

PREPORUKE ZA ODGOVORNU UPOTREBU BENZODIJAZEPINA U ZAŠTITI DUŠEVNOG ZDRAVLJA

PRIKAZ KNJIGE

BOOK REVIEW

RECOMMENDATIONS FOR THE RESPONSIBLE USE OF BENZODIAZEPINES IN MENTAL HEALTH CARE IN SERBIA

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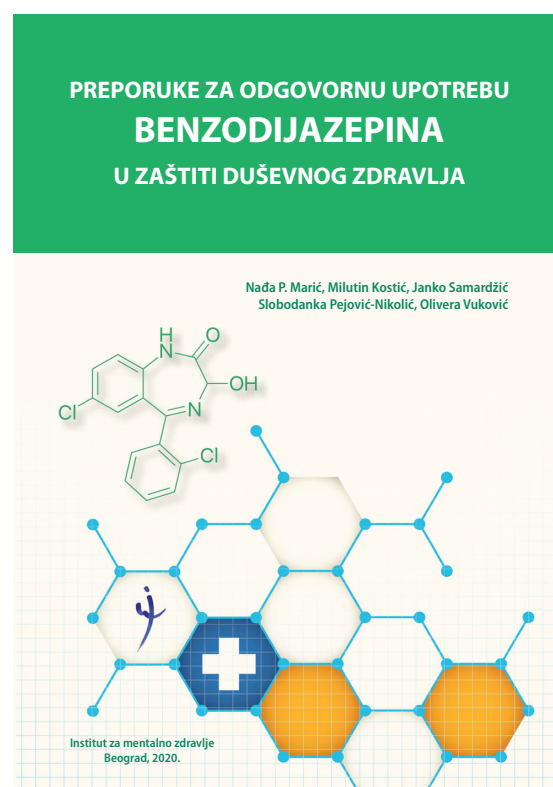
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Knjiga „Preporuke za odgovornu upotrebu benzodijazepina u zaštiti duševnog zdravlja” autora Marić NP, Kostić M, Samardžić J, Pejović- Nikolić S i Vuković O, izdata od strane Instituta za mentalno zdravlje u Beogradu, 2020. godine, predstavlja moderno, sveobuhvatno delo namenjeno psihijatrima, drugim zdravstvenim radnicima, saradnicima i studentima, kao i svim čitaocima zainteresovanim za primenu lekova koji danas spadaju među najupotrebljavanije u opštoj populaciji, globalno, pa i u Srbiji. Ove preporuke su izdate u godini kada se navršava šest decenija od kada je prvi molekul iz grupe benzodijazepina registrovan za terapijsku upotrebu.

Benzodijazepini su jedni od farmakoloških agensa koji se najčešće propisuju pacijentima i koji se sve više upotrebljavaju u mnogim zemljama sveta. Pored terapijske primene, poslednjih godina beleži

Recommendations for the responsible use of benzodiazepines in mental health care in Serbia, written by Marić NP, Kostić M, Samardžić J, Pejović- Nikolić S and Vuković O, and published in 2020 by the Institute of Mental Health in Belgrade, is a contemporary and comprehensive book intended for psychiatrists, other health workers, associates and students, as well as all readers interested in the application of medicines which are amongst the most frequently used medications in the general population, both globally and in Serbia. These recommendations have been published in the year marking six decades since the first molecule from the benzodiazepine group was registered for therapeutic application.

Benzodiazepines are one of the pharmacological agents that are most frequently prescribed to patients and which are used more and more in many countries all over the world. In addition to application in clinical

se i nemedicinska upotreba kao i zloupotreba benzodijazepina, što predstavlja rastući javno-zdravstveni problem. Procena je da 20% osoba u Srbiji koristi neki od benzodijazepina, a kod preko 4% je ta upotreba na kritičnom nivou, mereno brojem prijema na urgentno lečenje usled prekomerne upotrebe depresora CNS-a.

Knjiga „Preporuke za odgovornu upotrebu benzodijazepina u zaštiti duševnog zdravlja“ nastala je u trenutku kada se globalno suočavamo sa pandemijom izazvanom SARS-COV-2 virusom, ali i sa neizvesnošću i nepoznanicama koje ona nosi, što sledstveno vodi narušavanju duševnog zdravlja stanovništva. Imajući u vidu aktuelnu zakonsku regulativu u Srbiji, lekari opšte prakse imaju veliku odgovornost, jer su u mogućnosti da znatno duže propisuju benzodijazepine od datih preporuka, bez konsultacija sa specijalistom. Ovo nameće potrebu modifikovanja ovakve regulative, ali i naglašava značaj postojanja ovakvih preporuka.

Grupa nastavnika i saradnika, iz oblasti psihijatrije i farmakologije, sa Medicinskog fakulteta Univerziteta u Beogradu, prihvatila se izazovnog zadatka i sistematično je prikupila i dala prikaz domaće i strane literature, kao i nivoe dokaza o upotrebi benzodijazepina. Kao primer dobre prakse izdvojene su preporuke iz Vodiča koje je izdalo Ministarstvo zdravlja Singapura, još 2008. godine¹, uz navedene nivoe dokaza i kategoriju preporuka koje su korišćene.

Knjiga „Preporuke za odgovornu upotrebu benzodijazepina u zaštiti duševnog zdravlja“ sadrži tri poglavlja i priloge. U uvodnom poglavlju opisana je istorija razvoja i primene benzodijazepina, i prikazane su njihove farmakološke karakteristike (farmakokinetika i farmakološki profil dejstva). Opisani su i rizici koje upotreba benzodijazepina nosi, a koji su do danas bili često zanemarivani, kao što su padovi, prelomi, saobraćajne nesreće i povrede na radu. Dat je prikaz benzodijazepina prema Anatomsko-terapijsko-hemijskoj (ATC) klasifikaciji. Predstavljani su najčešće korišćeni benzodijazepini i „Z“ lekovi: alprazolam, bromazepam, diazepam, lorazepam, midazolam, klonazepam i zolpidem, uz detaljan tabelarni prikaz farmakokinetičkih svojstava ovih lekova. Jasno je prikazana paralela farmakokinetičkih svojstava najpropisivanijih benzodijazepina iz grupe anksiolitika i najpropisivanijeg „Z leka“, ekvivalentna doza u odnosu na 10 mg diazepama, vreme do postizanja maksimalne koncentracije u krvi kao i prosečno vreme eliminacije. Predstavljene su osnovne regulative propisivanja benzodijazepina, kao i epidemiološki podaci o njihovoj upotrebi i nemedicinskoj upotrebi.

therapy, non-medical use and abuse of benzodiazepines is also registered, representing an increasingly present public health problem. It is estimated that 20% of the people in Serbia use one of the benzodiazepines, and that in more than 4% of the cases this use is at a critical level, as measured by the number of emergency admissions resulting from the overuse of CNS depressors.

The book *Recommendations for the responsible use of benzodiazepines in mental health care in Serbia* has appeared at a time when we are faced with the global pandemic caused by the SARS-COV-2 virus, but also with the uncertainty and all the unknowns that it brings with it, consequently leading to the deterioration of mental health in the population. Bearing in mind the legislation that is currently in effect in Serbia, general practitioners have a great responsibility, since they are authorized to prescribe benzodiazepines, without consulting a specialist, for significantly longer periods than the recommendations suggest. This necessitates the modification of such legislation, but also emphasizes the significance of the recommendations.

A group of psychiatry and pharmacology professors, teaching fellows and assistants from the Faculty of Medicine of the Belgrade University took upon itself a challenging task and systematically gathered and presented a review of Serbian and international literature as well as levels of proof on benzodiazepine use. As an example of good practice, recommendations from the Guidebook issued by the Singapore Ministry of Health in 2008¹ have been presented in the book, together with stated levels of proof and the category of recommendations applied.

The book *Recommendations for the responsible use of benzodiazepines in mental health care in Serbia* has three chapters and appendices. The first chapter describes the history of the development and application of benzodiazepines as well as their pharmacological characteristics (pharmacokinetics and the pharmacological profile). It also describes the risks that the use of benzodiazepines carries, which have been neglected until now; such as falls, fractures, traffic accidents and work-related injuries. An overview of benzodiazepines according to Anatomical Therapeutic and Chemical (ATC) Classification is also given. The most frequently used benzodiazepines and “Z drugs”: alprazolam, bromazepam, diazepam, lorazepam, midazolam, clonazepam and zolpidem are presented as well, with a detailed tabular overview of the pharmacokinetic characteristics of these drugs. The parallel between the pharmacokinetic characteristics of the most commonly prescribed benzodiazepines from the anxiolytic

¹ MOH Clinical Practice Guidelines 2/2008 [Internet]. Ministry of Health, Singapore; 2008. Available from: <http://www.moh.gov.sg/cpg>

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Drugo poglavlje sadrži opis indikacija, dužine primene, kontraindikacija i interakcija sa drugim lekovima. Data je preporuka lekarima da pre propisivanja bilo kojeg od lekova iz grupe benzodijazepina razmotre dužinu upotrebe za akutne tegobe svakog pojedinačnog pacijenta. Striktno su navedene indikacije za primenu benzodijazepina, koje uključuju panični poremećaj, generalizovani anksiozni poremećaj, socijalnu fobiju i nesanicu, zatim katatoniju, kao i simptome koji nastaju tokom obustave alkohola, epileptični napad, akutnu distoniju, uvod u anesteziju i akutnu hipertenzivnu krizu. U opisu kontraindikacija posebno se naglašava da su lekovi kontraindikovani kod dece i adolescenata, kao i da je potrebno usklađivanje doze u populaciji starih. Naglašeno je da se benzodijazepini preporučuju uz veliki oprez u terapiji post-traumatskog stresnog poremećaja. Detaljno su navedene grupe lekova sa kojima benzodijazepini interaguju, kao i interakcije sa drugim supstancama, npr alkoholom. Dat je predlog za detaljnu procenu interakcija, njihovo sprečavanje ili ublažavanje uz usmeravanje čitaoca na relevantne baze podataka.

U trećem poglavlju autori ovih preporuka ističu opasnost zloupotrebe, zavisnosti i „rekreativne“ upotrebe ove grupe lekova, što je potkrepljeno savremenim činjenicama. Poseban osvrt je dat na trajanje efekata i rizike upotrebe kao i na odgovoran pristup u lečenju benzodijazepinima. Objašnjen je značaj razvoja tolerancije uz gubitak efikasnosti, prikazano je da ne postoje dokazi o dugoročnoj efikasnosti i efikasnosti izvan indikacija. Istaknute su vulnerabilne grupe i navedeno je da se korišćenje benzodijazepina može smanjiti tamo gde je psihoterapija lakše dostupna. Izdvojeni su tipovi korisnika benzodijazepina, uz posebno naglašavanje primene benzodijazepina kod osoba sa psihotičnim poremećajima, upozorenja na ovakvu praksu i neželjene efekte primene benzodijazepina u ovoj grupi pacijenata, koja je povezana sa pojačanjem kognitivnih smetnji, disfunkcionalnosti i sa višom stopom mortaliteta.

Kao jedna od značajnih osetljivih kategorija označene su i trudnice i žene tokom laktacije; navedeni su neželjeni efekti primene benzodijazepina tokom trudnoće na novorođenče.

Poseban osvrt je napravljen na primenu benzodijazepina zajedno sa antidepresivima, kao i na prednosti i nedostatke njihove kombinovane primene, ali i na nedostatak konzistentnih dokaza o ovom problemu.

Način izlaganja i prezentacije su savremeni i pristupačni za upotrebu zdravstvenim profesionalcima. Preporuke su jednostavne za primenu, nedvosmislene i ne ostavljaju prostor za različita tumačenja. Autori su svoje tvrdnje potkrepili raznovrsnim dokazima iz literature, sa posebno pažljivim osvrtom u slučajevima

group of drugs and the most commonly prescribed “Z drug” has also been presented clearly, together with the equivalent dose as compared to 10 mg of diazepam, the time needed for the medication to reach peak plasma concentration following drug administration, as well as the average elimination time. The basic regulations regarding benzodiazepine prescription are presented, as are the epidemiological data on the application of these drugs and their non-medical use.

The second chapter contains the description of the indications, length of application, contraindications, and interactions of benzodiazepines with other drugs. A recommendation is given to doctors that, when prescribing any of the drugs from the benzodiazepine group, they should carefully consider the length of use for acute complaints in every individual patient. The indications for the application of benzodiazepines, which include panic disorder, generalized anxiety disorder, social phobia, insomnia, catatonia, as well as symptoms occurring during alcohol discontinuation, epileptic seizure, acute dystonia, putting a patient under anesthesia and acute hypertensive crisis, are precisely listed and described. In the description of the contraindications it is especially emphasized that these medications are contraindicated in children and adolescents, as well as that the dosage needs to be adjusted in elderly patients. It is also stressed that benzodiazepines are recommended with great caution in the treatment of post-traumatic stress disorder. The groups of drugs that benzodiazepines interact with are listed in detail, as well as the interactions with other substances, for instance alcohol. A recommendation is given regarding detailed assessment of interactions, their prevention or mitigation and the reader is referred to relevant data bases.

In the third chapter, the authors of these recommendations emphasize the danger of abuse, dependency and “recreational” use of this group of drugs, which is backed by current information. Special attention is given to the duration of the effects and the risks of use, as well as to the responsible approach to treatment with benzodiazepines. The importance of the development of drug tolerance coupled with loss of effectiveness is explained and it is stressed that there is no proof of long-term effectiveness or of effectiveness outside the prescribed indications. Vulnerable groups are outlined, and it is stated that benzodiazepine use can be decreased where psychotherapy is more easily accessible. The types of benzodiazepine users are defined, with special attention to the application of benzodiazepines in patients with psychotic disorders, and a warning against the practice of prescribing these drugs to this group of patients, stating the resulting side-effects, is noted, since their application in such cases is associated with an increase in cognitive

nekonzistentnih dokaza. Imajući u vidu visoku učestalost upotrebe i nemedicinske upotrebe benzodijazepina u Srbiji, priručnik koji objedinjuje preporuke na jednom mestu, ali i skreće pažnju na neželjena dejstva kako kratkotrajne, tako i dugotrajne upotrebe ovih lekova, od velikog je značaja.

Ovaj pionirski poduhvat može se visoko oceniti i ostavlja prostor za dalji rad sa pojavom novih naučnih dokaza. Preporuke mogu biti značajne za sve lekare u celokupnom sistemu zdravstvene zaštite, na svim njegovim nivoima, primarnom, sekundarnom i tercijarnom, i za sve one koji se bave zaštitom i unapređenjem zdravlja stanovništva i koji se, u svojoj svakodnevnoj kliničkoj praksi, susreću sa pacijentima kojima su propisani lekovi iz grupe benzodijazepina.

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difficulty, dysfunctionality and with a higher mortality rate. Pregnant and lactating women are marked as one of the important vulnerable categories, and adverse effects of benzodiazepine application, in pregnancy, on the newborn are described. Insight is provided into the application of benzodiazepines in combination with antidepressants, as well as into the advantages and disadvantages of their combined use, but also into the lack of consistent proof related to this problem.

The way that the book is written, and the presentation of the data is contemporary and accessible for application by health professionals. The recommendations are simple to implement, they are unambiguous and leave no room for different interpretation. The authors have substantiated their assertions with a variety of proof from literature, with an especially careful insight into cases of inconsistent proof. Bearing in mind the high frequency of benzodiazepine use and non-medical use in Serbia, a guidebook which unites recommendations in one place, but also draws attention to the adverse effects of both short-term and long-term use of these drugs, is of great importance.

This pioneer undertaking can be assessed very highly, and it leaves room for further work with the emergence of new scientific evidence. These recommendations can be significant for all doctors in the entire system of health care, at all of its levels, primary, secondary and tertiary, and for all those involved in population health care and health improvement, and who, in their everyday clinical practice, come into contact with patients who have been prescribed drugs belonging to the benzodiazepine group.

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