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UPOTREBA PSIHOAKTIVNIH SUPSTANCI U REGIONALNOM METADONSKOM CENTRU U SRBIJI

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SAŽETAK

Uvod/Cilj: Pacijenti na metadonskoj supstitucionoj terapiji (MST) često upotrebljavaju psihoaktivne supstance (nikotin, alkohol, kanabis, kokain, amfetamin i slične stimulanse, sedative, hipnotike, halucinogene i dr.), što može negativno uticati na terapijske ishode. Cilj ovog istraživanja je bio da se odredi prevalencija i modeli upotrebe psihoaktivnih supstanci kod pacijenata koji su na MST.
Metode: Istraživanje je sprovedeno u Metadonskom centru Univerzitetskog kliničkog centra Vojvodine u periodu avgust - oktobar 2022. godine. Podaci o upotrebi psihoaktivnih supstanci su prikupljeni pomoću opšteg i ASSIST (engl. *The Alcohol, Smoking and Substance Involvement Screening Test*) upitnika. Deskriptivna statistika je korišćena za analizu prikupljenih podataka.
Rezultati: Ukupno, 60 pacijenata na MST je uključeno u istraživanje. Među njima, bilo je najviše korisnika nikotina (98,3%), a zatim alkohola (10,0%) i nelegalnih psihoaktivnih supstanci (kanabisa, kokaina i meskalina) (5,1%) unutar tri meseca koja su prethodila istraživanju. Upotreba nelegalnih psihoaktivnih supstanci je uglavnom bila povremena. Tri pacijenta su imala ASSIST skor >27, što je ukazivalo na visok rizik od razvoja zavisnosti, alkoholne (2 pacijenta) ili kanabionoidne (1 pacijent).
Zaključak: Istraživanje je ukazalo na značajnu razliku u učestalosti upotrebe legalnih i nelegalnih psihoaktivnih susptanci. Zbog toga bi njihovu upotrebu trebalo pratiti na osnovu redovne i povremene analize urina.

Ključne reči: metadonska supstituciona terapija, psihoaktivne supstance, prevalencija, ASSIST skor, rizik od zavisnosti

Uvod

Metadon je najčešće korišćeni i najefikasniji lek u lečenju zavisnosti od opijata (1,2). Suzbija čežnju, ublažava simptome obustave i dovodi do tolerancije na euforične efekte opijata.

Psihoaktivne supstance mogu smanjiti adherencu prema metadonu i kompromitovati uspeh supstitucionog lečenja (3). Osim toga, one su neurotoksične i prouzrokuju kognitivne i bihejvioralne poremećaje (4,5), te različite oblike rizičnog ponašanja (rizični seksualni kontakti, upotreba nesterilnih špriceva i igala) koji povećavaju rizik od HIV infekcije (4). Pacijenti na metadonskoj supstitucionoj terapiji (MST) ih često (zlo)upotrebljavaju, jer je, npr., učešće pušača iznad 80%, a onih koji konzumiraju alkohol 25-35% (6-9). Takođe, jedno istraživanje je ukazalo da 65% pacijenata na supstitucionoj terapiji opioidnim agonistima (metadonom ili buprenorfinom/naloksonom) zloupotrebljava benzodiazepine (48,3%), amfetamin (41,7%), opioide (6,7%), kanabis (30%), nove psihoaktivne supstance (8,3%) i psihotropne lekove (25%), kao što su pregabalin, gabapentin, kvetiapin i bupropion (10).

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USE OF PSYCHOACTIVE SUBSTANCES IN THE REGIONAL METHADONE CENTER IN SERBIA

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SUMMARY

Introduction/Aim: Patients on methadone maintenance therapy often use psychoactive substances (nicotine, alcohol, cannabis, cocaine, amphetamine-type stimulants, sedatives, hypnotics, hallucinogens and others), which can negatively affect therapeutic outcomes. The aim of this study was to determine the prevalence and pattern of psychoactive substance use among patients on methadone maintenance therapy.
Methods: The study was conducted in the Methadone Center of the University Clinical Center of Vojvodina in the period August-October 2022. Substance use data were collected through general and ASSIST (The Alcohol, Smoking and Substance Involvement Screening Test) questionnaires, respectively. Descriptive statistics was used to analyze the collected data.
Results: In total, 60 patients on methadone maintenance therapy were included in the study. Among them, the prevalence of the use of nicotine, alcohol and illicit psychoactive substances was 98.3%, 10% and 5.1%, respectively, in the last 3 months preceding the investigation. The use of illicit psychoactive substances was mostly occasional. Three patients had ASSIST score >27 which was associated with a high risk of developing dependence to alcohol (two patients) or cannabis (1 patient).
Conclusion: The study indicated a significant difference in the prevalence of the use of licit and illicit psychoactive substances. Therefore, their use should be monitored through regular and occasional urinalysis.

Keywords: methadone maintenance therapy, psychoactive substance, prevalence, ASSIST score, risk of dependence

Introduction

Methadone is the most frequently used and most effective medication in the treatment of addiction to opioid drugs (1,2). It suppresses cravings, alleviates withdrawal symptoms and leads to tolerance to the euphoric effects of opioids.

Psychoactive substances can reduce the adherence to methadone and compromise the success of maintenance therapy (3). In addition, they are neurotoxic and cause cognitive and behavioral disorders (4,5), and therefore, various forms of risky behavior (risky sexual contacts, use of non-sterile syringes and needles) that increase the risk of HIV infection (4). Patients on methadone maintenance therapy (MMT) often (mis)use them because there are more than 80% of smokers and 25-30% of those who use alcohol (6-9). Also, one study has shown that 65% of patients on maintenance therapy involving opioid agonists (methadone or buprenorphine/naloxone) abuse benzodiazepine (48.3%), amphetamine (41.7%), opioids (6.7%), cannabis (30%), new psychoactive

Različite demografske i kliničke karakteristike se povezuju sa upotrebom psihoaktivnih supstanci kod osoba na MST. Demografske karakteristike su mlađe životno doba (11-13), muški pol (14), nezaposlenost i niži stepen obrazovanja (12), dok se među kliničkim karakteristikama navode lošije zdravstveno stanje (npr. depresija) (13). Upotreba psihoaktivnih supstanci kod osoba na MST može biti različita i nedovoljno je istražena i na nivou geografskih regiona (14,15).

Stoga, cilj ovog istraživanja je bio da se odredi prevalencija i modeli upotrebe psihoaktivnih supstanci kod pacijenata na MST u Univerzitetskom kliničkom centru Vojvodine, Novi Sad (Srbija), kao i da se predože odgovarajuće mere za optimizaciju ishoda terapije.

Metode

Istraživanje je sprovedeno između avgusta i oktobra 2022. godine u Metadonskom centru pri Klinici za psihijatriju Univerzitetskog kliničkog centra Vojvodine (KCV), Novi Sad (Srbija). Uloga Metadonskog centra je da implementira, sprovodi i kontroliše sprovođenje MST u regionu (16).

U istraživanje su uključeni pacijenati koji su bili na MST i koji su pristali da budu uključeni, što su i potvrdili potpisivanjem informisanog pristanka. Oni su bili stariji od 18 godina, imali su prethodnu istoriju neuspelih pokušaja lečenja od zavisnosti, jaku motivaciju za izlečenje kroz supstitucionu terapiju i jedan od međunarodnih dijagnostičkih kriterijuma opioidne zavisnosti (17).

Podaci o sociodemografskim karakteristikama i upotrebi psihoaktivnih supstanci su prikupljeni kroz intervju pacijenata u Metadonskom centru neposredno nakon izdavanja metadona. Intervjuisanje je trajalo između pet i 15 minuta. Za prikupljanje podataka su korištena dva instrumenta Opšti upitnik o sociodemografskim karakteristikama i ASSIST upitnik (engl. *The Alcohol, Smoking and Substance Involvement Screening Test*) o upotrebi psihoaktivnih supstanci (18).

Opšti upitnik je posebno razvijen za potrebe ovog istraživanja. Sastojao se od sedam pitanja koja su se odnosila na životnu dob (godine), pol (muški/ženski), bračni status (neoženjen/neudata, oženjen/udata, razveden/razvedena, udovac/udovica), decu (da/ne), obrazovanje (osnovna, srednja, viša i visoka škola), zaposlenost (da/ne) i stanovanje (selo/grad).

ASSIST upitnik je razvila Svetska zdravstvena organizacija, jer je upotrebu psihoaktivnih supstanci (nikotin, alkohol, kanabis, kokain, amfetamin i slični stimulansi, sedativi i hipnotici, halucinogeni, inhalanti, opioidi i druge) prepoznala kao rizik za javno zdravlje (18). On sadrži osam pitanja na osnovu kojih se mogu dobiti podaci o upotrebi psihoaktvnih supstanci bilo kada u životu ili unutar tri meseca koja su prethodila istraživanju (nikad/jedan do dva puta/mesečno/nedeljno/svakodnevno ili gotovo svakodnevno), kao i o problemima vezanim za njihovu upotrebu.

Navedena pitanja su zatvorenog tipa sa ponuđenim odgovorima koji se skoruju. Ukupni skor može biti u opsegu od 0 do 39 (osim za nikotin gde je skor u opsegu od 0 do 31), i njegovo tumačenje je sledeće: nizak rizik od razvoja zavisnosti ukoliko je skor u opsegu od 0 do 3 (osim za alkohol gde je skor u opsegu od 0 do 10), umeren ako je skor 4-26 (osim za alkohol gde je skor u opsegu od 11 do 26), a visok ako je skor ≥ 27 (18).

Prikupljeni podaci su numerički opisani pomoću mera deskriptivne statistike. Mere učestalosti (brojevi, proporcije) su korištene za numeričko opisivanje kvalitativnih podataka, a mere centralne tendencije (srednja vrednost) i mere varijabilnosti (opseg, standardna devijacija) su korištene za numeričko opisivanje kvantitativnih podataka. Deskriptivna statistika je sprovedena u statističkom program IBM Statistics SPSS za Windows verzija 20.0 (*IBM Corporation, Armonk, New York*).

Istraživanje je sledilo principe i etičke norme Helsinške deklaracije, i odobrila ga je Etička komisija Univerzitetskog kliničkog centra Vojvodine, Novi Sad (Srbija) (broj 00-08/332).

Rezultati

Ukupno, 60 pacijenata na SMT je uključeno u istraživanje. Njihove sociodemografske karakteristike su predstavljene u Tabeli 1. U proseku, imali su 42,18 godina (SD=6,33; minimalno 30, a maksimalno 60 godina). Bili su uglavnom muškog pola (75,0%), sa završenom srednjom školom (78,3%), nezaposleni (78,3%) i gotovo dve trećine je bilo neoženjeno/ neudato (65%).

Celoživotna prevalencija upotrebe psihoaktivnih supstanci je bila u opsegu od 66,7% (za inhalante) do 100% (za alkohol i opioide), dok je prevalencija njihove upotrebe unutar tri meseca

substances (8.3%) and psychotropic drugs (25%), such as pregabalin, gabapentin, quetiapine, bupropion (10).

Different demographic and clinical characteristics are associated with the use of psychoactive substances among persons on MMT. Demographic characteristics include younger age (11-13), male gender (14), unemployment and lower levels of education (12), while clinical characteristics include poor health condition (e.g. depression) (13). The use of psychoactive substances in persons on MMT can be different and it has not been sufficiently investigated at the level of geographical regions (14,15).

Therefore, the aim of this study was to determine the prevalence and modes of psychoactive substance use in patients on MMT at the University Clinical Center of Vojvodina, Novi Sad (Serbia), as well as to propose appropriate measures for the optimization of treatment outcomes.

Methods

The study was conducted at the Methadone Center within the Clinic for Psychiatry of the University Clinical Center of Vojvodina, Novi Sad (Serbia) from August to October 2022. The role of the Methadone Center is to implement, conduct and control the implementation of MMT in the region (16).

The study included patients on MMT who agreed to be included, which they confirmed by signing the written consent. They were older than 18, they had the previous history of unsuccessful attempts to treat addiction, strong motivation for getting cured with the help of maintenance therapy and one of international diagnostic criteria of opioid addiction (17).

Data on sociodemographic characteristics and use of psychoactive substances were collected through patient interviews at the Methadone Center immediately after methadone was dispensed. The interview lasted between 5 and 15 minutes. The following two instruments were used for the collection of data: the General questionnaire on sociodemographic characteristics and the ASSIST questionnaire (Alcohol, Smoking and Substance Involvement Screening Test) on the use of psychoactive substances (18).

The general questionnaire was specially developed for the needs of this study. It included seven questions relating to age (years), sex (male/female), marital status (single, married, divorced, widowed), children (yes/no), education (elementary, high school, college, university), employment (yes/no) and place of residence (town/village).

The ASSIST questionnaire was developed by the World Health Organization because it recognized the use of psychoactive substances (nicotine, alcohol, cannabis, cocaine, amphetamine and similar stimulants, sedatives and hypnotics, hallucinogens, inhalants, opioids and others) as a risk to public health (18). It contains eight questions based on which data can be obtained on the use of psychoactive substances at any time in life or in the last three months preceding the research (never/one to two times,/monthly/ weekly/daily or almost daily), as well as problems related to their use.

The above mentioned questions are closed-ended with the provided answers which are scored. The total score ranges between 0 and 39 (except for nicotine where the score ranges between 0 and 31), and its interpretation is as follows: low risk of developing addiction if the score ranges between 0 and 3 (except for alcohol where the score ranges between 0 and 10), moderate risk if the score ranges between 4 and 26 (except for alcohol where the score ranges between 11 and 26), and high when the score is > 27 (18).

The collected data were numerically described with the help of descriptive statistics measures. Frequency measures (numbers, proportions) were used for the numerical description of qualitative data, while measures of central tendency (mean value) and variability measures (range, standard deviation) were used for the numerical description of quantitative data. Descriptive statistics was performed in the statistical program IBM Statistics SPSS for Windows version 20.0 (IBM Corporation, Armonk, New York).

The study followed the principles and ethical norms of the Declaration of Helsinki, and it was approved by the Ethics Committee of the University Clinical Center of Vojvodina, Novi Sad (Serbia) (number 00-08/332).

Tabela 1. Sociodemografske karakteritike pacijenata na metadonskoj supstitucinoj terapiji u Univerzitetskom kliničkom centru Vojvodine (N=60)

Karakteristike	N	%
Uzrast (godine) (AS ± SD)	42,18	6,33
Pol		
Muiški	45	75,0
Ženski	15	25,0
Bračni status		
Neoženjen/neudata	39	65,0
Oženjen/udata	10	16,7
Razveden/razvedena	8	13,3
Udovac/udovica	3	5,0
Deca		
Da	20	33,3
Ne	40	66,7
Obrazovanje		
Osnovna škola	9	15,0
Srednja škola	47	78,3
Viša škola	3	5,0
Visoka škola	1	1,7
Zaposlenost		
Da	13	21,7
Ne	47	78,3
Mesto stanovanja		
Grad	46	76,7
Selo	14	23,3

AS – aritmetička sredina, SD - standardna devijacija.

koja su prethodila istraživanju bila u opsegu od 1,7% (za halucinogen meskalin) do 98,3% (za nikotin) (tabela 2).

Prevalencija upotrebe legalnih naspram nelegalnih psihoaktivnih supstanci je predstavljena u tabeli 3. Tri (5%) pacijenta su upotrebljavala nelegalne psihoaktivne supstance (kanabis, kokain i meskalin) unutar tri meseca koja su prethodila istraživanju, uglavnom povremeno (Tabela 2). Takođe, jedan pacijent je upotrebljavao dve psi-

Tabela 2. Prevalencija upotrebe psihoaktivnih supstanci kod pacijenata na metadonskoj supstitucionoj terapiji u Univerzitetskom kliničkom centru Vojvodine (N=60)

Psihoaktivna supstanca	Celoživotna		Poslednja 3 meseca	
	N	%	N	%
Nikotin	59	98,3	59	98,3
Alkohol	60	100,0	6	10,0
Kanabis	54	90,0	2	3,4
Kokain	50	83,3	1	1,7
Amfetaminski stimulansi	55	91,7	0	0,0
Inhalanti	40	66,7	0	0,0
Sedativi/Hipnotici	52	86,7	0	0,0
Halucinogeni	47	78,3	1	1,7
Opioidi	60	100,0	0	0,0
Drugi lekovi	0	0,0	0	0,0

*Učestalost upotrebe psihoaktivnih supstanci: nikotin – svakodnevno (59 pacijenata); alkohol – svakodnevno (2 pacijenta) i jedan do dva puta nedeljno (4 pacijenta); kanabis – svakodnevno (1 pacijent) i jedan do dva puta nedeljno (1 pacijent); kokain – jedanput nedeljno (1 pacijent), meskalin: jedanput unutar poslednja tri meseca (1 pacijent).

Table 1. Sociodemographic characteristics of patients on methadone maintenance therapy at the University Clinical Center of Vojvodina (N=60)

Characteristics	N	%
Age (Years) (Mean±SD)	42.18	6.33
Sex		
Male	45	75.0
Female	15	25.0
Marital status		
Single	39	65.0
Married	10	16.7
Divorced	8	13.3
Widowed	3	5.0
Children		
Yes	20	33.3
No	40	66.7
Education		
Elementary school	9	15.0
High school	47	78.3
College (three years)	3	5.0
University	1	1.7
Employment		
Yes	13	21.7
No	47	78.3
Place of living		
Town / city	46	76.7
Village	14	23.3

SD - standard devijation

Results

In total, 60 patients on MMT were included in the study. Their sociodemographic characteristics are presented in Table 1. On average, they were 42.18 years old (SD=6.33; minimum 30 and maximum 60 years). They were mostly male (75.0%), with a high school diploma (78.3%), unemployed (78.3%) and almost two thirds were single (65%).

The lifetime prevalence of the use of psychoactive substances ranged from 66.7%

Table 2. Prevalence of psychoactive substance use in patients on methadone maintenance therapy at the University Clinical Center of Vojvodina (N=60)

Psychoactive substance	Lifetime		Last 3 months*	
	N	%	N	%
Tobacco products	59	98.3	59	98.3
Alcohol	60	100.0	6	10.0
Cannabis	54	90.0	2	3.4
Cocaine	50	83.3	1	1.7
Amphetamine-type stimulants	55	91.7	0	0.0
Inhalants	40	66.7	0	0.0
Sedatives/Hypnotics	52	86.7	0	0.0
Hallucinogens	47	78.3	1	1.7
Opioids	60	100.0	0	0.0
“Other” drugs	0	0.0	0	0.0

*Frequency of use of psychoactive substances: nicotine - daily (59 patients); alcohol - daily (2 patients) and once to twice a week (4 patients); cannabis – daily (1 patient) and once to twice a week (1 patient); cocaine – once a week (1 patient), mescaline: once in the last three months (1 patient).

Tabela 3. Upotreba legalnih i nelegalnih psihoaktivnih supstanci kod pacijenata na supstitucionoj terapiji metadonom u Univerzitetskom kliničkom centru Vojvodine (N=60)

Psihoaktivna supstanca	Celoživotna		Poslednja 3 meseca	
	N	%	N	%
Legalne	60	100	59	98,3
Nelegalne	60	100	3	5,0

hoaktivne supstance (kokain i kanabis) unutar tri meseca koja su prethodila istraživanju.

Rizik od razvoja zavisnosti od psihoaktivnih supstanci je procenjen na osnovu ASSIST skora (tabela 4). Za sedam supstanci (nikotin, kokain, amfetamin i slični stimulansi, inhalanti, sedativi/hipnotici, halucinogeni i opioidi), ASSIST skor je bio u opsegu 0-3 ili u opsegu 4-26, što je ukazivalo da su pacijenti imali nizak ili umereni rizik od razvoja zavisnosti.

Za dve supstance (alkohol i kanabis), ASSIST skor je bio u tri opsega (0-3, 4-26 i iznad 27) što ukazuje da su pacijenti imali nizak, umereni ili visok rizik od razvoja zavisnosti (Tabela 4). Kada je reč o visokom riziku od razvoja zavisnosti, kod dva pacijenta (3,4%) se odnosio na alkohol a kod jednog pacijenta (1,7%) na kanabis (Tabela 4).

Diskusija

Celoživotna upotreba psihoaktivnih supstanci (legalnih i nelegalnih) bila je veoma zastupljena (npr. nikotin: 98,3%; alkohol: 100%; sedativi/hipnotici: 86,7%; kanabis: 90%) među pacijentima u Metadonskom centru Univerzitetskog kliničkog centra Vojvodine. I to je uobičajeni nalaz epidemioloških istraživanja (19-21), gde, po pravilu, upotreba nikotina i/ili alkohola prethodi upotrebi kanabisa, a upotreba kanabisa prethodi upotrebi drugih nelegalnih psihoaktivnih supstanci.

Kada je reč o upotrebi psihoaktivnih supstanci unutar tri meseca koja su prethodila istraživanju, najzastupljenija je bila upotreba nikotina. Gotovo svi pacijenti na MST su bili pušači (98,3%). Rezultati su uporedivi sa rezultatima drugih istraživanja gde je upotreba nikotina takođe bila izuzetno zastupljena (>80%) (6,22). Značajna proporcija pušača među pacijentima na MST može se objasniti „korisnim" interakcijama. Naime, nikotin, kao i druge psihoaktivne supstance koje izazivaju zavisnost, aktivira mezolimbički put i povećava oslobađanje dopamina u zoni n*ucleus accumbens*, što pojačava efekte euforije koju prouzrokuje metadon. Takođe, nikotin može ublažiti neželjena dejstva metadona koja se ispoljavaju kao agitacija i uznemirenost. I, generalno, pojačanje efekata euforije i ublažavanje agitacije i uznemirenosti su razlozi zbog kojih pacijenti na MST koriste psihoaktivne supstance (23).

Upotreba alkohola u ovom istraživanju je bila druga po zastupljenosti. Naime, 10% pacijenata ga je povremeno (6,7%) ili svakodnevno (3,3%) konzumiralo unutar tri meseca koja su prethodi-

Tabela 4. Rizik od razvoja zavisnosti kod pacijenata na metadonskoj supstitucionoj terapiji u Univerzitetskom kliničkom centru Vojvodine (N=60)

Psihoaktivna supstanca	Nizak		Umereni		Visok	
	N	%	N	%	N	%
Nikotin	0	0,0	59	98,3	0	0,0
Alkohol	54	90,0	4	6,7	2	3,4
Kanabis	52	86,7	1	1,7	1	1,7
Kokain	49	81,7	1	1,7	0	0,0
Amfetaminski stimulansi	55	91,7	0	0,0	0	0,0
Inhalanti	40	66,7	0	0,0	0	0,0
Sedativi/Hipnotici	52	86,7	0	0,0	0	0,0
Halucinogeni	47	78,3	0	0,0	0	0,0
Opioidi	0	0,0	60	100	0	0,0
Drugi lekovi	0	0,0	0	0,0	0	0,0

*Rizik je procenjen na osnovu ASSIST skora.

Table 3. Use of legal and illegal psychoactive substances in patients on methadone maintenance therapy at the University Clinical Center of Vojvodina (N=60)

Psychoactive substances	Lifetime		Last 3 months	
	N	%	N	%
Legal	60	100	59	98.3
Illegal	60	100	3	5.0

(for inhalants) to 100% (for alcohol and opioids), while the prevalence of their use in the last three months preceding the study ranged from 1.7% (for hallucinogen mescaline) to 98.3% (for nicotine) (Table 2).

The prevalence of the use of legal psychoactive substances compared to illicit psychoactive substance use is presented in Table 3. Three (5%) patients had used illicit psychoactive substances (cannabis, cocaine, and mescaline) in the last three months preceding the study, mostly occasionally (Table 2). Also, one patient had used two psychoactive substances (cocaine and cannabis) in the last three months preceding the study.

The risk of developing addiction to psychoactive substances was assessed based on the ASSIST score (Table 4). For seven substances (nicotine, cocaine, amphetamine and similar stimulants, inhalants, sedatives/hypnotics, hallucinogens, and opioids), the ASSIST score ranged between 0-3 or between 4 and 26, which indicated that patients had a low or moderate risk of developing addiction.

For two substances (alcohol and cannabis), the ASSIST score had three ranges (0-3, 4-26, and above 27), which indicated that patients had a low, moderate or high risk of developing addiction (Table 4). When it comes to the high risk of developing addiction, in two patients (3.4%), this risk was connected with alcohol and in one patient (1.7%) with cannabis (Table 4).

Discussion

The lifetime use of psychoactive substances (legal and illegal) was highly prevalent (e.g. nicotine: 98.3%; alcohol: 100%; sedatives/hypnotics: 86.7%; cannabis: 90%) among patients at the Methadone Center of the University Clinical Center of Vojvodina. This is a common finding of epidemiological studies (19-21), where, as a rule, the use of nicotine and/or alcohol precedes the use of cannabis, while the use of cannabis precedes the use of other illicit psychoactive substances.

When it comes to the use of psychoactive substances in the last three months preceding the study, the most common was the use of nicotine. Almost all patients on MMT were smokers (98.3%). The results can be compared to the results of other studies, where the use of nicotine was also very common (>80%) (6,22). A significant proportion of smokers among patients on MMT can be

Table 4. Risk of developing dependence in patients on methadone maintenance therapy at the University Clinical Center of Vojvodina (N=60)

Psychoactive substances	Low		Moderate		High	
	N	%	N	%	N	%
Tobacco products	0	0.0	59	98.3	0	0.0
Alcohol	54	90.0	4	6.7	2	3.4
Cannabis	52	86.7	1	1.7	1	1.7
Cocaine	49	81.7	1	1.7	0	0.0
Amphetamine-type stimulants	55	91.7	0	0.0	0	0.0
Inhalants	40	66.7	0	0.0	0	0.0
Sedatives/Hypnotics	52	86.7	0	0.0	0	0.0
Hallucinogens	47	78.3	0	0.0	0	0.0
Opioids	0	0.0	60	100	0	0.0
“Other” drugs	0	0.0	0	0.0	0	0.0

*Rizik je procenjen na osnovu ASSIST skora.

la istraživanju. Rezultati nisu u skladu sa najvećim brojem epidemioloških istraživanja jer je u njima ta prevalencija bila između 25% i 35% (7-9). Uočena razlika se ne može povezati sa načinom na koji su podaci prikupljani, jer je upotreba alkohola u navedenim epidemiološkim istaživanjima, takođe, dobrovoljno prijavljivana. Ipak, moguće je da su pacijenti u ovom istraživanju nastojali da prijavljivanje bude socijalno prihvatljivo.

Prevalencija upotrebe kanabisa je bila 3,3% unutar tri meseca koja su prethodila istraživanju, dok je celoživotna prevalencija iznosila 90%. Sa druge strane, jedno istraživanje koje je sprovedeno na klinikama u pet kineskih provincija je ukazalo na prevalenciju upotrebe kanabisa od 0,3% unutar meseca koji je prethodio istraživanju, i celoživotnu prevalenciju od svega 4,4% (13). Nekonzistentni rezultati između istraživanja se mogu povezati sa razlikama u zakonskoj regulativi, dostupnosti, ceni i potentnosti kanabisa na nivou geografskih regiona (24,25). U Kini su, primera radi, na snazi striktne politike kažnjavanja za upotrebu, promet te proizvodnju psihoaktivnih supstanci uključujući i kanabis (26).

Samo jedan pacijent (1,7%) je povremeno koristio kokain unutar tri meseca koja su prethodila istraživanju. To je konzistentno sa rezultatima drugih istraživanja gde su pacijenti takođe dobrovoljno prijavljivali upotrebu nelegalnih, psihoaktivnih supstanci (7,13). Na primer, pacijenti na MST u tri vijetnamske klinike nisu koristili kokain (7), dok je u nekoliko regiona u Kini svega osam pacijenata (0,3%) koristilo kokain unutar meseca koji je prethodio intervju (13). U istraživanjima gde je urin analiziran na prisustvo psihoaktivnih supstanci, prevalencija upotrebe kokaina je bila značajno veća (25–60%) (27,28). Takođe, istraživanja ukazuju da pacijenti na MST koriste kokain povremeno (14,7%) ili redovno (10,7%) (28).

Razlika u prevalenciji upotrebe legalnih (nikotin, alkohol) i nelegalnih (kokain, kanabis, meskalin) psihoaktivnih susptanci je bila značajna u ovom istraživanju. Nikotin je koristilo 98,3% pacijenata, a zatim alkohol 10%, kokain 1,7%, kanabis 3,3% i meskalin 1,7% pacijenata. Slična razlika je uočena i u drugim istraživanjima (7,13). Na primer, Le i saradnici su ukazali da alkohol koristi 24,8%, cigarete 68,6% i nelegalne psihoaktivne supstance 6% pacijenta na MST (7). Razlika u upotrebi legalnih i nelegalnih psihoaktivnih supstanci može se povezati sa pristrasnošću prijavljivanja (engl. *reporting bias*). *Khalili* i saradnici su tako sproveli jedno istraživanje kako bi procenili validnost prijavljivanja upotrebe psihoaktivih supstanci (opiuma, metadona, amfetamina i kanabisa). Kada je reč o opioidima, 4,2% pacijenata je prijavilo njihovu upotrebu, a 8,5% pacijenata je imalo pozitivan nalaz urina (29). S obzirom da upotreba psihoaktivnih supstanci smanjuje adherencu i kompromituje ishode MST, nosioci politika u nekim zemljama (npr. Kina) insistiraju da se kod pacijenata upotreba heroina prati (redovno ili povremeno) na osnovu analize urina (13).

Pacijenti su uglavnom imali ASSIST skor u opsegu od 0 do 3 za psihoaktivne supstance koje nisu upotrebljavali unutar tri meseca koja su prethodila istraživanju. To je ukazivalo na nizak rizik od razvoja zavisnosti pa nije zahtevalo intervenciju nego podršku i motivaciju da se psihoaktivne supstance ne zloupotrebljavaju u budućnosti (18).

Pacijenti koji su bili pušači (98,3%) su imali ASSIST skor u opsegu od 4 do 26, što je ukazivalo na umereni rizik od razvoja nikotinske zavisnosti. Kada se rezultati porede sa rezultatima drugih istraživanja uočava se značajna razlika (30-31). Do i saradnici su tako ukazali na umereni rizik od nikotinske zavisnosti kod 12,9% pacijenata u nekoliko metadonskih centara u Vijetnamu (31). Međutim, istraživači su za procenu rizika od nikotinske zavisnosti koristili Fagerstremov upitnik. Za razliku od ASSIST upitnika, on pacijente grupiše u pet grupa: „veoma nizak", „nizak", "umeren", „visok" ili „veoma visok" rizik od nikotinske zavisnosti. Ta razlika koja se odnosi na istraživačke metode otežava poređenje rezultata istraživanja.

Kao što je navedeno, pacijenti koji su bili pušači su imali umereni rizik od razvoja zavisnosti. S tim u vezi, kod njih je bila potrebna samo kratka intervencija odnosno informisanje o ASSIST skoru i verovatnoći javljanja zdravstvenih problema (18). Primera radi, nikotin, osim na nervnom, ispoljava neželjena dejstva i na kardiovaskularnom (arterijska hipertenzija) i respiratornom (infekcije, alergije, hronična opstruktivna bolest pluća, astma) sistemu, a katrani iz duvanskog dima se povezuju sa hroničnim bronhitisom, karcinomom pluća, jednjaka, pankreasa i mokraćne bešike (32).

Tri (5%) pacijenta su imala ASSIST skor iznad 27, što je ukazivalo na visok rizik od razvoja zavisnosti, alkoholne (2 pacijenta) ili kanabinoidne (1 pacijent). To je zahtevalo intervenciju kao što je upućivanje na specijalistički pregled i odgovarajuće lečenje (18).

explained by "beneficial" interactions. Namely, nicotine, like other psychoactive substances that cause addiction, activates the mesolimbic pathway and increases the release of dopamine in the nucleus accumbens zone, which enhances the effects of euphoria caused by methadone. Also, nicotine can alleviate the unwanted effects of methadone, which manifest as agitation and restlessness. Also, generally speaking, enhancing the effects of euphoria and alleviating agitation and anxiety are the reasons why patients on MMT use psychoactive substances (23).

The use of alcohol in this study was the second according to its prevalence. Namely, 10% of patients had consumed it occasionally (6.7%), or daily (3.3%) in the last three months preceding the study. The results are not in accordance with the largest number of epidemiological studies because the prevalence in these studies ranges between 25% and 35% (7-9). The observed difference cannot be connected to the way in which data were collected, because the use of alcohol in the above mentioned epidemiological studies was also voluntarily reported. However, it is possible that patients in this study tried to make reporting socially acceptable.

The prevalence of cannabis use was 3.3% in the last three months preceding the study, while the lifetime prevalence amounted to 90%. On the other hand, a study, which was conducted at clinics in five Chinese provinces, indicated the prevalence of cannabis use of 0.3% in the last month preceding the study, and a lifetime prevalence of only 4.4% (13). Inconsistent results between studies may be linked to differences relating to legal regulations, availability, price and potency of cannabis at the level of geographic regions (24,25). In China, for example, strict punishment policies are in force for the use, trafficking and production of psychoactive substances, including cannabis (26).

Only one patient (1.7%) had occasionally used cocaine in the last three months preceding the study. This is consistent with the results of other studies where patients also voluntarily reported the use of illicit psychoactive substances (7,13). For example, patients on MMT in three clinics in Vietnam did not use cocaine (7), while in several regions in China, only eight patients (0.3%) had used cocaine in the month preceding the interview (13). In studies, where urine was analyzed for the presence of psychoactive substances, the prevalence of cocaine was significantly higher (25-60%) (27,28). Also, studies indicate that patients on MMT use cocaine occasionally (14.7%) or regularly (10.7%) (28).

The difference in the prevalence of the use of legal (nicotine, alcohol) and illegal (cocaine, cannabis, mescaline) psychoactive substances was significant in this study. Nicotine was used by 98.3% of patients, followed by alcohol 10%, cocaine 1.7%, cannabis 3.3% and mescaline by 1.7% of patients. A similar difference was observed in other studies (7,13). For example, Le and associates indicated that 24.8% of patients on MMT used alcohol, 68.6% used cigarettes, and 6% used illegal psychoactive substances (7). The difference in the use of legal and illegal psychoactive substances can be associated with the reporting bias. Khalili and associates conducted a study to assess the validity of reporting the use of psychoactive substances (opium, methadone, amphetamine and cannabis). When it comes to opioids, 4.2% of patients reported their use, and 8.5% of patients had a positive urine test (29). Given that the use of psychoactive substances reduces adherence and compromises MMT outcomes, policy makers in some countries (e.g. China) insist that heroin use should be monitored in patients (regularly or occasionally) based on urinalysis (13).

Patients' ASSIST score mainly ranged between 0 and 3 for psychoactive substances that they had not used in the last three months preceding the study. This indicated a low risk of developing addiction, and therefore, it did not require intervention, but support and motivation so as not to abuse psychoactive substances in the future (18).

Patients who were smokers (98.3%) had an ASSIST score ranging between 4 and 26, which indicated a moderate risk of nicotine addiction. When the results are compared with the results of other studies, a significant difference is observed (30-31). Do et al. thus pointed to the moderate risk of nicotine addiction in 12.9% of patients in several methadone centers in Vietnam (31). However, the researchers used Fagerström Test to assess the risk of nicotine addiction. Unlike the ASSIST questionnaire, it groups patients into five groups: "very low", "low", "moderate", "high" or "very high" risk of nicotine addiction. This difference relating to research methods makes it difficult to compare research results.

Dakle, kod ovih pacijenata osim lečenja opioidne zavisnosti trebalo je razmotriti i lečenje alkoholne odnosno kanabinoidne zavisnosti.

Ovo istraživanje ima nekoliko nedostataka. Prvo, sprovedeno je u jednoj zdravstvenoj ustanovi i na malom uzorku, što može ograničiti generalizaciju zaključaka na druge zdravstvene ustanove i regione. Drugo, istraživanje je transverzalno (studija preseka) te stoga nije bilo moguće ustanoviti uzročno-posledičnu vezu između demografskih karakteristika i upotrebe psihoaktivnih supstanci. U te svrhe idealno bi bilo sprovesti longitudinalno istraživanje. Treće, podaci o dozi metadona, trajanju lečenja, prisustvu komorbiditeta, kao i o njihovom lečenju nisu prikupljani, što upućuje na potrebu da se prikupe, i da se istraži njihova veza sa upotrebom psihoaktivnih supstanci. Konačno, prikupljanje podataka o upotrebi nelegalnih psihoaktivnih supstanci kroz dobrovoljno prijavljivanje je moglo biti socijalno prihvatljivo i nerealno. Uprkos navedenim nedostacima, rezultati ovog istraživanja bi mogli biti od koristi kod planiranja javnozdravstvenih politika za metadonske centre.

Zaključak

Istraživanje je ukazalo na značajnu razliku u prevalenciji upotrebe legalnih i nelegalnih psihoaktivnih susptanci. S obzirom da su pacijenti dobrovoljno prijavljivali njihovu upotrebu, moguće je da su nastojali da prijavljivanje bude socijalno prihvatljivo. Stoga bi upotrebu psihoaktivnih supstanci trebalo pratiti na osnovu redovne i povremene analize urina. Konačno, tri pacijenta su imala ASSIST skor > 27, što je ukazalo na visok rizik od razvoja zavisnosti, alkoholne (2 pacijenta) odnosno kanabinoidne (1 pacijent). Zbog toga su potrebne intervencije, koje podrazumevaju upućivanje na specijalistički pregled i lečenje.

Konflikt interesa

Autori su izjavili da nema konflikta interesa.

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As noted, patients who were smokers had a moderate risk of developing addiction. In this regard, they only needed a short intervention, that is, information about the ASSIST score and the probability of occurrence of health problems (18). For example, nicotine, in addition to its adverse effects on the nervous system, has adverse effects on the cardiovascular (arterial hypertension) and respiratory (infections, allergies, chronic obstructive pulmonary disease, asthma) system, while tars from tobacco smoke are associated with chronic bronchitis, lung cancer, esophageal, pancreatic and bladder cancer (32).

Three (5%) patients had an ASSIST score above 27, which indicated a high risk of developing addiction, alcohol (2 patients) or cannabinoid (1 patient) addiction. This demanded intervention such as referring to a specialist examination and appropriate treatment (18). Therefore, in these patients, in addition to the treatment of opioid addiction, the treatment of alcohol or cannabinoid addiction should also be considered.

This study has several shortcomings. First, it was conducted in one healthcare institution on a small sample, which can limit the generalization of conclusions in other health institutions and regions. Second, the study is a transversal (cross-sectional) study, and therefore, it is impossible to prove a causal link between demographic characteristics and use of psychoactive substances. To conduct a longitudinal study would be ideal for this purpose. Third, data on methadone dose, duration of treatment, the presence of comorbidities, as well as their treatment were not collected, which indicates the need to collect them and to investigate their relationship with the use of psychoactive substances. Finally, the collection of data on the use of illicit psychoactive substances through voluntary reporting could have been socially acceptable and unreal. In spite of the above mentioned shortcomings, the results of this research could be of use when planning the public health policies for methadone centers.

Conclusion

The study indicated a significant difference in the prevalence of use of legal and illegal psychoactive substances. Considering the fact that patients reported their use voluntarily, it is possible that they tried to make their reporting socially acceptable. Therefore, the use of psychoactive substances should be monitored based on regular and occasional urinalysis. Finally, three patients had an ASSIST score > 27, which indicated a high risk of developing addiction, alcohol addiction (2 patients), that is, cannabinoid addiction (1 patient). Therefore, interventions are needed, including referring to a specialist examination and treatment.

Competing interests

The authors declared no competing interests.

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