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

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

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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

Sažetak

Uvod. Benzodiazepini (BZD) 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 BZD.

Metod. Retrospektivna studija o upotrebi BZD 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 zdravstvenih kartona (EZK) pacijenata starijih od 18 godina. Pacijenti s dijagnozama mentalnih bolesti nisu uključeni u studiju. Studijom je obuhvaćeno 8.560 EZK, ali je 259 pacijenata s dijagnozama mentalnih oboljenja isključeno.

Rezultati. U desetogodišnjem periodu od ukupno 8.301 analiziranog EZK, kod 1.044 (12,58%) pacijenta pronađen je najmanje jedan recept za BZD. Žene koriste BZD u većem procentu – 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%. Najpropisivaniji BZD je bio bromazepam – 80,17%.

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

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

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Introduction

Benzodiazepines (BZDs) are efficient drugs, mostly prescribed to reduce anxiety, treat insomnia, cause myorelaxation, and prevent seizures¹. Clinical guidelines generally recommend short-term use of these drugs for up to 6 weeks². The recommendations for the short-term use limit are based on drug tolerance and addiction³.

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%^{4,5}. 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 population⁶.

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 prescribed⁷. 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 medicine⁸. 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 diagnoses⁹.

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 understood¹⁰.

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 areas¹¹⁻¹².

In our country, a small number of studies on the topic of prevalence and use of benzodiazepines were conducted. The available data⁹, 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 nesanice, izazivaju miorelaksaciju i sprečavaju epileptične napade¹. Klinički vodiči generalno preporučuju kratkotrajnu upotrebu ovih lekova, a najduže do 6 nedelja². Preporuke za kratkoročnu upotrebu su zasnovane na toleranciji i zavisnosti od ovih lekova³.

Međutim, bez obzira na sve preporuke, *Obrazac propisivanja i upotreba BZD* širom sveta je u porastu. U Sjedinjenim Američkim Državama (SAD) propisivanje BZD primarno za anksiozne poremećaje i nesanicu, povećano je za 320% tokom 1996-2013. god. U istom periodu, procenat smrti koje se povezuju s predoziranje benzodiazepinima povećan je za 500%^{4,5}. Prema izveštaju Nacionalnog instituta za zloupotrebu narkotika (NIDA) iz 2004. godine, 48 miliona ljudi starijih od 12 godina koristi BZD u SAD, što je približno 20% ukupne populacije⁶.

Obimna studija o upotrebi lekova, sprovedena 1996 - 2002. god. na Univerzitetu za farmakologiju Britanska Kolumbija, Vankuver, Kanada, pokazala je da su BZD među najpropisivanijim lekovima. Samo tokom 2002. god. propisano je 84 miliona tableta BZD⁷, 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 medicine⁸. U Studiji o propisivanju BZD sprovedenoj u Republici Srpskoj (Bosna i Hercegovina) tokom 2011-2018. godine, 2,98% svih propisanih recepata BZD odnosilo se na 10,63% pacijenata, a 23,81% BZD na nepsihijatrijske dijagnoze⁹.

Mnogi lekari često propisuju BZD pacijentima s depresijom, anksioznošću, kardiovaskularnim i gastrointestinalnim bolestima, tenzionom glavoboljom, bolom u grudima ili bolom u leđima. Izgleda da BZD ne smanjuju samo anksioznost, već i somatske tegobe uzrokovane kardiovaskularnim ili gastrointestinalnim bolestima mada tačan patofiziološki mehanizam još uvek nije poznat¹⁰.

Rezultati brojnih studija otkrivaju da BZD češće koriste pacijentkinje, starije osobe (>65 godina), pacijenti s hroničnim bolestima i pacijenti koji žive u gradskim sredinama¹⁰⁻¹².

U našoj zemlji je sproveden manji broj studija na temu pretežne upotrebe BZD. Dostupni podaci⁹ 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 i da 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

Cilj rada

Cilj rada je bio da ispitamo *Obrazac propisivanja BZD* kod lekara porodične medicine, za odrasle pacijente bez dijagnoze mentalne bolesti, kao i uticaj sociodemografskih karakteristika na korisnike BZD (pol, godište, nivo obrazovanja, bračni status, mesto stanovanja - grad ili selo).

Metod

Istraživanje predstavlja retrospektivnu studiju deseto-godišnje upotrebe BZD (2009-2019). Studija je 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 Foči 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 u toku posmatranih deset godina. Podaci o propisivačkim obrascima 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 obrasca 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, koštano-mišićne bolesti, karcinomi); klasa upotrebljenih BZD (bromazepam, diazepam, alprazolam, drugi); dužina trajanja terapije (<6 nedelja, ≥6 nedelja do 1 godine, 2-5 godina, 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.

Za statističku analizu, a u vezi sa starošću ispitanika, pacijenti su podeljeni u četiri grupe: 18-30 godina, 31-45 godina, 46-64 godina i ≥65 godina. Prema obrazovnom nivou, pacijenti su takođe podeljeni u četiri grupe: bez formalnog obrazovanja, sa završenom osnovnom školom, sa srednjom školom i sa fakultetom. Što se tiče bračnog statusa pacijenata, takođe su podeljeni u četiri grupe: u braku, samci, razvedeni i udovice/udovci. Prema mestu stanovanja, pacijenti su podeljeni u dve grupe: urbana i ruralna. Pacijenti iz Banjaluke dodeljeni su u grupu sa urbanim mestom stanovanja jer su tri tima porodične medicine lečila populaciju koja živi u urbanoj

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).

sredini, a pacijenti iz Foče i Čelinca su raspoređeni u grupu sa ruralnim mestom stanovanja jer su timovi porodične medicine iz oba mesta uglavnom lečili stanovništvo iz ruralnih krajeva.

Istraživanje je sprovedeno u skladu sa Helsinškom deklaracijom o medicinskim istraživanjima i principima dobre kliničke prakse. Odobrenje za sprovođenje studije dobijeno je od Etičkog komiteta Doma zdravlja Banjaluka.

Statistička analiza

Sakupljeni podaci su prikazani za najmanje 95% uključenih pacijenata. Kategoričke varijable su predstavljene kao brojevi i procenti i upoređivane su korišćenjem χ^2 testa. Kontinuirane varijable su predstavljene kao srednja vrednost sa standardnom devijacijom ili kao sredina sa interkvartalnim opsegom i upoređivani su *Studentovim t*-testom ili *Man-Vit-nijevim U* testom, prema distribuciji podataka i broju grupa. *Kolmogorov-Smirnov* test i vizuelna procena korišćeni su za određivanje normalne distribucije kontinuiranih varijabli. Univarijantna, kao i multivarijantna binarna logistička regresija su korišćene da bi se identifikovala nezavisna predviđanja vrste lečenja 'po potrebi'. Sve statističke analize su izvedene korišćenjem *IBM SPSS Statistics*, verzija 25,0 (Njujork, SAD).

Rezultati

Od ukupnog broja analiziranih zdravstvenih kartona (8.301) u desetogodišnjem periodu, 1.044 pacijenta (12,58%) su koristila BZD, najčešće žene (71,07%), zatim stariji od 65 godina (44,54%), pacijenti koji žive u urbanim sredinama (75,96%) i oni sa hroničnim bolestima (88,60%). Bračni partneri su češće koristili BZD, kao i pacijenti sa završenom srednjom školom (60,44%) (Tabela 1).

Veliki broj recepata za BZD nisu preporučili porodični lekari, već drugi specijalisti (65,42%). Većini pacijenata BZD nisu preporučeni kao kontinuirana terapija, već "po potrebi" - 732 (70,11%). Što se tiče dužine trajanja terapije, većina pacijenata je koristila ove lekove 2-5 godina, a mali broj pacijenata - 169 (16,19%) po preporukama (< 6 nedelja).

Najčešće korišćeni BZD kod naših pacijenata su bili bromazepam 837 (80,17%), diazepam 116 (11,11%) i alprazolam 61 (5,84%), dok su drugi BZD korišćeni u manjem procentu (Tabela 1).

Table 1. The characteristics of patients using benzodiazepines (n=1044)**Tabela 1.** Karakteristike pacijenata koji koriste benzodiazepine (n=1044)

Variables/ <i>Varijable</i>	N	%
Gender/<i>Pol</i>		
Female/ <i>Žene</i>	742	(71.07)
Male/ <i>Muškarci</i>	302	(28.93)
Age (years)/ <i>Starost (godine)</i>		
18-30	24	(2.30)
31-45	114	(10.92)
46-64	441	(42.24)
>65	465	(44.54)
Recommended for use by/<i>Preporučeni za upotrebu od strane</i>		
Family physicians/ <i>Porodičnog lekara</i>	361	(34.58)
Other specialists / <i>Drugih specijalista</i>	683	(65.42)
Education/<i>Obrazovanje</i>		
No education/ <i>Bez obrazovanja</i>	67	(6.42)
Primary school/ <i>Osnovna škola</i>	200	(19.16)
Secondary school/ <i>Srednja škola</i>	631	(60.44)
Faculty/ <i>Fakultet</i>	146	(13.98)
The presence of chronic diseases/<i>Prisustvo hroničnih bolesti</i>		
Yes/ <i>Da</i>	925	(88.60)
No/ <i>Ne</i>	119	(11.40)
Course of treatment/ <i>Način lečenja</i>		
Continuous / <i>Kontinuirano</i>	312	(29.89)
„As needed“/„ <i>po potrebi</i> “	732	(70.11)
Marital status/ <i>Bračni status</i>		
Married / <i>U braku</i>	660	(63.22)
Single/ <i>Samac</i>	83	(7.95)
Divorced / <i>Razveden</i>	56	(5.36)
Widowed/ <i>Udovica/ udovac</i>	245	(23.47)
Treatment duration (years)/<i>Trajanje lečenja (godine)</i>		
<6 weeks/ <i>nedelja</i>	169	(16.19)
6 weeks/ <i>nedelja</i> - 1 year/ <i>godina</i>	276	(26.43)
2-5	560	(53.64)
6-9	36	(3.45)
≥10	3	(0.29)
Class of used benzodiazepine/<i>Klasa korišćenih benzodiazepina</i>		
Bromazepam	837	(80.17)
Diazepam	116	(11.11)
Alprazolam	61	(5.84)
Other/ <i>Drugi (Zolpidem)</i>	30	(2.88)
Residence/<i>Mesto stanovanja</i>		
Urban area/ <i>Urbano područje</i>	793	(75.96)
Rural area/ <i>Ruralno područje</i>	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).

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).

Graph 1. The numerical and percentage overview of benzodiazepine use in all patients, patients in urban and rural area

Grafikon 1. Brojčani i procentualni pregled upotrebe benzodiazepina kod svih pacijenata, pacijenata u gradskim i seoskim područjima

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).

Žene u urbanim područjima koriste BZD mnogo češće nego one iz ruralnih područja - statistička značajnost ($p=0.048$). Pacijenti koji su završili srednju školu i pacijenti stariji od 65 godina, u urbanim sredinama, koriste BZD mnogo češće nego oni u ruralnim područjima - statistička značajnost ($p<0.01$). Pacijenti u urbanim područjima koriste BZD u dužem periodu nego oni u ruralnim, što je, takođe, pokazalo statističku značajnost ($p<0.01$). Porodični lekari iz urbanih sredina su samostalno češće propisivali BZD nego njihove kolege iz ruralnih sredina - statistička značajnost ($p<0.01$). Što se tiče načina uzimanja terapije (kontinuirano ili 'po potrebi'), bračnog statusa i prisustva hroničnih bolesti, nije nađena statistički značajna razlika u upotrebi BZD između pacijenata iz urbanih i ruralnih krajeva (Tabela 2).

Table 2. The characteristics of patients using benzodiazepines in urban and rural areas**Tabela 2.** Karakteristike pacijenata koji koriste benzodiazepine u urbanim i ruralnim područjima

	Urban area/ <i>Gradsko područje</i> (n=793) N (%)	Rural area/ <i>Seosko područje</i> (n=251) N (%)	P*
Gender/<i>Pol</i>			0.048
Male/ <i>Muškarci</i>	217 (27.36)	85 (33.86)	
Female/ <i>Žene</i>	576 (72.64)	166 (66.14)	
Education/<i>Obrazovanje</i>			<0.01
No education / <i>Bez obrazovanja</i>	36 (4.54)	31 (12.35)	
Primary school/ <i>Osnovna škola</i>	165 (20.81)	35 (13.95)	
Secondary school/ <i>Srednja škola</i>	480 (60.53)	151 (60.16)	
Faculty/ <i>Fakultet</i>	112 (14.12)	34 (13.54)	
Class of used BZD/<i>Klasa korišćenih BZD</i>			<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/<i>Način lečenja</i>			0.99
Continuous/ <i>Kontinuirani</i>	237 (29.89)	75 (29.88)	
„As needed “/ <i>„po potrebi“</i>	556 (70.11)	176 (70.12)	
Recommended for use by/<i>Preporučeni od strane</i>			<0.01
Family physician/ <i>Porodičnog lekara</i>	223 (28.12)	138 (54.98)	
Other specialist/ <i>Drugi specijalista</i>	570 (71.88)	113 (45.02)	
Marital status/<i>Bračni status</i>			0.203
Married/ <i>U braku</i>	514 (64.81)	146 (58.17)	
Single/ <i>Samac</i>	58 (7.31)	25 (9.96)	
Divorced/ <i>Razveden</i>	39 (4.92)	17 (6.77)	
Widowed/ <i>Udovac/udovica</i>	182 (22.95)	63 (25.10)	
Chronic diseases/<i>Hronične bolesti</i>			0.219
Yes/ <i>Da</i>	708 (89.28)	217 (86.45)	
No/ <i>Ne</i>	85 (10.72)	34 (13.55)	
Age/<i>Starost</i>			<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/<i>Trajanje lečenja</i>			<0.01
< 6 weeks/ <i>nedelja</i>	106 (13.37)	63 (25.10)	
6 weeks to 1 year/ <i>6 nedelja do 1 godine</i>	210 (26.48)	66 (26.29)	
2-5 years/ <i>godina</i>	473 (59.65)	87 (34.66)	
6-9 years/ <i>godina</i>	4 (0.50)	32 (12.75)	
≥10 years/ <i>godina</i>	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); $p = 0.011$).

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); $p = 0,011$).

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

Tabela 3. Multivarijantna logistička regresiona analiza koja pokazuje vezu između različitih faktora i 'po potrebi' lečenja (n=1.044)

	Univariate/Univarijantna		Multivariate/Multivarijantna	
Variables/Varijable	OR/NV (95% CI)	p	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/Obrazovanje	1.04 (0.87-1.24)	0.662		
Another specialist recommendation/ Preporuka drugog specijaliste	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 period¹³. 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 antidepressants¹⁴.

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-

Diskusija

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 poređeni.

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 godine¹³. 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 antidepresiva¹⁴.

Studija sprovedena u Pakistanu imala je za cilj da istraži rasprostranjenost upotrebe BZD kod prigradske i gradske populacije 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 područja¹⁵.

nificantly more when compared to the subjects from the urban areas¹⁵. 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 periods⁹. 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 drugs¹⁶. 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 benzodiazepines³.

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^{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, and 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^{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 periodu⁹. 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 lekova¹⁶. 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, nesanica i briga u vezi sa porodičnim finansijskim problemima, svakodnevni život i egzistencijalni problemi, pominju se kao najčešći razlozi za hroničnu upotrebu BZD³.

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^{17,18}. Porodični lekari imaju važnu ulogu u smanjenju dugoročne upotrebe BZD. Pacijentima bi trebalo preporučiti kratkotrajno lečenje ovim lekovima, po mogućstvu do 4 nedelje, i u najmanjoj efikasnoj dozi za lečenje izražene anksioznosti, paničnih poremećaja i reakcija u akutnim krizama. Umesto propisivanja BZD za lečenje blage anksioznosti i nesanice, treba predložiti savetovanje, kognitivno-bihevioralnu terapiju, higijenu spavanja i strategije za samopomoć. Porodični lekari treba da upoznaju pacijente sa sporednim efektima ovih lekova, uključujući i uticaj na vožnju, upravljanje mašinama i zavisnost, pre nego što im propišu BDZ. Indikacije za hroničnu upotrebu su izuzetno retke. U tim situacijama najbolje je potražiti mišljenje psihijatra^{19,20}.

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.

Zaključak

Rezultati naše studije su pokazali da je upotreba BZD kod pacijenata bez mentalnih oboljenja vrlo visoka, mnogo više nego što je preporučeno. Ove lekove češće koriste žene, stariji, ljudi sa hroničnim bolestima, što je slično rezultatima iz drugih studija. Pacijenti u urbanim područjima više koriste BZD nego oni u ruralnim, Strategije za smanjenje propisivanja BZD, koje bi uključile obrazovanje i lekara i pacijenata, neophodne su radi smanjenja hronične upotrebe ovih lekova.

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