

**CARACTERÍSTICAS COMPARATIVAS DO ESTADO DE TECIDOS DENTÁRIOS DUROS EM PACIENTES DEPENDENTES DE DROGAS QUE USAM HEROÍNA, E METADADONA COMO TERAPIA DE SUBSTITUIÇÃO****COMPARATIVE CHARACTERISTICS OF THE STATE OF HARD DENTAL TISSUES IN DRUG-DEPENDENT PATIENTS WHO USE HEROIN, AND METHADONE AS REPLACEMENT THERAPY****СРАВНИТЕЛЬНАЯ ХАРАКТЕРИСТИКА СОСТОЯНИЯ ТВЕРДЫХ ТКАНЕЙ ЗУБОВ У НАРКОЗАВИСИМЫХ ПАЦИЕНТОВ, УПОТРЕБЛЯЮЩИХ ГЕРОИН И МЕТАДОН В КАЧЕСТВЕ ЗАМЕСТИТЕЛЬНОЙ ТЕРАПИИ**

SEVBITOV, Andrei<sup>\*</sup>;TIMOSHIN, Anton; DOROFEEV, Aleksei; DAVIDYANTS, Alla; ERSHOV, Kirill; KUZNETSOVA, Maria

Department of Propaedeutic of Dental Diseases  
of I.M. Sechenov First Moscow State Medical University (Sechenov University)

*\* Correspondence author*  
*e-mail: avsevbitov@mail.ru*

Received 12 November 2019; received in revised form 19 January 2020; accepted 22 January 2020

**RESUMO**

De acordo com o serviço Federal de controle de drogas da Rússia, atualmente, 8,5 milhões de pessoas consomem drogas, incluindo maconha - 6,2 milhões, drogas sintéticas - 1,5 milhão e heroína - 800.000 pessoas. De acordo com a literatura estrangeira e nacional, o consumo de narcóticos na população cresce continuamente, principalmente na juventude e na adolescência: na estrutura dos drogados, 20% são pacientes com idades entre 9 e 16 anos, 60% - 17 a 30 anos, 20% - 30 anos ou mais. Além disso, muitos autores observam o fato de que mesmo em jovens com uso a por um curto período de metadona, aumenta acentuadamente a intensidade de cárie dental com subsequente perda rápida de dentes. Desde 2005, a OMS incluiu a droga metadona na lista de medicamentos essenciais para o tratamento da dependência de opióides. No entanto, de acordo com a literatura mais recente, o efeito negativo da metadona no corpo como um todo e a saúde bucal são muito mais pronunciados do que quando se toma heroína. As alterações na cavidade oral ao consumir heroína e metadona na literatura não são suficientemente abordadas, portanto, é considerado relevante estudar a patologia dentária nesse grupo de pacientes. Este artigo apresenta os resultados de uma análise comparativa dos efeitos adversos da heroína e da metadona nos tecidos duros dos dentes de pacientes dependentes de drogas. Nos pacientes que tomavam heroína e metadona, houve uma deterioração nos indicadores de status dentário. As principais manifestações do uso de narcóticos são o desenvolvimento do processo carioso, doenças inflamatórias da cavidade oral, violação da salivação, formação e disseminação de infecção odontogênica crônica. O efeito negativo da metadona é mais pronunciado em comparação com a heroína devido ao contato da droga em forma de comprimido com a mucosa oral.

**Keywords:** *cárie dentária, toxicod dependência, heroína, metadona.*

**ABSTRACT**

According to the Federal service for drug control in Russia, currently, 8.5 million people take drugs, including marijuana-6.2 million, synthetic drugs-1.5 million, and heroin-800,000 people. According to foreign and domestic literature, the population's consumption of narcotic drugs is continuously growing, especially in the youth and adolescence: in the structure of drug addicts, 20% are patients aged 9-16 years, 60% - 17-30 years, 20% - 30 years and older. Besides, many authors note the fact that even in young people with short-term use of methadone sharply increases the intensity of dental caries with subsequent rapid loss of teeth. Since 2005, the WHO has included the drug methadone in the list of essential medicines for the treatment of opioid dependence. However, according to the latest literature, the negative effect of methadone on the body as a

whole, and dental health is much more pronounced than when taking heroin. Changes in the oral cavity when taking heroin and methadone in the literature are not covered enough, so it is considered relevant to study dental pathology in this group of patients. This article presents the results of a comparative analysis of the adverse effects of heroin and methadone on the hard tissues of the teeth of drug-dependent patients. In patients taking heroin and methadone, there was a deterioration in dental status indicators. The main manifestations of taking narcotic drugs are the development of the carious process, inflammatory diseases of the oral cavity, violation of salivation, the formation and spread of chronic odontogenic infection. The negative effect of methadone is more pronounced in comparison with heroin due to the contact of the tablet form of the drug with the oral mucosa.

**Keywords:** *dental caries, drug addiction, heroin, methadone.*

## АННОТАЦИЯ

По данным Федеральной службы по контролю за оборотом наркотиков в России в настоящее время наркотики принимают 8,5 млн. человек, из них марихуану — 6.2 млн., синтетические наркотики — 1,5 миллиона, а героин — 800 000 человек. По данным зарубежной и отечественной литературы потребление населением наркотических препаратов постоянно растет, особенно в молодежной среде и подростковом возрасте: в структуре наркозависимых 20% составляют пациенты в возрасте 9–16 лет, 60% — 17–30 лет, 20% — от 30 лет и старше. Кроме того, многие авторы отмечают тот факт, что даже у лиц молодого возраста при непродолжительном приеме метадона резко увеличивается показатель интенсивности кариеса зубов с последующей быстрой потерей зубов. С 2005 года ВОЗ был включен препарат метадон в перечень основных лекарственных средств для лечения опиоидной зависимости. Однако по последним данным литературы, отрицательное влияние метадона на организм в целом и на стоматологическое здоровье значительно более выражено, чем при приеме героина. Изменения в полости рта при приеме героина и метадона в литературных источниках освещены недостаточно, поэтому актуальным считается изучение стоматологической патологии у данного контингента пациентов. В данной статье приведены результаты сравнительного анализа отрицательного воздействия героина и метадона на твердые ткани зубов у наркозависимых пациентов. У пациентов, принимающих героин и метадон, отмечено ухудшение показателей стоматологического статуса. Основными проявлениями приема наркотических препаратов являются развитие кариозного процесса, воспалительных заболеваний ротовой полости, нарушение саливации, формирование и распространение хронической одонтогенной инфекции. Отрицательное влияние метадона более выражено по сравнению с героином вследствие контакта таблетированной формы препарата со слизистой оболочкой полости рта.

**Ключевые слова:** *кариес зубов, наркомания, героин, метадон.*

## 1. INTRODUCTION

According to foreign and domestic literature, the population's consumption of narcotic drugs is constantly growing, especially in the youth and adolescence: in the structure of drug addicts, 20% are patients aged 9-16 years, 60% - 17-30 years, 20% - 30 years and older. [Silva *et al*, 2019; Gupta *et al*, 2012; Mateos-Moreno *et al*, 2013]. According to sociological research in recent years, every seventh student has tried drugs at least once. Over the past ten years, the number of adolescents with drug addiction has increased 13 times [Evstratenko *et al*, 2018; Sevbitov *et al*, 2019].

According to the Federal service for drug control in Russia, currently, 8.5 million people take drugs, including marijuana - 6.2 million, synthetic drugs - 1.5 million, and heroin-800,000 people.

Since 2005, WHO has included the drug methadone in the list of essential medicines for the treatment of opioid dependence. However, according to the latest literature, the negative effect of methadone on the body as a whole and dental health is much more pronounced than when taking heroin. Changes in the oral cavity when taking heroin and methadone in the literature are not covered enough, so it is considered relevant to study dental pathology in this group of patients [Martusevich *et al*, 2014; Mazzeo *et al*; 2013].

Methadone (6dimethylamino-4,4-diphenyl-3heptanon) is a synthetic opioid, an analgesic with narcotic properties, first obtained in 1946. Initially, the drug was supposed to be used as a substitute for morphine due to the similarity of the physiological effects caused, except for analgesia, less pronounced in cases of methadone use. Nevertheless, in 1949, the effectiveness of reducing doses of methadone for

the treatment of heroin withdrawal was shown. In 1964 V. P. Dole and M. A. Nyswander offered methadone for the treatment of patients with heroin addiction, and since then, the drug has been used in medicine mainly for the relief of heroin withdrawal attacks and as a means of replacement therapy [Simonova *et al*, 2014; Timoshin *et al*; 2018].

In the mid-60s of the last century, methadone programs were proposed, which are still being implemented in the United States, Great Britain, Denmark, Sweden, the Netherlands and other countries. The goal of these programs is not drug withdrawal, but social rehabilitation, reducing the level of criminogenic behavior, as well as inhibiting HIV infection and the development of AIDS. Also, in several countries in Europe, Latvia, Lithuania, Ukraine, and the United States, there are similar programs that aim to gradually transfer patients who use heroin to another synthetic drug, such as methadone. In Russia, such programs are banned or are limited in their use. In Ukraine, the methadone program lasted about nine years. In Crimea, during this time, the number of patients receiving an opium antagonist has increased from 9 to 800 people. After the return of Crimea to the Russian Federation, this program was discontinued. When adapting patients after methadone addiction, many drug addicts were further rehabilitated in other cities of Russia (Moscow, St. Petersburg, Rostov-on-don). Moreover, this process continues today because it turned out that the dependence on methadone is long-lasting and much more severe than on other opiates [Vaijayanthimala *et al*, 2015; Voloshina *et al*, 2018; Dos Silva *et al*; 2019].

According to the results of foreign studies of the effectiveness of methadone replacement therapy programs, it was noted that about 60% of the patients who participated in them, together with the use of methadone, continued to use "street" drugs. Besides, after replacement therapy, only 5-10% of patients with heroin addiction have remission of more than one year. Despite the above, it is stated that currently, methadone is used by drug users mainly for substitution purposes against the background of already formed heroin addiction [Silva *et al*, 2019; Gigena *et al*, 2015; Walter *et al*, 2015].

It should be borne in mind that systematic uncontrolled use of methadone for only one month due to the parallel development of tolerance to the drug and addiction to it, can lead to an increase in a single dose of methadone five times (1 g). It is also shown that the rate of

development of tolerance and dependence in the use of methadone is proportional to the length of use and the daily dose of heroin. Besides, if heroin withdrawal lasts for several days, then methadone-a few weeks. Unlike heroin, when you cancel methadone, the addict is not able to give up the drug on their own. Also, methadone overdose is much more common than heroin due to the slowness of its action and the unpredictable rate of development of tolerance to the drug. This does not allow you to assess the necessary dose, which does not threaten fatal consequences [Yang *et al*, 2015; Gupta *et al*, 2012].

Rapid acquisition of tolerance to the drug is also a problem of substitution therapy since many patients are subsequently forced to take methadone for years. It should be noted that while methadone maintenance therapy significantly increased mortality from overdoses. With increasing rates, acute methadone poisoning also prevails in the structure of acute opiate drug poisoning (the ratio of heroin/methadone was 3/1 in 2011, 1/3 in 2012 and 1/5 in the first six months of 2013).

To date, the spread and non-medical use of narcotic substances naturally leads to an increase in social tension and personal and public danger: an increase in crime, accidents, and suicides, severe problems with their health and the health of future offspring, a decrease in life expectancy, prostitution, the spread of HIV infection, hepatitis C [Mateos-Moreno *et al*, 2013; Protrka *et al*; 2013].

It is stated that drug addiction of any nature is a severe threat not only to the mental, somatic but also to the dental status of patients. It was found that the frequency and severity of oral diseases significantly increased in patients with drug dependence who use heroin [Du M. *et al*, 2001; Dukić *et al*, 2013].

Significant changes in the dental status of heroin-dependent patients are associated with the reluctance to lead a healthy lifestyle, comply with basic hygiene standards of oral care, and regularly visit the dentist. An important role is played by the reduction of the body's immunity, its protective and adaptive abilities against the background of taking drugs [Vehkalahti *et al*; 1996].

According to most authors, the main problems of dental heroin-dependent patients are the following [Girardin *et al*, 2019]:

- destruction of hard tissues of teeth;

- development of periodontal diseases of inflammatory origin;
- changes in the oral mucosa;
- violation of salivation;
- spread of foci of chronic odontogenic infection.

Based on the above, the purpose of the work is to conduct a comparative analysis of the negative impact on the hard tissues of the teeth of patients taking heroin and methadone as replacement therapy based on a set of objective studies [Di Fazio *et al*, 2018; Fiorentin *et al*, 2018].

## 2. MATERIALS AND METHODS

All research methods under this article have been conducted in accordance with the relevant guidelines and regulations. All experimental protocols were approved by the Local Ethics Committee of I. M. Sechenov First Moscow State Medical University (Sechenov University) protocol number № 05-16 from 18.05.2016. Prior to the study, informed consent was obtained from all patients for the upcoming study.

A set of clinical material was carried out from 2015 to 2017 in the clinic for the treatment and rehabilitation of drug-dependent patients of the medical center "Profmed". These were patients with various types of drug addiction, but the bulk - using opioid drugs (97%)

A total of 110 patients aged 20 to 50 years and more were examined, men-68, women-42, who are in the rehabilitation period.

According to the goals and objectives of the study, patients were selected who in addition to heroin mainly did not take other drugs (group 1-53 patients), and patients who received methadone as replacement therapy at different times (group 2-57 patients) Their distribution by sex, age, and duration of use of the drug are presented in Table 1 and 2.

Depending on the duration of the drug, group 1 patients are divided into two subgroups: 1A-patients with a duration of administration from 1 to 3 years and 1B-with a duration of administration of 3-5 or more years.

Similarly, patients were divided into two groups. Patients in subgroups 2A and 2B were taken mainly oral methadone, according to the scheme prescribed by the doctor-narcologist in the form of syrup or tablets.

Examination of the oral cavity included the determination of the hygienic state, detection of pathological changes in the oral mucosa, periodontal, hard tissues of the tooth.

At the same time, it was revealed that all 100% of the examined patients need various types of dental care. It was also revealed that all their previous visits to the dentist were motivated by the development of pain syndrome, that is, for emergency indications and, mainly, to the dentist to remove an inappropriate tooth treatment or to open an abscess.

Based on a survey of patients, it was found that planned oral sanitation was rejected, as a rule, due to problems of adaptation to dental treatment, fear of pain, and there were various life restrictions due to drug use and the duration of stages of dental treatment.

To assess the hygienic state of the oral cavity, the Green-Vermillion index was calculated, which includes the plaque index and the Tartar index.

An instrumental survey was also conducted. The teeth were examined using a dental mirror and a probe. When analyzing the intensity of the carious process, we used the values of the CFR indices of teeth, where C – the number of carious (untreated) teeth, F (filling) - the number of treated (sealed) teeth, R - the number of removed or to be removed teeth. The sum (C+F+R) of all affected and lost teeth characterizes the intensity of the carious process in a particular person.

The prevalence of caries was also assessed. The prevalence of dental caries is the ratio of the number of persons who have at least one of the signs of dental caries (carious, filled or removed teeth) to the total number of examined, expressed as a percentage.

## 3. RESULTS AND DISCUSSION:

Among the 100 people examined in the rehabilitation center for drug addicts, there was not a single person who did not complain about the general state of health and did not have pathological changes in the oral cavity. All 100% of those examined needed dental care. When conducting a survey of patients, it was found that women were motivated to take drugs for economic reasons in 32.7% of cases, moral and psychological in 43.2%, the influence of a drug-dependent husband, or another sexual partner.

In men, the main reasons were: interest to

try something "new" - 71.4%, dissatisfaction with work, career, family life-17.3%, the influence of friends, and the environment-11.3%.

Age-related terms of initiation of drug use in men and women were not revealed – the average age was 17.3 years, which has a substantial negative impact on the development of the body as a whole and, in particular, in the formation of the dental system.

It was revealed that the expressed drug dependence and the appearance of signs of withdrawal syndrome for the first time in women were formed approximately 6-8 months, in men-in 1-1.2 years, that is, two times later, which can be explained by the different frequency of taking drugs.

The negative manifestation of drug use men noted as the development of various somatic diseases (weakness, fatigue, heart pain, violation of the chair), women-the development of female dysfunction, memory loss, anorexia.

In the structure of complaints about hard tissues of the teeth, complaints about the destruction of teeth prevailed. All the examined patients had an unsatisfactory state of oral hygiene. Against the background of the general pathology of the body of drug-dependent patients, this is one of the main factors in the development of inflammatory processes in the oral cavity (Fig. One).

It was found that supragingival and subgingival deposits were reliably encountered in patients of both groups (100%), while solid supragingival and subgingival deposits prevailed.

#### *Hygienic state of the oral cavity when using heroin and methadone.*

The hygienic state of the oral cavity is not only a reflection of the general state of the body but also, in a certain way, plays a role in the prediction and development of major dental diseases. This indicator was evaluated by calculating the Green-Vermilion index (1964). The data obtained are presented in Tables 3 and 4 and Figure 1.

As can be seen from table 3, the hygienic state of the oral cavity in patients taking heroin can be assessed as "bad" and "very bad" - in 49% of patients in subgroup 1A and 45.2% of patients in subgroup 1B. Satisfactory hygiene was observed only in 5.7% of patients in subgroup 1A.

In a comparative analysis of hygiene indicators in different age groups of subgroup 1A,

it was found that 20-40 year-old patients had a level of hygiene with a rating of "bad" and "very bad" 2 times more often than in the age group of 41-50 years (33.9% and 15.1% of patients, respectively). A similar pattern is observed in subgroup 1B (33.9% and 11.3%).

The dependence of the hygiene index on the duration of drug use was not revealed by us: "bad" and "very bad" hygiene was detected in 49% of the examined patients with drug use lasting up to 3 years and in 45.2 patients taking drugs for more than three years.

Similarly calculated indicators of hygiene in the 2nd group (Tab. 4).

From the data obtained in table 4, it can be seen that satisfactory oral hygiene in patients of subgroup 2A is 3.4%, in subgroup 2B - 5.2%

"Bad" and "very bad" hygiene was found in 49.2% of patients in subgroup 2A and 41.9% of patients in subgroup 2A and 41.9% of patients in subgroup 2B, satisfactory-in 3.4% of patients in group 2A and 5.2% of patients in group 2B.

In group 2, there is also a dependence on the state of oral hygiene on age, as in group 1 ("bad" and "very bad" hygiene in 36.9% of patients 20-40 years and 12.3% aged 41-50 years). In subgroup 2B, these figures were 29.7% and 12.2%, respectively.

Thus, a poor and very poor state of oral hygiene has been established in all patients. At the same time, the indicators in both groups do not have much difference. It should be noted that patients often did not pay attention to such factors as the need to rinse the mouth after eating, a certain choice of toothpaste and brushes, because no preventive work was done with them [Cone *et al*, 2012; Kunkel *et al*, 2015; Grabenauer *et al*; 2018].

#### *Features of the clinic of the carious process in the use of drugs.*

Parenteral use of heroin contributes to an increase in the prevalence (96-100%) and intensity of dental caries due to toxic effects on the oral cavity. There was a correlation between the experience of heroin use and the intensity of dental caries: the longer the experience, the more likely the development of multiple caries, which later turns into pulpitis and periodontitis of a sluggish course [Pesce *et al*, 2012; Rook *et al*, 2005; Wasels *et al*, 1994; Presley *et al*, 2003; Sordi *et al*, 2017].

A characteristic feature of this group of patients is the absence of dental complaints and

the development of "pain-free caries".

The prevalence of caries in the examined patients was 100%, CFR-16.7%

The index of prevalence and intensity of caries was calculated separately for each subject, and then the average values were derived. The results are presented in Table 5.

As follows from table 5 in subgroup 1A (29 patients), the prevalence of caries was 87.8 in the age group of 20-40 years%.

In the age group from 41 to 50 years of this subgroup, the same figure was 98.1%.

The prevalence of caries in subgroup 1B was: at the age of 20-40 years, the prevalence was 87.9%, over 41 years - respectively 98.8%.

Thus, from the presented data, it can be stated that according to the WHO assessment, these values indicate a high prevalence of caries in people who take drugs. In this case, the indicators tend to increase depending on the age of patients and the timing of drug use.

The rate of caries intensity was 4.3 in subgroup 1A in the age group 20-40 years, and 5.8 in the age group 41-50 years.

In subgroup 1B, this indicator was 6.3 in the age group of 20-40 years and 6.8 in the age group of 41-50 years, i.e., the same relationship is observed as in the prevalence of caries: the intensity index tends to increase depending on the age of the patient and the duration of heroin use.

Similarly, we studied the prevalence and intensity of caries in patients transferred to methadone replacement therapy (group 2).

As can be seen from Table 6, the following data were obtained in group 2: in subgroup 2A, the prevalence in patients aged 20-40 years was 89.3%, in group 41-50 years – 94.2%.

The intensity index was in subgroup 2A in the age group 20-40 years - 5.8; and in the age group 41-50 years - 7.1.

In subgroup 2B, the prevalence of caries in people aged 20 to 40 years was 96.6%, and in the older age group, 99.6%. Accordingly, the intensity – 6.7, and in the older age group-8.7.

Thus, in the 2nd group, as in the 1st, there is a dependence (deterioration) of the prevalence and intensity of caries on the age of patients and the duration of drug use.

#### 4. CONCLUSIONS:

Heroin use has a toxic effect on the oral organs: clinically, there are high rates of prevalence and intensity of caries, especially in the age group of 41-50 years. When using methadone as replacement therapy, the prevalence of caries in 41-50 year olds is slightly higher than in the age group of 20-40 years (by 4%), the intensity of caries is similar (by 1.3 points or higher). The use of methadone as a replacement therapy has a more negative effect on the hygiene of the oral cavity and the condition of the hard tissues of the teeth than with the use of heroin.

A special feature of the treatment of patients suffering from drug addiction is the need for rapid preventive measures, rehabilitation of the oral cavity, including the removal of destroyed teeth and teeth with 3 degrees of mobility, treatment of dental caries and its complications. Given the high prevalence of dental diseases in drug-dependent patients, it is recommended to use high-quality care with annual planned rehabilitation to improve the quality of life. The use of modern therapeutic and orthopedic materials will improve the quality of dental care.

Given the peculiarities of caries in drug-dependent patients, the occurrence of which is connected, including, with hypocalvaria recommended as a filling material to use polyalkenoate blocks of cement having series-production properties due to the content of fluoride ions.

#### 5. ACKNOWLEDGMENTS:

This work was done at Sechenov University with supported by the "Russian Academic Excellence Project 5-100".

#### 6. REFERENCES:

1. Evstratenko, V. V., Sevbitov, A. V., Platonova, V. V., Selifanova, E. I., Dorofeev, A. E. The characteristics of crystallization of mixed saliva in patients using heroin and methadone. *Klinicheskaya Laboratornaya Diagnostika*, **2018**, 63(4), 223-227.
2. Sevbitov A.V., Dorofeev A.E., Kuznetsova M.Yu., Timoshin A.V., Ershov K.A. Comparative characteristics of the crystallogram of the oral fluid in patients who use heroin and methadone. *Periodico Tchê Quimica*, **2019**, 16(33), 94-101

3. Martusevich, A. K., Yanchenko, V. A., Zhdanova, O. B., Artese, F., Napisanova, L. A., Virbalene, R. Crystallization characteristics of biological fluids of patients with postoperative alveococcosis. *Sovremennye Tehnologii v Medicin*, **2014**, 6(2), 38-42.
4. Mazzeo, M. A., Linares, J. A., López, M. M., Bachmeier, E., Wietz, F. M., Galván, V., Valentinuzzi, M. C., Riveros, J. A., Finkelberg, A. Analysis of saliva samples from oncological patients treated with 5-fluorouracil and leucovorin calcium by scanning electron microscopy with energy dispersive system. *Journal of Oral Pathology and Medicine*, **2013**, 42(10), 788-792.
5. Simonova, Z. G., Martusevich, A. K., Shubina, O. I., Emanuel, V.L. Structuring characteristics of biological fluids of patients with combined cardiovascular and gastrointestinal pathology. *Sovremennye Tehnologii v Medicin*, **2014**, 6(3), 64-70.
6. Timoshin, A. V., Dorofeev, A. E., Davidyants, A. A., Ershov, K. A., Pustokhina, I. G., Danshina, S. D. Features of the dental status of patients taking narcotic smoking mixtures. *Indo American Journal of Pharmaceutical Sciences*. **2018**, 5(9), 9114-9117.
7. Vijayanthimala, V., Lee, D. K., Kim, S. V., Yen, A., Tsai, N., Ho, D., Chang, H.-C., Shenderova, O. Nanodiamond-mediated drug delivery, and imaging: Challenges and opportunities. *Expert Opinion on Drug Delivery*. **2015**. 12(5), 735-749.
8. Voloshina, I. M., Borisov, V. V., Sevbitov, A.V., Davidyants, A.A., Mironov, S. N., Kuznetsova, M. Yu., Ergesheva, E. V. Distinctive features of microcrystallization of mixed saliva in children with different levels of activity of carious process. *Asian Journal of Pharmaceutics*, **2018**, 12(S3), 1017-1020.
9. Dos Silva, D. S., De Yamaguchi, K. K. L. Drug chemistry, and self-medication awareness as a tool in teaching organic functions. *Periodico Tchê Química*, **2019**, 16(31), 223-234
10. Silva, P. D. C., Santos, B. L. C. D., Soares, G.L., Oliveira, W.A.D. Anti-Candida albicans activity of the association of citronelal with anfotericin B or with cetoconazole. *Periodico Tchê Química*, **2019**, 16(31), 250-257
11. Gigena, P. C., Comejo, L. S., Lescanode-Ferrer, A. Oral health in drug addict adolescents and non-psychoactive substance users. *Acta Odontol Latinoam*, **2015**, 28(1), 48-57.
12. Walter M., Bentz D., Schick Tanz N., Milnik A., Aerni A., Gerhards C., Schwegler K., Vogel M., Blum J., Schmid O., Roozendaal B., Lang UE, Borgwardt S., de Quervain D. Effects of cortisol administration on craving in heroin addicts. *Transl Psychiatry*. **2015**, 28(5), 610.
13. Yang T., Guo X., Wang H., Fu S., Wen Y., Yang H. Magnetically optimized SERS assay for rapid detection of trace drug-related biomarkers in saliva and fingerprints. *Biosens Bioelectron*. **2015**, 15(68), 350-357.
14. Gupta T., Shah N., Mathur V. P., Dhawan A. Oral health status of a group of illicit drug users in Delhi, India. *Community Dent Health*, **2012**, 29(1), 49-54.
15. Mateos-Moreno M. V., Del-Río-Highsmith J., Riobóo-García R., Solá-Ruiz M. F., Celemín-Viñuela A. Dental profile of a community of recovering drug addicts: Biomedical aspects. Retrospective cohort study. *Med Oral Patol Oral Cir Bucal*. 2013 Jul 1;18(4):e671-9
16. Protrka N., Katunarić M., Filipović I., Verzak Z. Caries prevalence in heroin addicts. *Acta Clin Croat*. **2013**, 52(4), 436-43.
17. Du M., Bedi R., Guo L., Champion J., Fan M., Holt R. Oral health status of heroin users in a rehabilitation centre in Hubei province, China. *Community Dent Health*, **2001**, 18(2), 94-8.
18. Dukić W., Dobrijević T. T., Katunarić M., Lesić S. Caries prevalence in chronic alcoholics and the relationship to salivary flow rate and pH. *Cent Eur J Public Health*, **2013**, 21(1):43-7.
19. Vehkalahti M., Nikula-Sarakorpi E., Paunio I. Evaluation of salivary tests and dental status in the prediction of caries increment in caries-susceptible teenagers. *Caries Res*, **1996**, 30(1), 22-8.
20. Girardin F., Hearmon N., Negro F., Eddowes L., Bruggmann P., Castro E. Increasing hepatitis C virus screening in people who inject drugs in Switzerland using rapid antibody saliva and dried blood spot testing: A cost-effectiveness analysis. *J Viral Hepat*. **2019**, 26(2), 236-245.

21. Di Fazio V., Wille S. M. R., Toennes S. W., van Wel J. H. P., Ramaekers J. G., Samyn N. Driving under the influence of cocaine: Quantitative determination of basic drugs in oral fluid obtained during roadside controls and a controlled study with cocaine users. *Drug Test Anal*, **2018**, 10.
22. Fiorentin T. R., Scherer J. N., Marcelo M. C. A., Sousa T. R. V., Pechansky F., Ferrão M. F., Limberger R. P. Comparison of Cocaine/Crack Biomarkers Concentrations in Oral Fluid, Urine, and Plasma Simultaneously Collected From Drug Users. *J Anal Toxicol*, **2018**, 42(2), 69-76.
23. Cone E. J. Oral fluid results compared to self reports of recent cocaine and heroin use by methadone maintenance patients. *Forensic Sci Int*. **2012**, 10(215), 88-91.
24. Kunkel F., Fey E., Borg D., Stripp R., Getto C. Assessment of the use of oral fluid as a matrix for drug monitoring in patients undergoing treatment for opioid addiction. *J Opioid Manag*. **2015**, 11(5), 435-42.
25. Grabenauer M., Moore K. N., Bynum N. D., White R. M., Mitchell J. M., Hayes E. D., Flegel R. Development of a Quantitative LC-MS-MS Assay for Codeine, Morphine, 6-Acetylmorphine, Hydrocodone, Hydromorphone, Oxycodone and Oxymorphone in Neat Oral Fluid. *J Anal Toxicol*. **2018**, 42(6), 392-399
26. Pesce A., West C., Gonzales E., Rosenthal M., West R., Mikel C., Almazan P., Latyshev S., Horn P. Illicit drug use correlates with negative urine drug test results for prescribed hydrocodone, oxycodone, and morphine. *Pain Physician*, **2012**, 15(5), E687-92.
27. Rook E. J., Hillebrand M. J., Rosing H., van Ree J. M., Beijnen J. H. The quantitative analysis of heroin, methadone, and their metabolites and the simultaneous detection of cocaine, acetylcodeine, and their metabolites in human plasma by high-performance liquid chromatography coupled with tandem mass spectrometry. *J Chromatogr B Analyt Technol Biomed Life Sci*. **2005**, 824(1-2), 213-21.
28. Wasels R., Belleville F. Gas chromatographic-mass spectrometric procedures used for the identification and determination of morphine, codeine, and 6-monoacetylmorphine. *J Chromatogr A*. **1994**, 674(1-2), 225-34.
29. Presley L., Lehrer M., Seiter W., Hahn D., Rowland B., Smith M., Kardos KW, Fritch D., Salamone S., Niedbala R. S., Cone E.J. High prevalence of 6-acetylmorphine in morphine-positive oral fluid specimens. *Forensic Sci Int*, **2003**, 133(1-2), 22-5.
30. Sordi M. B., Massochin R. C., Camargo A. R., Lemos T., Munhoz E. A. Oral health assessment for users of marijuana and cocaine/crack substances. *Braz Oral Res*, **2017**, 31, 102.



**Table 1.** Distribution of heroin users by gender, age, and duration of use (group 1)

Drug	Total patients	Gender	Age	Duration of use		Total
				1-3 years (group 1A)	3-5 or more years (group 1B)	
Methadone	53	M	20-30 years	6	6	12
		W		3	3	6
		M	31-40 years	7	7	14
		W		4	2	6
		M	41-50 and more	5	3	8
		W		4	3	7
<b>Total:</b>				29	24	53

**Table 2.** Distribution of methadone users by gender, age, and duration of use (group 2)

Drug	Total patients	Gender	Age	Duration of use		Total
				1-3 years (group 1A)	3-5 or more years (group 1B)	
Methadone	57	M	20-30 years	5	5	10
		W		5	4	9
		M	31-40 years	8	6	14
		W		4	4	8
		M	41-50 and more	5	5	10
		W		3	3	6
<b>Total:</b>				30	27	57

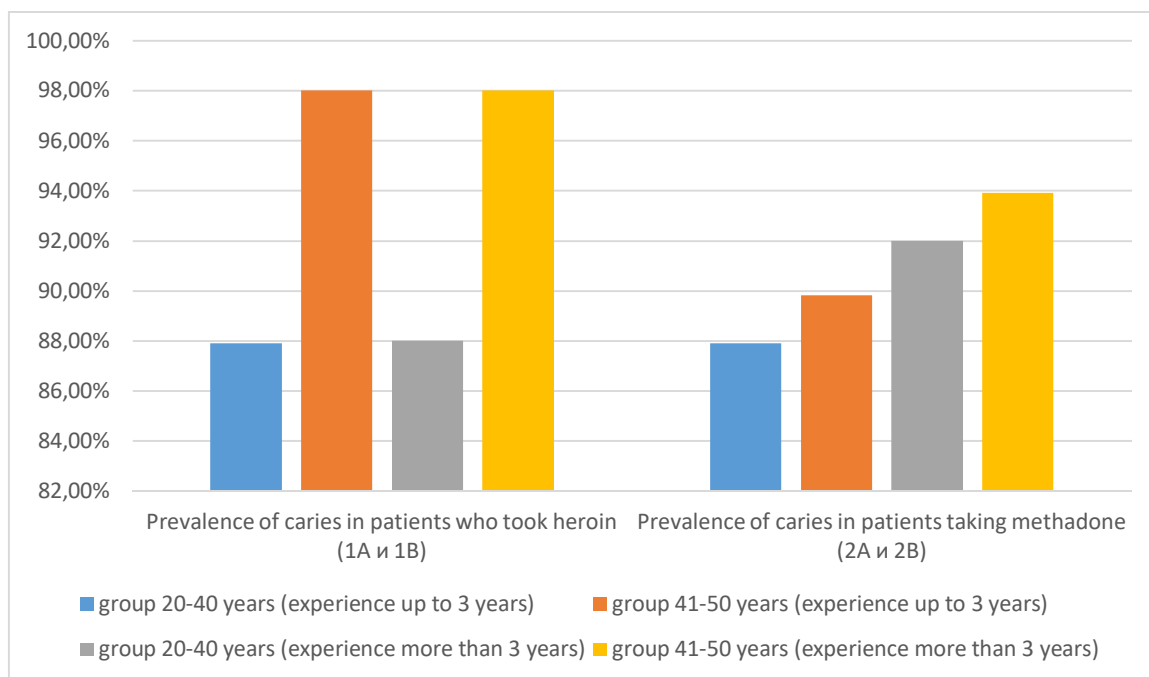
**Table 3.** Indicators of the hygienic state of the oral cavity in patients of the 1st group (previously used heroin)

The index level of hygiene, the rate of indicators	Group 1 (n=53)			
	Subgroup 1A		Subgroup 1B	
	20-40 year n-20	41-50 year n-9	20-40 year n-18	41-50 year n-6
<b>Good</b> 0-0,6	-	-	-	-
<b>Satisfactory</b> 0,7-1,6	2 (3,8%)	1 (1,9%)	-	-
<b>Bad</b> 1,7-2,5	7 (13,2%)	2 (3,8%)	4 (7,5%)	3 (5,6%)
<b>Very bad</b> >2,6	11 (20,7%)	6 (11,3%)	14 (26,4%)	3 (5,7%)

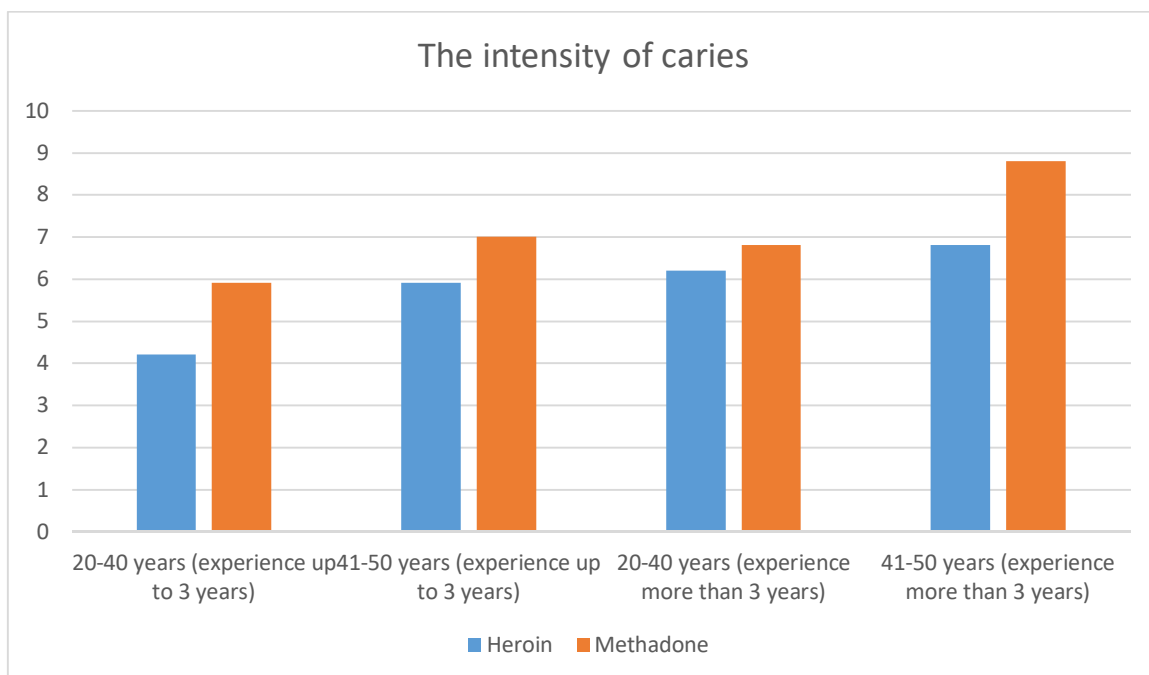
**Table 4.** Indicators of the hygienic state of the oral cavity in patients of the 2nd group (substitution therapy with methadone)

The index level of hygiene, the rate of indicators	Group 1 (n=53)			
	Subgroup 1A		Subgroup 1B	
	20-40 year n-22	41-50 year n-8	20-40 year n-19	41-50 year n-8
<b>Good</b> 0-0,6	-	-	-	-
<b>Satisfactory</b> 0,7-1,6	1 (1,7%)	1 (1,7%)	2 (3,5%)	1 (1,7%)
<b>Bad</b> 1,7-2,5	3 (5,3%)	2 (3,5%)	9 (15,7%)	1 (1,7%)
<b>Very bad</b> >2,6	18 (31,6%)	5 (8,8%)	8 (14%)	6 (10,5%)

**Table 5.** Prevalence of caries in patients taking heroin and methadone, depending on age and duration of use



**Table 6.** The intensity of caries in patients who took heroin and methadone, depending on the age and duration of use





**Figure 1.** Patient P. Methadone replacement therapy for 6 years. Chronic periodontitis of the upper dentition, chronic generalized periodontitis