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Anxiety and depression in opiate addicts treated with methadone and buprenorphine

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Summary – *Objective:* To examine anxiety and depression in opiate addicts treated with methadone and buprenorphine. *Subjects and methods:* The study was conducted in the Association 'Margina' and the Center for Prevention and Out-patient Treatment of Addiction Diseases in Mostar. It included 100 patients who were divided into two groups: the first group consisted of drug subox- on users (N=50) and the other group consisted of subjects addicted to methadone, which was divided into two subgroups: M + and M– (recurrent). For the purposes of the research, Beck 's Anxiety and Depression Scale, Self-assessment Questionnaire for Anxiety (STAI), socio-demographic questionnaire specifically made for this research and Health Survey SF -36 (Short – Form Health Survey – 36th) were used. *Results:* Significantly higher numbers of addicts were living in the city (p = 0.034). The recurrent methadone users were significantly more depressed (> 20 %), while this percentage was somewhat lower in SBX users and M + subjects (20%). There was no statistically significant difference between the latter two groups (p=0.216). SBX users displayed most anxiety (10 %), while it was lowest among the users of methadone (<10 %). There was a statistically significant difference between the users of methadone M+ and M– (p = 0.034). *Conclusion:* Users of methadone were significantly more

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anxious than the drug buprenorphine users, while there were no statistically significant differences between the groups considering the depression

Keywords: opiate addicts, anxiety, depression, methadone, buprenorphine

INTRODUCTION

Psychoactive substances represent a problem dating from the fifties and starting to threaten the usual standards of life. People who get addicted to psychoactive substances become slaves of their problem and try to focus all their abilities towards providing a certain amount of psychoactive substance, weakening their integrity even further. The average age when the substance is taken for the first time is about 15 years, first injection happens about 21 (18 in the age group 18–24), while the time of the first addiction treatment ranges between 22–25 years of age.

It is a rule that an addict takes more substances at the same time, usually starting with alcohol and marijuana and then quickly turning to opiates.[1] Opiates include psychoactive substances of herbal origin, first of all opium, the dried milky juice from the not yet ripe fruits of white poppies, from which the morphine is later extracted. By means of twice-acetallizing the morphine, heroin (half-synthetic drug) is produced. This group also includes synthetic derivates of morphine, codeine and methadone, with similar effect.[2] Addiction to heroin is in most cases very difficult to cure. So nowadays, it is usual to try to help the individuals and their families by means of replacing the expensive illegal psychoactive drug with narcotics heptanone (methadone) and buprenorphine. Patients receive these substances directly from their doctors.[3] Methadone is widely used in treating the addiction throughout the world since 1960, while it was introduced to Croatia in 1990. The effects of methadone differ from the effects of other narcotics, because they last longer and there is no initial euphoria. The effect of methadone lasts up to 24 hours, thus enabling the patients to take it just once a day.[4] The main effects of methadone are alleviating the craving, suppressing the withdrawal symptoms and blocking the euphoric effect of opiates. It is a paradox that the use of methadone has resulted in greater number of fatalities due to the drug overdose.[5] Buprenorphine is used as a substitution therapy in treating the opiate addiction. It is used also as a substitution for methadone therapy if and when a patient decides to stop taking methadone. As opposed to methadone, buprenorphine may be given 3 times a week, enabling the users to have a better professional and social rehabilitation and generally, better quality of life. Higher doses of buprenorphine

are better tolerated than high doses of methadone, seldom lead to the development of tolerance and is less addictive than methadone.[6]

Anxiety

Anxiety is a painful state of helplessness and vulnerability. It is a state of being tense, worried and expecting something terrible to happen. The feeling of anxiety, along with accompanying organic and physiological disturbances, or more precisely, with secretory and motoric discharge, overwhelms the person and in the most severe cases, represents an unbearable state and an incomparable experience.[7] Anxiety is a constitutive part of life and we all feel it from time to time. We consider it a disease only when the anxiety is always present (general anxiety disorder), happening in particular situations which are usually not frightening, i.e. entering an elevator or taking a tram ride, leaving the house, social situations (phobias) or when it appears abruptly as an attack of particularly strong feeling of anxiety, called panic (panic disorder) and when that anxiety significantly limits the individual in achieving her/his personal, professional and other goals in life, thus reducing the quality of life. Not all anxiety should be feared, because it is common and informs the individual if he was in an alarming situation.[8]

Anxiety is manifested with a variety of symptoms, such as heart thumping, sweating, tremor of hands and body, dry mouth, breathing difficulties, nausea, feeling warm or hot, muscle tension, feeling that we are unable to relax and feeling of having a globe in the throat. Furthermore, it is manifested by mental symptoms, such as feeling of imminent fainting, weakness, confusion, concentrating difficulties, fear of death. The patients report a fear that they will lose control over their actions, feel excessively worried and expect some unpleasant surprise to happen. Several factors influence the occurrence of anxiety, such as childhood experiences, stressful situations, personal susceptibility and the manners of coping with stress.[9]

The treatment of each person suffering from anxiety disorder should be approached individually and a specific plan of treatment tailored, consisting of medicamental treatment, psychotherapeutic and other non-medicamental procedures and most frequently, their combination. Whichever reasons lead to the development of anxiety, their basis is in brain, because they are psychologically and biologically connected. Thus, it is important to say that the anxiety disorders can be treated with drugs, particularly from the group of anti-depressants affecting the serotonin levels, which are also successful in treatment of depression. It is important to point out that the drugs should be taken continually throughout the period of several weeks, as prescribed.[10]

Depression

Depression is a frequent mental disorder, characterized with sadness, loss of interest or satisfaction, feeling of guilt or low self-esteem, sleep and appetite disturbances, fatigue and lack of concentration. It is estimated that 350 millions of persons are suffering from that illness. Etiology of depression can be studied through several theoretical models: c*ognitive, behavioral, connected with surroundings* and probably the most acceptable is the *model diathesis-stress*.

Cognitive model explains the depression by means of attributive styles which person uses to explain the negative outcomes and begins with the cognitive triad, where the depressive persons have a more negative perception of themselves (unsuccessful person), negative perception of the world around them (superior and cruel) and negative expectations from the future. The behavioral model finds the causes of depression in problems due to personal interactions with the surroundings, where the limited pleasant experiences, thoughts that promote sadness and lack of experiences improving the self-esteem contribute to the emotional discomfort. Among the classes of depression, there are:

1. *Unipolar depressions* are characterized by typical depressive episodes, where a person experiences depressive mood, loss of interest and satisfaction and lack of energy, leading to decreased activity and lasting for no less than two weeks. Depending on the number and severity of symptoms, depressive episodes can be mild, moderate or severe.
2. *Bipolar mood disorder* consists of manic and depressive episodes, separated with periods of normal behaviour. Manic episodes include increased or heightened sense of irritability, hyperactivity, speaking tension, inflated self-esteem and reduced need for sleep.[11]

Treatment is nowadays ever more shifted from the psychiatric hospitals towards the treatment in families, which requires meeting several conditions. Among those conditions, the most important are: early start of treatment, positive emotional attitude towards the patient, informing the family about the nature of disease, support of professional and wider social surroundings, positive attitude towards the treatment and frequent controls etc.[12]

The main aim of this study is to investigate anxiety and depression among the opiate addicts treated with methadone and buprenorphine in the area of Mostar, in the Association 'Margina' and Center for Prevention and Out-patient Treatment of Addiction Diseases.

Specific aims: Investigate which between the users taking subox-on, methadone M+ and M- (recurrent) are the most anxious. Investigate which between the users taking subox-on, methadone M+ and M- (recurrent) are the most depressed. Investigate the health level of users taking subox-on, methadone M+ and M- (recurrent) Investigate the number of users taking subox-on, methadone M+ and M- (recurrent) considering their sex, level of education and interpersonal relations.

Ethical implications

- Verbal acceptance of subjects to take the survey.
- Informing the group about the anonymity of the survey and confidentiality of data.
- Informing the subjects about the aim and specific goals of the study.
- Stressing to subjects that the data will be used in scientific purposes (graduate thesis).
- In agreement with heads of both centers, data analysis and conclusions will be delivered to the centers.

SUBJECTS AND METHODS

The investigation was carried out in the Association 'Margina' and the Center for Prevention and Out-patient Treatment of Addictions in Mostar in the period from 1st July to 20th August in the year of 2013. For the purposes of the study, Beck's scale of anxiety and depression (23), containing 21 questions about anxiety and 21 questions about depression, State-Trait Anxiety Inventory (STAI) self-assessment questionnaire (24), socio-demographic questionnaire tailored specifically for the purposes of this study and Short Form Health Survey-36 (25) were used. The study was done on 100 subjects of both sexes, 50 methadone addicts and 50 buprenorphine addicts, aged from 23–49 years. Participation in the study was voluntary and included the subjects of both sexes. Patients previously diagnosed with mental illnesses or mental retardation have been excluded from the study.

Statistical data analysis

For the statistical analysis, we have used the program package SPSS for Windows (Version 17.0., SPSS Inc, Chicago, Illinois, USA) and Microsoft Excel (Version 11.0., Microsoft Corporation, Redmond, WA, USA). All statistical data were expressed as percentages and shown by means of graphs and tables, calculated using the program Microsoft Excel 2007. To assess the differences of nominal and ordinal variables, χ^2-test was used. Where the frequencies had not proved as expected, Yates' correction was applied and in some cases, merging of several cells. Level of significance was set to $p \leq 0,05$.

RESULTS

During the investigation, the total number of 100 subjects registered in the Association 'Margina' and the Center for Prevention and Out-patient Treatment of Addictions in Mostar have been questioned. 19 female subjects and 81 male subjects have been tested.

The most obvious difference between the subjects divided according to sex was in subox-on use – 87,9 % of male and 12,1 % of female subjects, while the difference in methadone use was less apparent – 76,1 % of male and 23,9 % of female subjects The difference in therapy choice between the sexes is statistically significant, because the Pearson's coefficient equals p 0,420.

Users of subox-on mostly finished the secondary education (72,7%) while the smaller percentage of them finished trade schools (3%) and universities (3%). As in the previous group, the greatest percentage of methadone users had finished secondary school (58,7%) while a lesser percentage (6,5%) of them had graduated on universities or achieved a baccalaureate. The difference here is also statistically significant, because the Pearson's coefficient equals p 0,471*.

In all three groups of subjects, namely users of subox-on, methadone users and recurrent users of methadone, most of the subjects have reported their standard of living as average. SBX (54,5%), M+ (52,2%) and M– (47,6%). The smallest percentage of users taking subox-on and methadone have reported their standard of living as above average SBX (3%), M (0%), while the smallest number of recurrent methadone users reported their standard of living equally as above average and 'cannot estimate' (4,8%). The difference in Pearson's coefficients is obvious here and it equals p 0,813.*

In all three groups of subjects, namely users of subox-on, methadone and recurrent users of methadone, most subjects have reported to live with their families. In SBX

Table 1. Socio-demographic data

	Group						χ^2	p
	SBX		M+		M–			
	N	%	N	%	N	%		
Sex							1,736	0,420
F	4	12,1	11	23,9	4	19,0		
M	29	87,9	35	76,1	17	81,0		
Education							7,398	0,471*
Primary school	5	15,2	5	10,9	1	4,8		
Secondary school	1	3,0	8	17,4	4	19,0		
Trade school	24	72,7	27	58,7	15	71,4		
University baccalaureate	2	6,1	3	6,5	1	4,8		
University diploma	1	3,0	3	6,5	0	0,0		
Standard							6,363	0,813*
Above average	1	3,0	0	0,0	1	4,8		
Slightly above average	2	6,1	3	6,5	0	0,0		
Average	18	54,5	24	52,2	10	47,6		
Slightly below average	6	18,2	10	21,7	3	14,3		
Significantly lower than average	4	12,1	7	15,2	6	28,6		
Cannot estimate	2	6,1	2	4,3	1	4,8		
Living with							4,123	0,873*
Alone	7	21,2	13	28,3	5	23,8		
With family	18	54,5	22	47,8	10	47,6		
With one parent	3	9,1	3	6,5	4	19,0		
With relatives	1	3,0	2	4,3	1	4,8		
With friends	4	12,1	6	13,0	1	4,8		
Living in							5,997	0,034*
Country	0	0,0	7	15,2	1	4,8		
City	33	100,0	39	84,8	20	95,2		

*Fisher's exact test; SBX-Subox-on; M+ Methadone group (stable); M– Methadone group (recurrent)

group, the percentage of those equaled 54,5%, while in methadone users it equaled 47.8% and 47,6% in recurrent methadone users. The smallest was the percentage of

those who live with their relatives, 3% in SBX group, 4,3% in methadone users group and 4,8% in recurrent methadone users group. The same percentage of the latter group reported living with their friends. Pearson's coefficient equaled p= 0,873.

100% of subox-on users live in the city, while that percentage is slightly smaller for methadone users (84,8 %) and the recurrent methadone users (95,2%). The results show that most of the subjects live in the city, while a smaller percentage of methadone users (15,2%) and recurrent methadone users (4,8%) live in the country. The Pearson's coefficient equals p= 0,034.

SBX users were mostly satisfied with their relationships with mothers and that answer had been given by 57,6 % of them. Methadone users have been most satisfied with their relationships with fathers and that answer had been given by 56,5% of them, while the recurrent methadone users were most satisfied with their relation-

Table 2. Interpersonal relations

	Group						χ^2	p
	SBX		M+		M–			
	N	%	N	%	N	%		
Relationship with father							2,625	0,622
Satisfied	16	48,5	26	56,5	8	38,1		
ustrightNot satisfied and not unsatisfied	12	36,4	16	34,8	9	42,9		
Unsatisfied	5	15,2	4	8,7	4	19,0		
Relationship with mother							0,967	0,915
Satisfied	19	57,6	24	52,2	11	52,4		
Not satisfied and not unsatisfied	9	27,3	16	34,8	8	38,1		
Unsatisfied	5	15,2	6	13,0	2	9,5		
Relationship with friends							1,091	0,896
Satisfied	16	48,5	21	45,7	12	57,1		
Not satisfied and not unsatisfied	12	36,4	19	41,3	6	28,6		
Unsatisfied	5	15,2	6	13,0	3	14,3		
Confiding to							1,480	0,961
Friends	11	33,3	18	39,1	7	33,3		
Mother	10	30,3	12	26,1	7	33,3		
Father	6	18,2	6	13,0	2	9,5		
Brother/Sister	6	18,2	10	21,7	5	23,8		

ships with friends, 57,1% of them and least satisfied with their relationships with fathers, 19,0 %. Most of the users would primarily confide to their friends, SBX 33,3% and M+ 39,1%, while the recurrent methadone users would equally confide to their friends and mothers, 33,3%. The answer 'father' was the least frequent in all three groups.

It is evident that the most of recurrent methadone users were older than 30 years of age, while the methadone users were the youngest, around thirty. There is a statistically significant difference between the groups, because the Pearson's coefficient equals p= 0,019.

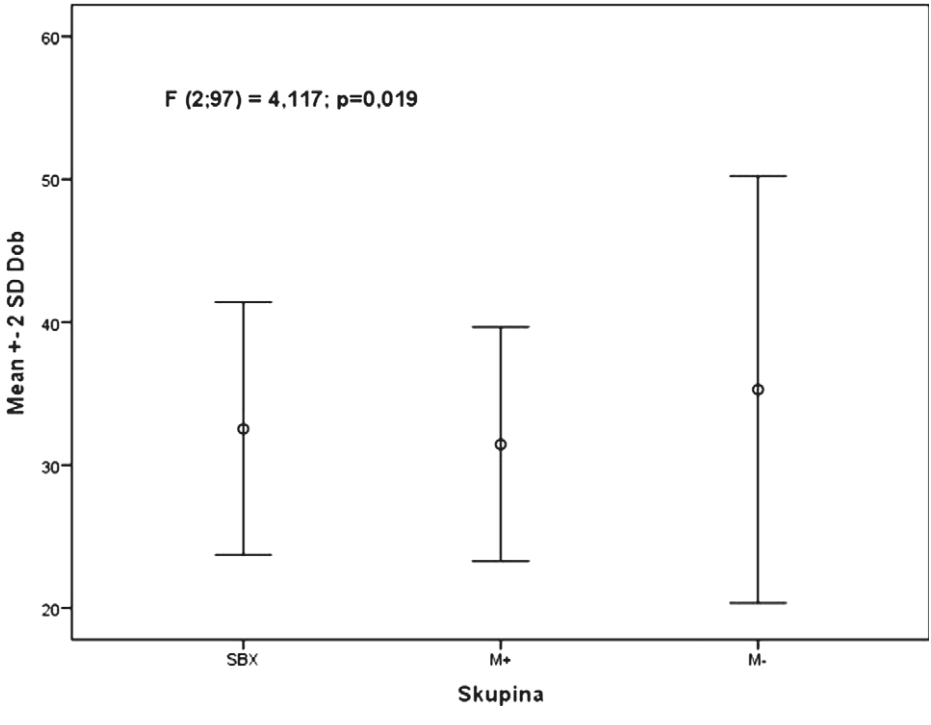

Figure 1. Distribution of subjects according to age

According to our data, the recurrent methadone users were the most depressive – over 20% of their total number, while the users of subox-on and methadone were equally depressive, around 20%. There is no statistically significant difference here, since the Pearson's coefficient equals p = 0,216.

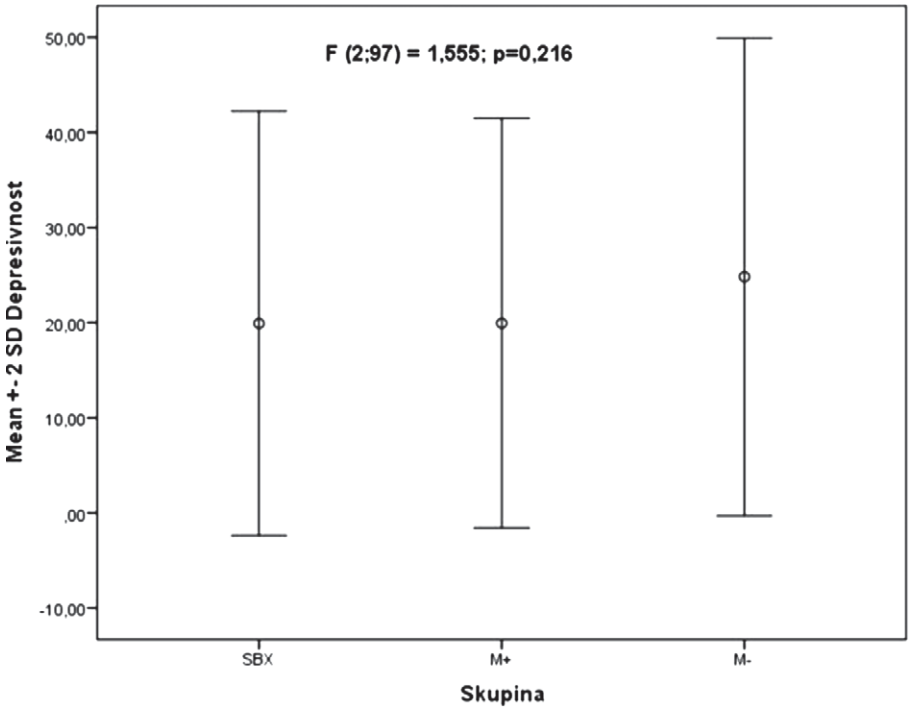

Figure 2. Distribution of subjects according to depression

According to our data, the subox-on users were the most anxious – 10%, while the percentage was lower in methadone users, under 10%. There is a statistically significant difference here, between the users of methadone M+ and recurrent methadone users M–. The difference is significant, p = 0,216.

Among the users of SBX, the most frequently reported was 'Physical pain', equaling X=63,42. The least frequently reported were 'Disturbances of physical functions', X=37,11 and 'Limitations due to the physical difficulties' X=37,50. Among the M+ users, the most frequently reported problem was also 'Physical pain', X equaling 78,93, and the least frequently reported were 'Disturbances of physical functions', X=24,64.

Among the recurrent methadone users, the most frequently reported were 'Disturbances of social functions', with X equaling 58,82 and the least frequently reported were, same as in other groups of users, 'Disturbances of physical functions', X=33,24.

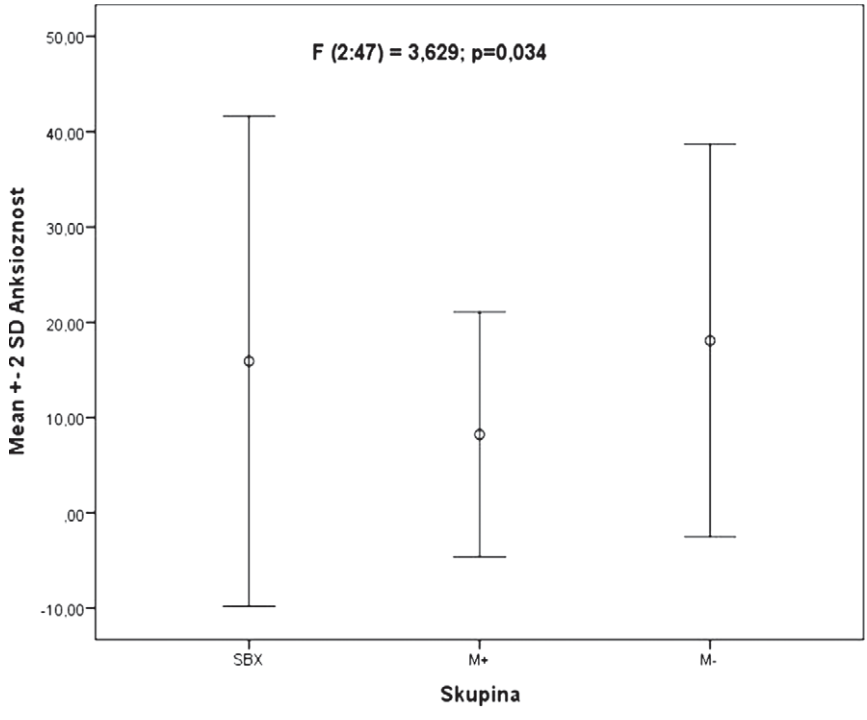

Figure 3. Distribution of subjects according to anxiety

Table 3. Differences in domains of SF 36 Questionnaire about the quality of life

SF 36	Group						F	P
	SBX		M+		M–			
	$\overline{X}$	SD	$\overline{X}$	SD	$\overline{X}$	SD		
Disturbances of physical functions	37,11	32,72	24,64	27,84	33,24	29,21	0,697	0,503
Limitations due to physical difficulties	37,50	36,63	41,07	28,77	44,12	39,06	0,152	0,859
Limitations due to emotional difficulties	45,61	43,33	57,14	44,20	45,10	33,21	0,428	0,654
Vitality	56,32	18,70	53,57	10,99	45,88	18,64	1,794	0,178
Mental health	60,00	17,54	60,00	16,38	47,29	21,92	2,547	0,089
Social functioning	59,87	24,85	69,23	19,51	58,82	20,62	0,959	0,391
Physical pain	63,42	30,20	78,93	19,46	54,26	31,18	3,004	0,059
Perception of general health	49,74	16,29	51,43	9,69	40,59	18,45	2,291	0,112

DISCUSSION

Together with alcoholism, addiction to psychoactive substances is, in broader sense, the leading social problem in the world and in the last few decades, also in our country. Recent data show that already in later classes of primary schools, children get their first experiences with psychoactive substances and that a significant number of kids had already tried marijuana, let alone alcohol. All of that represents a basis, together with a superficial attitude of parents towards raising and educating their kids, for the kids' inclination towards other types of behaviour and choosing the groups of peers at the margins of the usual and accepted social standards, which are, in fact, shaping the behaviour of an individual.[13]

According to data obtained in our study, from the total of 100 subjects, the greatest percentage of them have finished secondary schools – SBX 72%, M+ 58,7% and M– 71,4%, while less had graduated on universities SBX 3%, M+ 6,5% and M– 0% and colleges SBX 6,1%, M+ 6,5% and M– 4,8%. There is an interesting study, done by the Center for Addictions of Zagreb City, which showed that the probability that kid would try a psychoactive substance increases with higher education level of their parents.[14]

Considering the standard of living, a lesser number of subjects reported their standard was above average, namely SBX 6,1%, M+ 6,5% and M– 0,0%, while the greatest number reported that their standard of living was average – SBX 54,5%, M+ 52,2% and M– 47,6%. Lower than average standard of living was reported by 12,1% of SBX group, 15,2% of M+ group and 28,6% of M– group.

From the data dealing with characteristics of their households, we can see that most of the subjects live with their families, namely SBX 54,5%, M+ 47,8% and M– 47,6%, while a smaller number of them live alone – SBX 21,2%, M+ 28,3 and M– 28,3% or with one parent – SBX 9,1%, M+ 6,5% and M– 19%. The results of Prof. Janković's study show that one-parent families face a far greater number of difficulties compared to two-parent families and show significantly less potential in all areas of action and fulfilling the biological, psychological, emotional and social needs. The material status of one-parent families is also significantly worse than the status of complete families.[15]

Considering the interpersonal relations, our data suggest that our subjects have the best relations with their mothers – SBX 57,6%, M+ 52,2% and M– 52,4. While the SBX users are equally satisfied with their relationships with friends and fathers 48,5%, methadone users are more satisfied with their relationships with fathers

(56,5%) than with their relationships with friends (45,7%) and the recurrent methadone users are more satisfied with their relationships with friends (57,12%) than with their relationships with fathers (38,1%). From the study named *Family and School Fighting Against Addictions* by Fabijanić, we learn that girls addicted to psychoactive substances have rather negative opinions about their mothers. They find them frustrated, unsatisfied and neurotic as persons.[16] As a reason for that, they report that their mothers are not happy with their marital status and the role they have in their families, thus developing despair about their children.

As opposed to them, the boys do not share that opinion. They do not blame their mothers for things happening in their families, but see them as victims, suffering in their roles because of the insecurities of their partners. Thus, the boys are more inclined to blame their fathers.

From our questions dealing with depression, we learn that the recurrent methadone users were the most depressive (over 20 %), while that percentage was lower in SBX and M+ users, equaling about 20%. We found no statistically significant differences between these groups of subjects.

In the study carried out on addicts from Zadar, 9% of subjects had reported that depression and other forms of neurotic symptoms were their main motive for their first consumption of addictive substances.

In the studies carried out on young population of America, the data obtained show that 18% of depressive adolescents occasionally take light drugs and 7% of them drink alcohol at least once a week. In some other studies, the incidence of depressive disorders among the children and adolescent addicts ranged even up to 24,7%, with a significantly greater proportion of girls (48,2%) compared to boys (16,9%).

Analyzing the answers to questions dealing with anxiety, we can see that the SBX users were the most anxious (10%), while the methadone users were the least anxious (<10%). There is a significant difference between the methadone users (M+) and recurrent methadone users (M–). P-value equaled 0,034.

Considering the quality of life of our subjects, we found that the SBX users had suffered mostly from physical pain (X=63,42) and least frequently from physical difficulties (X=37,11) and from limitations due to the physical difficulties (X=37,50). The methadone users had suffered mostly from physical pain (X=78,93) and least frequently from physical difficulties (X=24,64). Among the recurrent methadone users, the most frequently reported problems were the disturbances of social functions (X=58,82) and the disturbances of physical functions were least frequently reported, same as in other groups of subjects (X=33,24).

CONCLUSIONS

1. According to their sex, education, standard of living and household members, we found no statistically significant differences between our groups of subjects.
2. In all three groups of subjects, significantly more subjects lived in cities than in rural areas p=0,034.
3. Considering the interpersonal relationships, we found no statistically significant differences between our groups of subjects.
4. The recurrent methadone users were more depressive (>20 %), while that percent is slightly lower in SBX and M+ users (around 20 %), but there were no statistically significant differences between the groups (p=0,216)
5. SBX users were the most (10%) and methadone users the least anxious (<10%). There is a statistically significant difference between the groups, p=0,034.
6. The quality of life is lower in M– group compared to the other two groups, especially considering the following characteristics – vitality, mental health, physical pain and general perception of health, but there were no statistically significant differences between the groups considering the quality of life.

ANKSIOZNOST I DEPRESIVNOST U OVISNIKA O OPIJATIMA LIJEČENIH METADONOM I BUPRENORFINOM

Sažetak – *Cilj:* Ispitati anksioznost i depresiju u ovisnika o opijatima liječenim metadonom i buprenorfinom. *Ispitanici i metode:* Ispitivanje je provedeno u Udruzi 'Margina' i Centru za prevenciju i ambulantno liječenje ovisnika u Mostaru. Uključeno je 100 pacijenata podijeljenih u dvije skupine: prva je skupina ovisna o lijeku subox-onu (N=50) i druga skupina ovisnika o metadonu, koja je podijeljena na dvije podskupine: M+ i M– (rekurentna). U svrhu istraživanja korištena je Beckova skala anksioznosti i depresivnosti, State-Trait Anxiety Inventory (STAI) upitnik za samoprocjenu, sociodemografski upitnik koji je namjenski sačinjen za ovo istraživanje i zdravstvena anketa SF-36 (Short Form Health Survey-36). *Rezultati:* Značajno je veći broj ispitanika koji žive u gradu (p=0.034). Više su deprimirani bili rekurentni korisnici metadona (> 20%), dok je ovaj postotak bio nešto niži kod korisnika SBX i u M+ skupini (20%). Između posljednje dvije skupine nije bilo statistički značajnih razlika (p=0.216). Korisnici SBX pokazali su najviše anksioznosti (10%), dok su najmanje anksiozni bili korisnici metadona (<10%). Postoji statistički značajna razlika između korisnika metadona M+ i M+ (p=0.034). *Zaključak:* Korisnici metadona bili su značajno više anksiozni od korisnika buprenorfina, dok glede depresivnosti nije nađeno statistički značajnih razlika.

Ključne riječi: ovisnici o opijatima, anksioznost, depresivnost, metadon, buprenorfin

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