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5. მნიშვნელოვანი სახელით შექმნილი სამართავი სიტყვა. უწყვეტი ძალიან მნიშვნელოვანი და ჟურნალური მასალების უნდა შექმნილი ბჟადალი. ხმალი, მაქს, დემოგრაფია - დამთავრებული, მოცარგია და საორნირო გადამტანი შესაძლებელი. ფიქსირებული უსაფრთხო პროცესში ჭეშმარიტი მინიმუმზედ ტარდამდე და რჩება თოვლის ფართობში, მაქსხში, დამთავრებით ფიქსირებული საბრძანო რეჟიმით. მაქსხში, დამთავრებით ფიქსირებული საბრძანო რეჟიმით.

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ORTHODONTIC TREATMENT ALGORITHM OF PATIENTS WITH A BURDENED DRUG ANAMNESIS. DRUGS THAT REDUCE BONE MINERAL DENSITY

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Abstract.
The large number of drugs available today for the treatment of various general somatic conditions poses the challenge of studying both the positive and negative effects of drugs on orthodontic tooth movement. To improve the efficiency, safety and quality of treatment, an orthodontic care algorithm has been developed for patients taking glucocorticoids (GCS), drugs for the treatment of diabetes mellitus (thiazolidinediones and SGLT-2 inhibitors), L-thyroxine, immunosuppressors, antidepressants, anticonvulsants, proton pump inhibitors (PPIs), misoprostol (copyright database IREG deposit certificate No. 2089354).

Out of 348 patients, who came for consultation and orthodontic treatment, 48 patients (13.8%), according to the algorithm, the active treatment and retention plans, appliance activation were adjusted taking into account the positive drug anamnesis. 9 patients were referred for consultations with doctors of other medical specialties to receive an information about general disease compensation degree, bone mineral density measurement and identification of possible contraindications for orthodontic treatment.

Key words. Anamnesis, orthodontic treatment, medications.

Introduction.
Numerous studies showed that different types of malocclusion are one of the most common maxillofacial pathology. Their frequency of occurrence ranges from 11 to 74%, depending on the region and age group [1,2].

Over 60% of children and adults who came for consultation and orthodontic treatment take medications or nutritional supplements on a regular basis [3].

A wide range of drugs available today for the treatment of various general somatic conditions poses the challenge of studying both the positive and negative effects of drugs on orthodontic tooth movement [4].

Orthodontic tooth movement is a well-studied process; however, it is not uncommon for an orthodontist to come across some difficulties during orthodontic treatment, the cause of which may not be obvious. The correct interpretation of the drug anamnesis and the development of a standard treatment plan for patients with a burdened drug anamnesis will improve the quality of treatment, will help to achieve a good clinical results and reduce the frequency of relapse.

Side effects of many drugs can manifest themselves in the oral cavity in the form of xerostomia, erosive and ulcerative lesions, gingival hypertrophy, etc. [5]. All this can also significantly complicate orthodontic treatment.

Wide range of medications can influence bone metabolism. Despite the relevance of the problem, there is no clear orthodontic treatment algorithm of patients, taking bone mineral density (BMD) reducing drugs on regular basis. Additional diagnostic procedures and necessary consultations with related medical specialists are not defined.

The aims of the study.
1. To analyze scientific literature on the effect of drugs on bone metabolism and orthodontic treatment outcome.
2. On the base of literature review to develop an orthodontic treatment algorithm for the patients taking BMD reducing drugs on regular basis.
3. To test the algorithm in clinical practice (to calculate the percentage of patients with burden drug history in routine orthodontic practice; to find the most commonly prescribed drugs which could reduce BMD; to check the distribution of the patients within decision tree leaf (ending states).

Materials and Methods.
An electronic search of published meta-analyses, systematic reviews, case reports, clinical and experimental studies included in databases (Cochrane Library, EMBASE and MEDLINE, Web of Science) was made using the following search terms in titles and abstracts: «orthodontic treatment»; «orthodontic tooth movement»; «drugs and bone metabolism»; «medications side effects»; «medications/oral health».

The search depth was 10 years. References from the found articles were scanned for additional relevant publications. The criteria for selecting published scientific studies are described in detail earlier [6].

All medications mentioned in this articles, and it possible side effects, which could have a negative impact on orthodontic tooth movement were included in orthodontic treatment algorithm.

General information on the medications and their effects derived from the following web sites: https://www.vidal.ru, https://www.rlsnet.ru. 348 patients (age 5 - 53 years) with any type of malocclusion were included in clinical part of our research. Anamnesis collection was made with an emphasis on drug intake history. The percentage of patients taking medications on regular basis with potential to reduce BMD was calculated and patients distribution according to the algorithm was verified.

Results.
The total number of articles found was 144. Based on latest literature review, an orthodontic treatment algorithm was developed for the patients taking drugs, reducing BMD, on regular basis (copyright database IREG deposit certificate No. 2089354). The algorithm provides clinical recommendations during active treatment and retention period for the patients taking following drugs: glucocorticoids (GCS), drugs for the treatment of diabetes mellitus (thiazolidinediones and SGLT-2 inhibitors), L-thyroxine, immunosuppressors, antidepressants, anticonvulsants, proton pump inhibitors (PPIs), misoprostol.
The algorithm is a graphic scheme, which allows the physician quickly to determine which actions should be performed at each stage of treatment. An accurate and logical algorithm scheme should help to reduce the frequency of medical errors (Figure 1).

Among 348 patients drug anamnesis collection revealed 48 patients (13.8%) 14 to 56 years of age who regularly take BMD reducing drugs. Of them, 27 patients (56.2%) regularly used corticosteroids in the form of ointments, sprays, inhalations or per os. 8 patients (16.7%) took L-thyroxine on a regular basis, 7 people (14.6%) - antidepressants, 4 people (8.3%) - PPIs. 1 patient each reported taking an anticonvulsant drug (2.1%) and immunosuppressive therapy (2.1%). (Figure 2).

According to the algorithm, during active orthodontic treatment of all patients with possible reduction of BMD, light force application and reduced interval between activations were recommended. However, this category of patients needs prolonged retention.

Due to the widespread use of corticosteroids, the presence of various forms of release, a wide range of both positive and negative effects, we have developed separate orthodontic treatment algorithms for patients taking corticosteroids [7].

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**Figure 1.** The orthodontic treatment algorithm of patients with burdened drug anamnesis. Drugs that reduce bone mineral density.
active orthodontic treatment, due to the increased bone resorption, the speed of tooth movement increases, however, a decrease in the new bone formation rate leads to an unstable result and a rapid relapse, up to 100% loss of treatment result [9].

The use of thiazolidinediones for glycemic control increases number of adipocytes, leads to a gradual replacement of the bone marrow with adipose tissue, reduces osteoblastogenesis and stimulates osteoclastogenesis. With prolonged use, thiazolidinediones increase concentration of bone resorption markers, decrease BMD, and violate its microarchitecture [10,11].

Inhibitors of the sodium-dependent glucose transporter type 2 or flozins contribute to weight loss and change phosphorus-calcium homeostasis due to increased calcium excretion, which inevitably leads to increased bone resorption and decreased mineral density [12,13].

The use of thyroid hormones for TSH reduction can provoke subclinical hyperthyroidism, which, in turn, can worsen BMD values [14]. The administration of L-thyroxine in large doses increases osteoclast activity and prostaglandin synthesis, which accelerate bone resorption and could promote osteoporosis development [15].

During orthodontic treatment planning for patients with endocrine pathology, it is very important to estimate the level of somatic disease compensation (for diabetes- glucose and HbA1c values, for thyroid diseases - TSH and T\(_{3}\) values). One of the immunosuppressants side effects is a skeleton atrophy, including the maxillofacial region. Immunosuppressants decrease bone volume, increase the number of osteoclasts, and decrease the number of osteoblasts [16]. The second indirect mechanism of action on bone tissue is an alteration of vitamin D and osteocalcin metabolism, which leads to the development of secondary hyperparathyroidism and osteopenia. The severity of side effects directly depends on the dosage and duration of immunosuppressant treatment [17].

Anticonvulsants are used not only for the treatment of epilepsy, but also as part of the complex therapy of migraine.
mental disorders, neuropathy, and chronic pain [18]. Many drugs in this group inactivate vitamin D and promote its catabolism, which leads to impaired absorption of calcium from the gastrointestinal tract. Long-term use of anticonvulsants contributes to the development of serious side effects on the skeletal system (osteomalacia, osteoporosis, increased risk of fractures and delay growth in children) [17,19].

The use of PPIs is associated with an increased risk of pathological fractures and osteoporosis development, especially with long-term use of high doses. Thus, according to Lau Y. (2012) [20], after one year of regular PPI intake, the risk of fractures increases up to 60%. One of the mechanisms of action may be a decrease in calcium absorption, leading to hypocalcemia, and, subsequently, to osteoporosis [21].

Antidepressants are among the most prescribed drugs and are used for the treatment of depression, phobias, bipolar, obsessive-compulsive disorders, peripheral neuropathy, fibromyalgia, chronic pain syndrome, etc. [17]. A side effect on skeletal system is expressed in an increased rate of bone loss and a decrease in its mineral density [22].

Misoprostol, being a synthetic analogue of prostaglandin E1, can significantly accelerate orthodontic tooth movement. This drug is prescribed to protect the gastrointestinal mucosa during long-term use of NSAIDs. For patients using misoprostol, it is necessary to specify the type of general somatic pathology and the length of treatment with NSAIDs. If indicated, the treatment can be adjusted according to the orthodontic treatment algorithm for patients taking NSAIDs on regular basis [6].

Pathological side effects of a wide range of drugs on BMD is well known. General doctors in parallel with the treatment of underlying disease, may prescribe to the patient osteoporosis preventing drugs and / or nutritional supplements. When planning treatment, an orthodontist should take into account the possible use by a patient of drugs that increase BMD (see specialized orthodontic care algorithm for the patients taking drugs that slow down bone metabolism) [6].

Certain drugs (immunosuppressants and anticonvulsants) may produce hypertrophic gingivitis. When such a complication occurs during orthodontic treatment, patients are recommended professional oral hygiene once every 3 months, the choice of appliance that facilitates oral hygiene as much as possible (self-ligating braces, fixation of molar tubes instead of bands, etc.). In some cases, gingivotomy is indicated. It is also necessary to take into account the possible unsatisfactory fixation of removable appliances.

Anticonvulsants and PPIs may cause xerostomia, which will complicate oral hygiene, increase the risk of caries and mucosal trauma during orthodontic treatment. When patients complained of dry mouth, we prescribed saliva substitutes.

If cortical support or removable appliances are needed during active orthodontic treatment as well as improvement stability of treatment results during retention period, consultations with related medical specialists are necessary to determine the possible complete drug withdrawal or the choice of an alternative without negative effect on skeleton and periodontal health.

Conclusion.

1. The analysis of published scientific studies has revealed a wide range of drugs with capacity to reduce BMD.

2. Orthodontic treatment algorithm contains practical recommendations for orthodontic treatment and additional diagnostic procedures for the patients taking on regular basis glucocorticoids (GCS), drugs for the treatment of diabetes mellitus (thiazolidinediones and SGLT-2 inhibitors), L-thyroxine, immunosuppressors, antidepressants, anticonvulsants, proton pump inhibitors (PPIs), misoprostol (copyright database IREG deposit certificate № 2089354).

3. 13.8% patients used on regular basis drugs with potential to reduce BMD. The result of the study showed patients distribution within almost all branches of the algorithm. The most frequently prescribed medications were corticosteroids, L-thyroxine, and antidepressants.

REFERENCES


Тезисы.
Большой ассортимент лекарственных препаратов, доступных сегодня для лечения различных общеизвестных состояний, ставит задачу изучения как положительных, так и негативных эффектов медикаментов на ортодонтическое перемещение зубов. Для повышения эффективности, безопасности и качества лечения на основании систематических обзоров и мета-анализов разработан алгоритм ортодонтической помощи пациентам, принимающим на постоянной основе глюкокортикоиды (ТКС), препараты для лечения сахарного диабета (тиазолидиниды и ингибиторы SGLT-2), L-тироксин, иммуносупрессоры, антидепрессанты, антиконвульсанты, ингибиторы протонной помпы (ИПП), мизопростол (свидетельство № 2089354).

При использовании предложенного алгоритма для 48 пациентов (13,8%) план ортодонтического лечения, режим активации аппаратуры и планирование ретенционного периода были скорректированы с учетом отягощенного лекарственного анамнеза. Из них 9 пациентов (18,7% человек) были направлены на консультации к специалистам лечебного профиля с вопросом о степени компенсации основного заболевания, определения МПК с целью выявления возможных противопоказаний к ортодонтическому лечению.

Ключевые слова: анамнез, ортодонтическое лечение, лекарственные препараты.