secondary school/Srednja škola                         | 631  | (60.44) |
| Faculty/Fakultet                                      | 146  | (13.98) |
| **The presence of chronic diseases/Prisustvo hroničnih bolesti** |  |         |
| Yes/Da                                                 | 925  | (88.60) |
| No/Ne                                                  | 119  | (11.40) |
| **Course of treatment/Način lečenja**                  |      |         |
| Continuous /Kontinuirano „As needed“/„po potrebi“      | 312  | (29.89) |
|                                                       | 732  | (70.11) |
| **Marital status/ Bračni status**                     |      |         |
| Married /U braku                                       | 660  | (63.22) |
| Single/Samac                                           | 83   | (7.95)  |
| Divorced /Razveden                                     | 56   | (5.36)  |
| Widowed/Udovica/udovac                                 | 245  | (23.47) |
| **Treatment duration (years)/Trajanje lečenja (godine)**|  |         |
| <6 weeks/nedelja                                       | 169  | (16.19) |
| 6 weeks/nedelja - 1 year/godina                        | 276  | (26.43) |
| 2-5                                                    | 560  | (53.64) |
| 6-9                                                    | 36   | (3.45)  |
| ≥10                                                    | 3    | (0.29)  |
| **Class of used benzodiazepine/Klasa korišćenih benzodiazepina** |  |         |
| Bromazepam                                             | 837  | (80.17) |
| Diazepam                                               | 116  | (11.11) |
| Alprazolam                                             | 61   | (5.84)  |
| Other/Drug (Zolpidem)                                  | 30   | (2.88)  |
| **Residence/Mesto stanovanja**                         |      |         |
| Urban area/Urbano područje                             | 793  | (75.96) |
| Rural area/Ruralno područje                            | 251  | (24.04) |
In relation to residence, all patients were divided into a group that lives mainly in an urban area (4,981 patients) and those who live mainly in a rural area (3.579 patients). The use of benzodiazepines was analyzed in relation to residence, as well as the influence of socio-demographic characteristics on the use of BZDs in these two groups of patients. Patients living in urban areas used BZDs in a considerably higher percentage when compared to those living in rural areas. Therefore, out of a total of 4981 analyzed EHRs from urban area residents, 793 (15.92%) were prescribed benzodiazepines, at least once, in the follow-up period. In the rural area, out of a total of 3579 analyzed EHRs, 251 (7.01%) were prescribed BZDs, at least once, in the follow-up period. (Graph. 1).

Females in urban area used BZDs more often than those in rural areas and it was statistically significant (p=0.048). The patients who graduated from secondary school and patients over 65, in urban areas, used benzodiazepines more often than those in rural areas, which was (p<0.01) statistically significant. The patients in urban areas used benzodiazepines for longer periods when compared to those from rural areas and the difference was statistically significant (p<0.01). The family physicians in urban areas independently prescribed benzodiazepines more often when compared to their colleagues working in rural areas and the statistical difference was significant (p<0.01). When considering the course of therapy (continuous or ‘as needed’ marital status, and the presence of chronic diseases, the statistically significant difference between the use of benzodiazepines in patients from urban and rural areas was not found, (Table 2).

U odnosu na mesto stanovanja, svi pacijenti su podeljeni u grupu koja uglavnom živi u urbanoj sredini (4.981 pacijenata) i one koji uglavnom žive u ruralnim područjima (3.579 pacijenata). Upotreba BZD je analizirana u odnosu na mesto stanovanja, a ispitivan je i uticaj sociodemografskih karakteristika na upotrebu BZD kod ove dve grupe pacijenata. Pacijenti koji žive u urbanim sredinama koristili su BZD u znatno većem procentu kada smo ih uporedili sa pacijentima koji žive u ruralnim područjima. Od ukupnog broja analiziranih EZK, kod 4.981 pacijenta iz urbanih područja, 793 (15.92%) je imalo propisan BZD najmanje jednom u periodu praćenja. U ruralnim područjima, od ukupnog broja 3.579 pregledanih EZK, 251 (7.01%) pacijent je imao propisan BZD najmanje jednom u periodu praćenja (Grafikon 1).
Table 2. The characteristics of patients using benzodiazepines in urban and rural areas

| Characteristic                              | Urban area/Gradsko područje (n=793) | Rural area/Seosko područje (n=251) | p*          |
|--------------------------------------------|-------------------------------------|----------------------------------|-------------|
| Gender/Pol                                  |                                     |                                  | 0.048       |
| Male/Muškarci                               | 217 (27.36)                         | 85 (33.86)                       |             |
| Female/Žene                                 | 576 (72.64)                         | 166 (66.14)                      |             |
| Education/Obradovanje                       |                                     |                                  | <0.01       |
| No education /Bez obrazovanja               | 36 (4.54)                           | 31 (12.35)                       |             |
| Primary school/Osnovna škola                | 165 (20.81)                         | 35 (13.95)                       |             |
| Secondary school/Srednja škola              | 480 (60.53)                         | 151 (60.16)                      |             |
| Faculty/Fakultet                            | 112 (14.12)                         | 34 (13.54)                       |             |
| Class of used BZD/Klasa korišćenih BZD     |                                     |                                  | <0.01       |
| Diazepam                                    | 74 (9.33)                           | 42 (16.73)                       |             |
| Bromazepam                                  | 662 (83.49)                         | 175 (69.72)                      |             |
| Alprazolam                                  | 35 (4.41)                           | 26 (10.36)                       |             |
| Other/Drugi                                 | 22 (2.77)                           | 8 (3.19)                         |             |
| Course of treatment/Način lečenja           |                                     |                                  | 0.99        |
| Continous/Kontinuirani                      | 237 (29.89)                         | 75 (29.88)                       |             |
| „As needed “po potrebi“                     | 556 (70.11)                         | 176 (70.12)                      |             |
| Recommended for use by/Preporučeni od strane|                                     |                                  | <0.01       |
| Family physician/Porodićnog lekara          | 223 (28.12)                         | 138 (54.98)                      |             |
| Other specialist/Družih specijalista        | 570 (71.88)                         | 113 (45.02)                      |             |
| Marital status/ Bračni status              |                                     |                                  | 0.203       |
| Married/U braku                             | 514 (64.81)                         | 146 (58.17)                      |             |
| Single/Samac                                | 58 (7.31)                           | 25 (9.96)                        |             |
| Divorced/Razveden                           | 39 (4.92)                           | 17 (6.77)                        |             |
| Widowed/Udovac/udovica                      | 182 (22.95)                         | 63 (25.10)                       |             |
| Chronic diseases/Hronične bolesti           |                                     |                                  | 0.219       |
| Yes/Da                                      | 708 (89.28)                         | 217 (86.45)                      |             |
| No/Ne                                       | 85 (10.72)                          | 34 (13.55)                       |             |
| Age/Starost                                  |                                     |                                  | <0.01       |
| 18-30                                       | 12 (1.51)                           | 12 (4.78)                        |             |
| 31-45                                       | 75 (9.46)                           | 39 (15.54)                       |             |
| 46-64                                       | 349 (44.01)                         | 92 (36.65)                       |             |
| >65                                         | 357 (45.02)                         | 108 (43.03)                      |             |
| Treatment duration/Trajanje lečenja          |                                     |                                  | <0.01       |
| < 6 weeks/nedelja                           | 106 (13.37)                         | 63 (25.10)                       |             |
| 6 weeks to 1 year/6 nedelja do 1 godine     | 210 (26.48)                         | 66 (26.29)                       |             |
| 2-5 years/godina                            | 473 (59.65)                         | 87 (34.66)                       |             |
| 6-9 years/godina                            | 4 (0.50)                            | 32 (12.75)                       |             |
| ≥10 years/godina                            | 0 (0.0)                             | 3 (1.20)                         |             |

*Statistically significant difference at p<0.05
*Statistički značajna razlika za p<0.05
In the regression analysis (Table 3), the BZDs recommendation by other specialists was more related to the ‘as needed’ course of treatment [OR 18.29 (12.91-25.89); p<0.001], while the treatment duration was a predictor of the continuous course of treatment (OR 0.89 (0.83-0.98); p=0.011).

Table 3. Multivariate logistic regression analysis showing associations between the different factors and ‘as needed’ treatment (n=1.044)

| Variables/Variable                        | Univariate/Univarijantna OR/NV (95% CI) | p    | Multivariate/Multivarijantna OR/NV (95% CI) | p    |
|------------------------------------------|----------------------------------------|------|------------------------------------------|------|
| Female/Žene                              | 1.89 (1.42-2.51)                       | <0.001 | 1.23 (0.86-1.77)                       | 0.253 |
| Age/Starost                              | 1.01 (0.98-1.02)                       | 0.257 |                                         |      |
| Education/Obradovanje                    | 1.04 (0.87-1.24)                       | 0.662 |                                         |      |
| Another specialist recommendation/Preporuka drugog specijalista | 20.57 (14.66-28.85)                   | <0.001 | 18.29 (12.91-25.89)                   | <0.001 |
| Presence of chronic diseases/Postoje hronične bolesti | 1.50 (1.01-2.23)                       | 0.046 | 1.05 (0.63-1.75)                       | 0.846 |
| Rural area/Seoska sredina                | 1.00 (0.73-1.36)                       | 0.999 |                                         |      |
| Treatment duration/Dužina lečenja         | 0.80 (0.75-0.86)                       | <0.001 | 0.89 (0.83-0.98)                       | 0.011 |
| Marital status/Bračni status             | 1.08 (0.97-1.20)                       | 0.185 |                                         |      |

*OR – Odds ratio  
*NV – Nivo verovatnoće

Discussion

The results of our study showed a high prevalence (12.58%) of benzodiazepine use in our patients. Female patients, patients over 65 years, and patients with chronic diseases used these drugs more often when compared to other groups of patients.

The results of other studies showed similar results considering the prescription and use of benzodiazepines. The study conducted in 2010 among the patients of a family medicine team in Primary Health care Center Banja Luka showed that even 20.41% of patients over the age of 18 got at least one prescription for benzodiazepines in a one-year period. The results of this study showed females and persons over 65 used benzodiazepines more often.

The results similar to ours were obtained in the study from Sweden. This study showed the factors related to the more frequent use of benzodiazepines were older age, female sex, living in an urban area, use of many other drugs, and simultaneous use of psychotropic drugs, especially antidepressants.

The study conducted in Pakistan aimed at investigating the prevalence of benzodiazepine use in suburban and urban population in the city of Karachi. The total prevalence of benzodiazepine use was 14%, which relates to our results. However, unlike our patients, the patients from the suburban areas, from this study, used benzodiazepines statistically sig-

U regresionoj analizi (Tabela 3) je pokazano da su preporuke za upotrebu BZD od strane drugih specijalista bile češće ‘po potrebi’ [NV 18,29 (12,91-25,89); p<0.001], dok je dužina lečenja bila prediktor kontinuirane upotrebe BZD (NV 0,89 (0,83-0,98); p=0,011).

**Discussion**

Rezultati naše studije su pokazali visoku prevalenciju, odnosno rasprostranjenost (12,58%) upotrebe BZD kod naših pacijenata. Pacijentkinje, zatim pacijenti preko 65 godina i pacijenti sa hroničnim bolestima koristili su ove lekove učestalije nego drugi pacijenti sa kojima su poredeni.

Rezultati drugih studija su prikazali slične rezultate u vezi s propisivanjem i upotrebom BZD. Studija sprovedena 2010. god. među pacijentima Doma zdravlja Banjaluka, pokazala je da čak 20,41% pacijenata, starosti iznad 18 godina, dobije najmanje jedan recept za BZD u toku jedne godine. Prema rezultatima ove studije, žene i osobe starije od 65 godina češće koriste BZD.

U studiji sprovedenoj u Švedskoj dobijeni su rezultati slični našim. Pokazano je da su faktori koji su u vezi sa češćom upotrebom BZD - starije doba, ženski pol, život u urbanoj sredini, upotreba mnogo lekova i istovremena upotreba psihotropnih lekova, naročito antidepressiva.

Studija sprovedena u Pakistanu imala je za cilj da istraži rasprostranjenost upotrebe BZD kod prigradskih i gradskih populacija grada Karači, koja je bila 14%, što je u skladu s našim nalazima. Međutim, za razliku od naših pacijenata, pacijenti iz prigradskih naselja u ovoj studiji koristili su BZD statistički značajno više nego pacijenti iz gradskih područja.
nificantly more when compared to the subjects from the urban areas\textsuperscript{19}. The results from the same study revealed that the most used benzodiazepines were bromazepam, followed by diazepam, which is the case in our patients, as well.

The study conducted in the Republic of Srpska, which also included patients with mental disorders, showed similar results as our study. Females, the elderly and patients living in urban areas used BZDs for longer periods\textsuperscript{16}. The same study also showed that people who live alone use BZDs more often, unlike the results of our study where married persons used BZDs more frequently.

The study conducted in the USA from 2003-2015 showed that the number of visits to a family doctor, due to benzodiazepine prescribing, has increased from 3.8\% in 2003 to 7.4\% in 2015. Family doctors prescribed approximately half of these drugs\textsuperscript{16}. Our study showed the opposite results, that is to say, the majority of benzodiazepines were prescribed following the recommendations of other specialists, and approximately one-third of these drugs were prescribed by family doctors independently.

Tension relieving, insomnia or worries due to one’s family financial problems, everyday life, and existential problems are mentioned as the most frequent reasons for chronic use of benzodiazepines\textsuperscript{3}.

Numerous researches showed a high prevalence of chronic use of benzodiazepines, which calls for the need to educate family physicians on methods that would decrease the overuse of these drugs\textsuperscript{17,18}. Family physicians play an important role in decreasing the long-term use of benzodiazepines. Patients should be prescribed a short-term course of these drugs, preferably for up to 4 weeks, and at the lowest effective dose for the treatment of severe anxiety, panic disorder, and acute crisis reactions. Instead of prescribing benzodiazepines for the treatment of mild anxiety and insomnia, counseling, cognitive-behavioral therapy, sleep hygiene, and strategies for self-help should be recommended. Family physicians should introduce patients with side effects of these drugs, including influence on driving, operating machinery, addiction, before benzodiazepines were being prescribed. Indications for chronic use are exceedingly rare. In these cases, it is best to ask for an opinion of a psychiatrist\textsuperscript{19,20}.

The results of our study showed that the patients in urban areas used benzodiazepines more than those in the mainly rural areas and this difference was statistically significant. We think that different lifestyles in these areas may be the reason why. It is an assumption that patients in mainly rural areas live with less stress, and they are more physically active and therefore have less need for the use of benzodiazepines.

Similar research on the topic of prescribing BZDs for patients without the diagnosis of mental disorders was not conducted in our country, as far as we know. With this study, we wanted to make a point on BZD overprescribing, and to encourage family doctors, as well as other doctors to correct their prescribing pattern and adjust them to the recommendations.

Rezultati iz iste studije su pokazali da je najčešće korišćen BZD bio bromazepam, zatim diazepam, što je slučaj i sa našim pacijentima.

Studija sprovedena u Republici Srpskoj, koja je uključila i pacijente s mentalnim oboljenjima, pokazala je slične rezultate kao naša studija. Žene, stariji pacijenti i oni koji žive u urbanim sredinama koristili su BZD u dužem periodu\textsuperscript{16}. U istoj studiji je, takođe, pokazano da ljudi koji žive sami češće koriste BZD, za razliku od naše studije gde su ljudi koji su u braku češće koristili BZD.

Studija sprovedena u SAD 2003-2015. god. pokazala je da je broj poseta porodičnom lekaru, zbog propisivanja BZD, povećan sa 3,8\% u 2003. god. na 7,4\% u 2015. god. Porodični lekari propisuju približno polovinu ovih lekova\textsuperscript{16}. Naša studija je pokazala suprotne rezultate, tj. većina BZD propisana je po preporuci drugih specijalista, a približno jedna trećina po mišljenju porodičnih lekara.

Smanjenje napetosti, nesanicu i brigu u vezi sa porodičnim finansijskim problemima, svakodnevni život i egzistencijalni problemi, pominju se kao najčešći razlozi za hroničnu upotrebu BZD\textsuperscript{19}.

Brojna istraživanja su pokazala visoku rasprostranjenost hronične upotrebe BZD, što ukazuje na potrebu za proširivanjem znanja porodičnih lekara o metodima koji bi doveli do smanjenja preterane upotrebe ovih lekova\textsuperscript{17,18}. Porodični lekari imaju važnu ulogu u smanjenju dugoročne upotrebe BZD. Pacijentima bi trebalo preporučiti kratkotrajno lečenje ovim lekovima, po mogućству do 4 nedelje, i u najmanjoj efikasnoj dozi za lečenje izražene anksioznosti, paničnih poremećaja i reakcija u akutnim krizama. Uметно propisivanja BZD za lečenje blage anksioznosti i nesanicu, treba predložiti savetovanje, kognitivno-bihejvioralnu terapiju, higijenu spavanja i strategije za samopomoć. Porodični lekari treba da uopšte najbolje ispitato, a približno jedna trećina po mišljenju porodičnih lekara.

Rezultati naše studije su pokazali da pacijenti iz urbanih sredina više koriste BZD nego oni iz ruralnih sredina i ta razlika je statistički značajna. Mišljenja smo da uzrok tome mogu biti različiti načini života u ovim oblastima. Pretpostavka je da su pacijenti koji žive mahom u ruralnim područjima izloženi manjem stresu, a i fizički su aktivniji, te otuda manja potreba za BZD.

Koliko je nama poznato, slično ispitivanje na temu propisivanja BZD pacijentima bez mentalnih bolesti, u našoj zemlji nije rađeno. Ovom studijom smo želeli da ukažemo na preterano propisivanje BZD i da ohrabrimo lekare porodične medicine, ali i druge lekare, da isprave svoju propisivačku praksu i prilagode je preporukama.
Conclusions

The results of our study showed that the use of benzodiazepines in patients without the diagnosis of mental disorder is high and considerably higher than it’s recommended. These drugs are used more by females, the elderly, and persons with chronic diseases, which is similar to the results of other studies. The patients in urban areas use benzodiazepines more than those in rural areas. The strategies to reduce the benzodiazepines prescription, which would include the education of physicians and patients, are necessary to reduce the chronic use of these drugs.

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