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## SIDE EFFECTS OF ANTIDEPRESSANTS ON ORAL HEALTH ACCORDING TO QUESTIONNAIRES OF PATIENTS AND HEALTHCARE PROFESSIONALS

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An anonymous survey was conducted of 31 visitors to pharmacies with prescriptions for antidepressants, 30 doctors who prescribe antidepressants, 51 pharmacy employees and 40 dentists. Less than half of doctors who prescribe antidepressants, pharmacists and only 12.9 % of patients were informed about the risk of adverse reactions from the oral cavity when using antidepressants. Complaints about the presence of caries or dryness/ulcers on the oral mucosa were noted in the questionnaires of 26 (83.9 %) patients. According to the data of 82.5 % of dentists, patients came to them with complaints of dry mouth due to the use of antidepressants. Therefore, among patients who use antidepressants, a high prevalence of caries and its complications, as well as the development of periodontal diseases against the background of dry mouth, was found, which may be partly related to the increase in the use of tricyclic antidepressants and the low awareness of patients and health care professionals about the peculiarities undesirable effects of antidepressants on the oral cavity condition.

**Key words:** anxiety, antidepressive agents, periodontal diseases, xerostomia, pharmacists

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## ВПЛИВ ПОБІЧНИХ ЕФЕКТІВ АНТИДЕПРЕСАНТІВ НА СТАН ЗДОРОВ'Я РОТОВОЇ ПОРОЖНИНИ ЗА ДАНИМИ АНКЕТУВАННЯ ПАЦІЄНТІВ ТА ФАХІВЦІВ ОХОРОНИ ЗДОРОВ'Я

Було проведено анонімне анкетування 31 відвідувача аптек із рецептами на антидепресанти, 30 лікарів, які призначають антидепресанти, 51 аптечного працівника та 40 лікарів-стоматологів. Менше половини лікарів, які призначають антидепресанти, фармацевтів і лише 12,9 % пацієнтів були поінформовані про ризик виникнення небажаних реакцій з боку ротової порожнини при вживанні антидепресантів. Скарги на наявність карієсу або сухості/виразок на слизовій оболонці рота відмічено у анкетах 26 (83,9 %) пацієнтів. За даними 82,5 % лікарів-стоматологів, до них звертались пацієнти із скаргами на сухість у роті, на фоні вживання антидепресантів. Отже, серед пацієнтів, які вживають антидепресанти, виявлено високу поширеність карієсу та його ускладнень, а також розвиток хвороб пародонта на фоні сухості ротової порожнини, що частково може бути пов'язано із зростанням вживання трициклічних антидепресантів і низькою поінформованістю пацієнтів та фахівців охорони здоров'я щодо особливостей небажаних ефектів антидепресантів на стан ротової порожнини.

**Ключові слова:** тривога, антидепресанти, захворювання пародонту, ксеростомія, фармацевти

*The study is a fragment of the research project "To justify the scientific approach in improvement of the methods of pharmaceutical care in case of socially significant diseases", state registration No 0123U101928*

War, natural disasters, and domestic violence are frequent causes of psychological injuries, and even many years after them, the patient may develop post-traumatic stress disorder (PTSD) [12]. It is known that medicinal products can have an undesirable side effect on the health of the oral cavity [2].

Patients with depression and PTSD have high rates of comorbidities and significantly worse oral health than the general population [8]. In particular, patients with depression often consult a dentist because of changes affecting the hard tissues of the tooth and soft tissues [10]. Caries [9] and periodontitis [7] are more often noted in them.

To a certain extent, the connection between anxiety-depressive disorders and dental health pathology is explained by the fact that depression is associated with the use of a large amount of carbohydrates, lack of interest in proper oral hygiene [10], abuse of tobacco [1], alcohol and/or psychostimulants [8], financial, geographic, and social barriers to access to oral health care.

However, impaired dental health can also be caused by the orofacial side effects of antidepressants [8], which are first-line drugs for the treatment of depression and anxiety disorders. Thus, it has been proven that fluoxetine provokes periodontitis [3], antidepressants from the group of selective serotonin reuptake inhibitors (SSRIs) can cause bruxism [6, 11].

**The purpose** of the study was to establish the frequency and nature of adverse reactions from the oral cavity in patients taking antidepressants.

**Materials and methods.** To study the frequency of side effects of the use of antidepressants, an anonymous survey of visitors to pharmacies with prescriptions for antidepressants, doctors who prescribe

antidepressants, pharmacy workers and dentists was conducted. Links to Google forms were sent to respondents in an e-mail and freely available on social networks. The survey was conducted during November 2022 – January 2023.

152 respondents took part in the survey (31 patients, 30 doctors who prescribe antidepressants, 51 pharmacy workers, 40 dentists). The results were evaluated by the frequency of responses (in percentages).

The questionnaires for health care professionals also specified the position, length of service, which antidepressants were more often prescribed (in the questionnaire of doctors who prescribe antidepressants), which antidepressants were more often dispensed (in the questionnaire for pharmacists), which changes in the oral cavity were detected (in the questionnaire for dentists).

Among the interviewed patients, 16 (51.6 %) were women, 15 (48.4 %) were men. The majority (74.2 %) of patients were young (25–44 years old), the rest – were middle-aged (45–60 years old).

Among the interviewed doctors who have experience in prescribing antidepressants, 6 doctors were psychiatrists, 6 were pediatricians, 6 were neurologists, 6 were family doctors, and the rest were doctors of various specialties (endocrinologists, therapists, etc.). Among them, only 1 (3.3 %) doctor had less than 2 years of work experience, 7 doctors (23.3 %) had experience from 2 to 7 years, the remaining 22 specialists had more than 7 years of experience.

Among the surveyed pharmacy workers, 7 (13.7 %) were pharmacy managers, 26 (51.0 %) were pharmacists, and 18 (35.3 %) were pharmacist assistants. 28 (54.9 %) pharmacy workers had work experience from 3 to 6 years, 20 (39.2 %) – less than 3 years, the remaining 3 (5.9 %) – more than 7 years.

Among dentists, 9 (22.5 %) had less than 3 years of experience, 26 (31.5 %) had 3–6 years of experience, and the remaining 5 (25 %) had more than 7 years of experience.

Statistical processing of the obtained data was carried out using the programs Microsoft Office Excel 2016, IBM SPSS Statistics Base version 22.0.

**Results of the study and their discussion.** Among the patients, 16 (51.5 %) are using antidepressants for the first time, and the rest – repeatedly. An increase in the body weight against the background of the use of antidepressants bothered 1 (3.2 %), insomnia – 7 (22.6 %), drowsiness and weakness during the day – 2 (6.45 %), dizziness – 3 (9.68 %) patients (Fig. 1). However, 26 (83.9 %) patients indicated the presence of caries or dryness/ulcers on the oral mucosa. 30 (96.8 %) respondents answered that they did not use other medicines at the same time as antidepressants (Fig. 1).

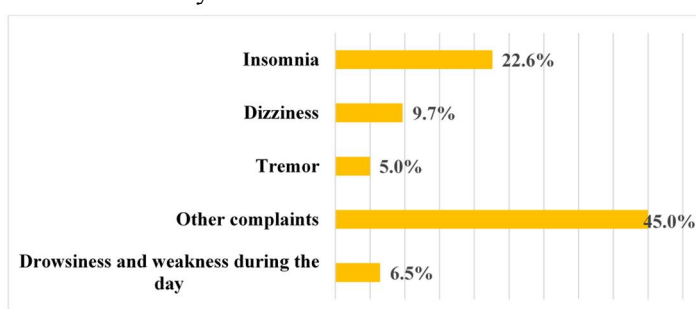


Fig. 1. Side effects in patients taking antidepressants

Most respondents (87.1 %) answered that the doctor warned them about specific side effects of antidepressants, but only 4 (12.9 %) patients said that they were informed about possible side effects from the oral cavity when taking antidepressants.

Amitriptyline is most often prescribed, this was indicated by 17 doctors (56.7 %), escitalopram is also often prescribed by 16 (53.3 %) doctors, fluoxetine – by 12 (40 %) doctors, paroxetine – by 10 (33.3 %)

doctors. 13 (43.3 %) doctors know about dry mouth as a side effect of antidepressants, 8 (26.7 %) doctors recommend consulting a dentist before taking antidepressants.

Among pharmacy workers, 46 (90.2 %) testified that they were approached by visitors with prescriptions for antidepressants. According to the data presented in Table 3, patients were more often prescribed escitalopram (54.9 %), fluoxetine (11.8 %), amitriptyline (7.8 %), trazodone (5.9 %), paroxetine (3.9 %) and doxepin (3.9 %), mirtazapine (2.0 %) (Table 1).

Table 1

**The frequency of prescribing antidepressants according to a survey of pharmacy workers**

Preparation	Number of respondents	%
Escitalopram	28	54.9
Fluoxetine	6	11.8
Amitriptyline	4	7.8
Trazodone	3	5.9
Doxepin	2	3.9
Paroxetine	2	3.9
Mirtazapine	1	2.0
Agomelatine	0	0
Clomipramine	0	0
They did not come across prescriptions for antidepressants	5	9.8

Prescriptions were mostly written for young patients, as indicated by 30 (65.2 %) pharmacy workers, while 15 (32.6 %) and 1 (2.2 %) of pharmacy workers 6 (11.8 %) pharmacy workers reported that patients complained about side effects from the oral cavity (caries or dryness/ulcers in the oral mucosa) against the background of taking antidepressants.

It should be noted that less than half (47.1 %) of pharmacy workers were informed about the oral side effects of antidepressants.

Only 20 dentists (50 %) noted that during the collection of anamneses they necessarily ask patients about the use of medicines, 14 (35.0 %) do this only when they are informed about the presence of a concomitant disease in the patient.

Among dentists, 35 (86.7 %) noted that they know about the effect of antidepressants on the condition of the oral cavity. 20 (50 %) noted caries or dryness/ulcers on the oral mucosa in patients taking antidepressants; among them, 5 (25 %) indicated that patients were mostly men, and 15 (75 %) were women; 10 (50 %) noted that the patients were mostly young (25–44 years old), 7 (35%) were middle-aged (45–60 years old); the remaining 3 (15 %) are older (over 60).

According to the questionnaire for dentists, the main complaints of patients against the background of taking antidepressants were dry mouth, which was indicated by 33 (82.5 %) dentists; accordingly, 28 (70.0 %) dentists noted the periodic appearance of ulcers on the mucous membrane of the oral cavity, the appearance of new carious cavities and the progression of caries – 24 (60.0 %), bleeding and inflammation of the gums – 21 (52.5 %) dentists.

It is emphasized that the features of the course of dental diseases were multiple caries, an acute course of caries with a predominant localization in the cervical areas of the teeth against the background of insufficient hygiene and dryness of the oral cavity. Unsatisfactory hygiene and chronic catarrhal gingivitis in patients taking antidepressants were diagnosed by 25 (76 %) doctors.

Fig.2 shows the state of oral health of a 26-year-old man. From the anamnesis: for 10 months he has been taking an antidepressant after experiencing stress. When prescribing the drug, the patient was not warned by the doctor about the need for periodic examination by the dentist. Before the onset of acute pain, he did not consult a dentist. During the last 6 months, he noted dry mouth, destruction of hard tooth tissues, bleeding gums.

Fig. 3 shows the clinical status of the oral health of a 28-year-old man. From the anamnesis: during the last 8 months, he has been using an antidepressant. Visits to the dentist have been postponed due to moving from the eastern regions of Ukraine. During the last 6 months, he lost fillings in his chewing teeth, the teeth were crumbling. The appearance of new carious cavities in the cervical regions. Complaints of bleeding and swelling of the gums.



Fig. 2. Clinical state of oral health of a 26-year-old man.



Fig. 3. Clinical status of oral health of a 28-year-old man.

As you know, antidepressants are divided into four groups: tricyclic antidepressants; SSRIs; atypical (heterocyclic second and third generation) antidepressants (including selective norepinephrine reuptake inhibitors); monoamine oxidase inhibitors.

Escitalopram and fluoxetine, as well as the tricyclic antidepressant amitriptyline, are among the most popular drugs from the group of antidepressants

that were dispensed in the pharmacy according to the survey of pharmacy workers. It should be noted that these drugs are included in the TOP-3 retail sales of antidepressants in 2022 of the analytical market research system “PharmXplorer” of the company “Proxima Research”. These three drugs are also among the top five drugs with the highest sales in defined daily doses. It is important to note that amitriptyline ranks 3rd in terms of consumption in defined daily doses.

The sale of drugs of the ATS classification group N06AB has increased significantly, which is due to an increase in the level of anxiety and depression against the background of the pandemic of the infection of COVID-19 and a full-scale war (Fig. 4).

The ATC classification group N06AA “Nonselective inhibitors of the reuptake of neuronal monoamines” has been characterized by a stable sales volume in recent years. However, considering the decrease in the number of the population due to migration in connection with military operations, the consumption of antidepressants of this group per capita increased (compare: the volume of pharmacy sales in natural terms in 2022 decreased by 21 %) (Table 2).

**Medicinal products – leaders (TOP-5) of retail sales of ATS group N06A (antidepressants)  
in natural terms (packages) in Ukraine in 2022**

Item number	Name (INN)	Quantity (packages)	Defined daily doses
1	Escitalopram	515941	20333713
2	Amitriptyline	419145	6908817
3	Fluoxetine	232524	4622370
4	Sertraline	217713	6764669
5	Paroxetine	198287	7154616

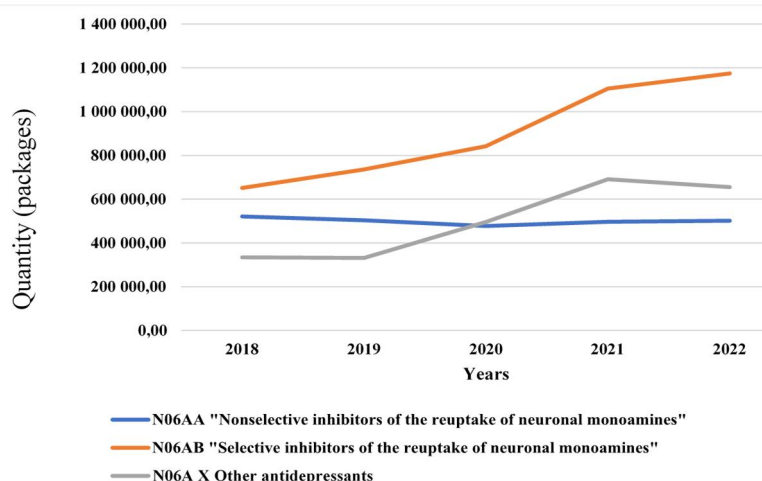


Fig. 4. Dynamics of the volume of sales in natural terms of medicinal products of groups N06AA, N06AB and N06AX in Ukraine (2018–2022)

Multiple studies have shown that antidepressants cause xerostomia [4, 10] by causing salivary gland hypofunction [5] or altering the dry mouth threshold, or they may do both effects [4]. According to the results of our study, 83.9 % of patients indicated the presence of caries or dryness/ulcers on the oral mucosa against the background of taking antidepressants. These complaints correspond to the frequency of clinical manifestations of oral cavity pathology detected by dentists in patients taking antidepressants: 82.5 % of doctors noted complaints of dryness in the mouth, 70.0 % – periodic appearance of ulcers on the mucous membrane of the oral cavity, 60.0 % – the appearance of new carious cavities and the progression of caries, 52.5 % – bleeding and inflammation of the gums.

As is known, SSRIs (fluoxetine, paroxetine, sertraline, escitalopram) cause side effects much less often (although nausea, nervousness, insomnia, headache, sexual dysfunction may be noted) compared to tricyclic antidepressants, the latter can block histamine H1 receptors (this leads to sedation, weight gain), muscarinic cholinergic receptors (causes dry mouth, impaired vision, delayed urination, etc.). It was established that in patients who took tricyclic antidepressants, the rate of saliva secretion in the parotid gland decreased by 58 %, and in patients who took SSRIs – by 32 %. Since saliva buffers organic acids formed by dental plaque and promotes the remineralization of hard dental tissues, a decrease in the rate of its secretion increases the risk of dental caries.

The high frequency of pathology of changes in the oral cavity revealed by us may reflect not only undesirable reactions of antidepressants, but also the presence of a premorbid background and a violation of the quality of care of the oral cavity in patients with depression. Severe changes in the oral cavity can be caused by the action of some of the specified factors, as well as the influence of drugs that suppress the activity of the salivary glands to a greater extent, and that important factor is the significant increase in the sale of amitriptyline. Since almost all patients stated that they did not use other medicines at the same time as antidepressants, it can be assumed that antidepressants were the trigger for the exacerbation of the pathology of the oral cavity.

It is worrying that less than half of health care professionals and only 12.9 % of patients were informed about the risk of adverse oral reactions when taking antidepressants, which indicates insufficient attention of doctors to this pathology.

### Conclusions

1. More than 80 % of patients taking antidepressants have significant oral health disorders, including a high prevalence of caries and its complications, as well as the development of periodontal disease against the background of dry mouth.
2. Less than 13 % of patients and less than half of healthcare professionals are informed about the risk of adverse oral reactions when taking antidepressants.
3. Among the directions of further research is the establishment of the contribution of various factors (premorbid background from the oral cavity, presence of anxiety-depressive disorders, changes in eating behavior, dose and group of antidepressants, etc.) in the violation of dental health.
4. It is important to establish the role of pharmaceutical care in the prevention and correction of periodontal diseases caused by antidepressants.

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Стаття надійшла 8.04.2022 р.

DOI 10.26724/2079-8334-2023-2-84-167-171

UDC 616.12-008.331.1-06-057.6(1-21/22):616-056]-042.2

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## COMPARATIVE ASSESSMENT OF QUALITY OF LIFE PARAMETERS IN RURAL AND URBAN RESIDENTS WITH COMORBID HYPERTENSION

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The study highlights the results of a comparative analysis of the quality of life of 152 patients with hypertension and its combined course with type 2 diabetes and coronary heart disease living in urban and rural areas. Quality of life parameters were determined using the SF-36 questionnaire. It was found that the patient's quality of life worsens with increased comorbidity. A clinically significant difference in the quality of life parameters depending on territorial affiliation was established. Thus, the level of quality of life in patients from rural areas is mainly reduced due to the mental component, manifested by a decrease in an emotional state and a decrease in vital activity, while in urban residents – due to the physical part of health, which led to the impossibility of performing everyday tasks.

**Key words:** hypertension, SF-36 questionnaire, comorbidity, mental component of health, physical component of health.

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## ПОРІВНЯЛЬНА ОЦІНКА ПОКАЗНИКІВ ЯКОСТІ ЖИТТЯ СІЛЬСЬКИХ І МІСЬКИХ ЖИТЕЛІВ З КОМОРБІДНИМ ПЕРЕБІГОМ ГІПЕРТОНІЧНОЇ ХВОРОБИ

У даній статті висвітлені результати порівняльного аналізу якості життя 152 пацієнтів з гіпертонічною хворобою та її поєднаним перебігом з цукровим діабетом 2 типу та ішемічною хворобою серця, що проживають у місті та в сільській місцевості. Параметри якості життя визначали за допомогою опитувальника SF-36. Виявлено, що якість життя хворих погіршується зі збільшенням коморбідності. Встановлено, клінічно значиму різницю показників якості життя в залежності від територіальної приналежності. Так, рівень якості життя у пацієнтів з сільської місцевості переважно знижується за рахунок психічного компоненту, що проявлялися зниженням емоційного стану, зниженням життєвої активності, тоді як у міських жителів – за рахунок фізичного компоненту здоров'я, що призводило до неможливості виконання повсякденних справ.

**Ключові слова:** гіпертонічна хвороба, опитувальник SF-36, коморбідність, психічний компонент здоров'я, фізичний компонент здоров'я.

*The study is a fragment of the research project “Study of the assessment of the combined effect of cardiovascular risk factors on the comorbid course of arterial hypertension, coronary heart disease and chronic kidney disease, features of prevention and rehabilitation”, state registration No. 0119U102851.*

According to the WHO, hypertension (HT) is the most important cause of mortality among chronic non-infectious diseases worldwide. The number of patients with arterial hypertension in the world is expected to increase by 15–20 % by 2025 and reach about 1 billion 560 thousand people [12]. According