





The current state of the problem of treatment adherence in patients with osteoporosis

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Received 05 Sep 2024

After peer review 28 Nov 2024

Accepted 30 Dec 2024

Compliance with the recommendations of a health professional by patients with chronic diseases is observed only in 50% of cases, and therefore, the problem of compliance is very relevant. The widespread occurrence of osteoporosis (OP) in Russia and the world, as well as the existing problem of reducing patient compliance, requires an analysis of existing data on the level of treatment adherence in patients with OP.

The aim. To analyze the current state of adherence to therapy in patients with OP.

Materials and methods. The article provides an overview of the available publications on the mentioned objective. Various databases and search engines were used to search for research by Russian and foreign authors: elibrary.ru, CyberLeninka, Russian National Library (RNB), PubMed, Scientific&Scholarly Research Database (Scilit), Google Academy. The information was searched by keywords and phrases: "osteoporosis", "osteoporosis", "adherence to therapy/treatment", "adherence to treatment", "compliance", as well as the corresponding MeSH terms.

Results. The current state of the OP problem has been studied, and the pharmacotherapy currently used in this pathology has been considered. The data on the compliance of patients with OP, the factors that negatively affect the adherence of patients, as well as the methods that contribute to the growth of this indicator, are analyzed, and the expediency of their use is demonstrated.

Conclusion. The problem of adherence to treatment of patients with OP is an important issue of modern healthcare. One of the most effective ways to improve compliance is to increase patients' awareness of the disease, its course, methods and expediency of pharmacotherapy. There is an urgent need to develop accessible and search for new methods to increase treatment adherence in patients with OP.

Keywords: osteoporosis; treatment commitment; compliance; patient awareness

Abbreviations: OP — osteoporosis; AR — adverse reaction.

For citation: A.M. Beitullaev, E.A. Egorova, A.V. Petrov, K.V. Bubley, A.V. Matveev, A.A. Bikbaev, A.G. Gevorkyan, T.K. Maltsev, M.N. Usamova. The current state of the problem of treatment adherence in patients with osteoporosis. *Pharmacy & Pharmacology.* 2024;12(5):350-361. DOI: 10.19163/2307-9266-2024-12-5-350-361

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Для цитирования: А.М. Бейтуллаев, Е.А. Егорова, А.В. Петров, К.В. Бублей, А.В. Матвеев, А.А. Бикбаев, А.Г. Геворкян, Т.К. Мальцев, М.Н. Усамова. Современное состояние проблемы приверженности лечению пациентов с остеопорозом. *Фармация и фармакология*. 2024;12(5):350-361. **DOI:** 10.19163/2307-9266-2024-12-5-350-361



Современное состояние проблемы приверженности лечению пациентов с остеопорозом

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Получена 05.09.2024

После рецензирования 28.11.2024

Принята к печати 30.12.2024

Соблюдение рекомендаций медицинского работника пациентами при хронических заболеваниях наблюдается лишь в 50% случаев, в связи с чем, проблема комплаентности является очень актуальной. Широкая распространённость остеопороза (ОП) в России и мире, а также существующая проблема снижения комплаентности пациентов требует проведения анализа существующих данных об уровне приверженности лечению у пациентов с ОП.

Цель. Провести анализ текущего состояния уровня приверженности терапии у пациентов с ОП.

Материалы и методы. В работе осуществлен обзор доступных публикаций по упомянутой тематике. Для поиска исследований российских и зарубежных авторов использовали различные базы данных и поисковые системы: elibrary.ru, КиберЛенинка, Российская национальная библиотека (PHБ), PubMed, Scientific&Scholarly Research Database (Scilit), Академия Google. Поиск информации проводился по ключевым словам и фразам: «остеопороз», «оsteoporosis», «приверженность терапии/лечению», «adherence to treatment», «комплаентность», «compliance», а также соответствующим MeSH терминам.

Результаты. Изучено современное состояние проблемы ОП, рассмотрена фармакотерапия, применяющаяся в данное время при упомянутой патологии. Проанализированы данные о комплаентности пациентов с ОП, факторы, негативно влияющие на приверженность больных, а также методы, способствующие росту данного показателя, а также продемонстрирована целесообразность их применения.

Заключение. Проблема приверженности лечению пациентов с ОП является важным вопросом современного здравоохранения. Одним из наиболее эффективных способов улучшения комплаентности является повышение осведомлённости пациентов о заболевании, его течении, методах и целесообразности проводимой фармакотерапии. Существует острая необходимость в разработке доступных и поиске новых методов повышения приверженности лечению пациентов с ОП.

Ключевые слова: остеопороз; приверженность лечению; комплаентность; осведомлённость пациентов **Список сокращений:** ОП — остеопороз; НР — нежелательная реакция; ЛП — лекарственный препарат.

INTRODUCTION

According to the International Classification of Diseases, Tenth Revision (ICD-10)¹, diseases of the musculoskeletal system include various syndromes and nosologicals caused by inflammatory and metabolic

lesions of the musculoskeletal system. These pathologies have a significant negative impact on the working capacity of the population, the economy, and the mental health of society [2]. In the structure of morbidity of the adult population of Russia, pathologies of the musculoskeletal system occupy one of the leading places [3], as well as 3rd place in terms of overall

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¹ International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). Available from: https://icd.who.int/browse10/2019/en



prevalence after diseases of the circulatory system and respiratory organs². The increase in morbidity and disability among various age groups emphasizes the need for priority attention to methods of prevention and treatment of the above-mentioned pathology [4].

Osteopathies and chondropathies account for only about 2% of the total number of diseases of the musculoskeletal system [3]. This is quite explainable by the low level of diagnosis and the long latent course of the pathological process, which causes a delay in patients seeking medical help [1]. Osteoporosis (OP), being the most common metabolic bone disease [5, 6], is characterized by a decrease in bone mass and a violation of the microarchitecture of bone tissue, which increases the risk of fractures even with minimal trauma³ [7]. This disease leads to millions of fractures worldwide every year, worsening the physical and psychological condition of patients, reducing the quality and shortening the duration of life [8, 9]. At the end of 2019, there were about 42 million patients with OP registered in the world, and by 2034 this number may exceed 200 million [10]. OP is a widespread disease in Russia [11–13], affecting about 14 million people, which is about 10% of the population [14]. While about 25% (34 million people) are at risk of osteoporotic fractures. Previously analyzed data, including the results of X-ray densitometry, show that 33.8% of women and 26.9% of men over 50 years of age in Moscow have signs of OP [15].

The risk group for the development of OP mainly includes elderly individuals. The reasons for the spread of OP among this category are related to changes in lifestyle and physiological changes in the body, as well as the development of inflammatory processes that negatively affect bone strength [5]. There are various factors causing the development of OP, including biological (gender, age, genetic predisposition), environmental, and behavioral (presence of bad habits, diet with insufficient calcium content, lack of physical activity) [16].

According to ICD-10 more than 20 forms of OP are distinguished, the most common of which is postmenopausal OP, caused by a decrease in estrogen levels [17]. Diagnosis of OP in postmenopausal women is based on the presence of a fragility fracture or low bone mineral density in the anamnesis, which is measured using densitometry [18]. After a hip fracture,

many women lose the ability to move independently, and the risk of death within a year after the injury doubles [19]. Women are more susceptible to the development of OP due to a decrease in the level of progesterone and estrogen, which is observed in this category of patients from 40–45 years of age [20].

The chronic nature of the disease requires prolonged pharmacotherapy, which, in turn, increases the risk of adverse reactions (ARs) from medicines and may also reduce the level of adherence to treatment in patients.

"Compliance" is usually considered as adherence to the regimen and scheme of treatment prescribed by a doctor, while "adherence to therapy" is a characteristic of the patient's behavior during treatment and the correspondence of this behavior to the doctor's recommendations [21]. These concepts are close in meaning, so they can be considered synonymous [22]. According to the World Health Organization, adherence to a healthcare professional's recommendations by patients with chronic diseases is observed in only 50% of cases⁴. Poor adherence to therapy is a complex problem that requires a multidisciplinary approach, requiring the involvement of various specialists for positive recovery dynamics and support for the quality of life of patients [23].

The widespread prevalence of OP in Russia and worldwide, as well as the existing problem of reduced patient compliance, prompted the authors to analyze existing data on the level of adherence to treatment in patients with osteoporotic pathology.

THE AIM. To analyze the current status of adherence to treatment in patients with OP.

MATERIALS AND METHODS

A review of available publications on the mentioned topic was carried out. Each author independently selected literary sources, after which a joint decision was made on the inclusion of a scientific publication in the analysis. Various databases and search engines were used to search for studies by Russian and foreign authors: elibrary.ru, CyberLeninka, Russian National Scientific&Scholarly Library, PubMed, Database (Scilit), Google Scholar, while PubMed and CyberLeninka were used by the authors as priority sources of information, the rest of the listed ones were additional. The search period covered all mentions of keywords available in the databases, from January 1, 1886 to October 31, 2024.

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² Healthcare in Russia. 2023: Federal State Statistics Service. Available from: https://rosstat.gov.ru/folder/210/document/13218

³ WHO. Kanis JA, on behalf of the WHO Scientific Group. Assessment of osteoporosis at the primary health-care level. Technical Report. WHO Collaboraiting Centre, University of Sheffield, UK; 2008:288. Available from: https://frax.shef.ac.uk/FRAX/pdfs/WHO_Technical_Report.pdf

⁴ WHO. Adherence to Long-term Therapies: Evidence for Action. World Health Organization;2003:198. Available from: https://doi.org/10.5144/0256-4947.2004.221



The selection of publications on the review of drug therapy for OP was carried out using keywords and phrases: "osteoporosis," "safety of pharmacotherapy," "side effects," "adverse reactions"; names of medicines and pharmacological groups used for OP ("bisphosphonates," "denosumab," etc.), as well as corresponding MeSH terms⁵.

The search for information to carry out an analysis of the state of adherence to treatment in patients with OP was carried out using keywords and phrases: "osteoporosis," "adherence to therapy/treatment," "compliance," as well as corresponding MeSH terms.

The process of selecting studies devoted to the problem of adherence to therapy in patients with OP is presented in Figure 1 and is based on the recommendations of the PRISMA system (Preferred Reporting Items for Systematic reviews and Meta-Analyses), 2020 [24].

The stage of identification of publications and pre-screening analysis implied the presence in the publication of several keywords on the topic, for example, "osteoporosis" and "adherence to treatment," "side effects" and "bisphosphonates."

The screening stage involved excluding publications from the sample that were published before 2020, thus, the data for the last 5 years were primarily reviewed. It should be noted that if a publication published before January 2020 contained data that, in the authors' opinion, are of key importance for the analysis, then such work underwent screening.

The stage of analyzing the acceptability of selection criteria involved assessing the relevance of information in the publication on the topic. The assessment involved the analysis by several authors of controversial publications for inconsistencies in the narrative or insufficiently reliable information, assessing the level of citation of publications, which may be one of the criteria for reliability and relevance, after which a collective conclusion was made.

RESULTS AND DISCUSSION

Drug therapy for osteoporosis: efficacy and safety profile

The chronic course of OP requires long-term pharmacotherapy aimed to improve the quality of life and prolonging remission of the disease^{6, 7}.

In medical practice, several pharmacological groups of medicines are used that affect various mechanisms of regulation of bone homeostasis, such as monoclonal antibodies, bisphosphonates, calcitonin, and molecular action drugs. The main goal of pharmacotherapy is to conduct primary (prevention of the first fracture in patients from a high-risk group) and secondary (prevention of repeated fracture) prevention of bone deformation [19]. Bisphosphonates — synthetic analogs of pyrophosphate, an endogenous regulator of bone mineralization, are the main medicines in this case [25, 26]. They act on osteoclasts, disrupting their metabolism and adhesion of tumor cells to the bone matrix, which suppresses their migration, invasion, and angiogenesis. Medicines are often used to treat metabolic bone diseases, including bone loss caused by glucocorticoids and other hormonal medicines [27]. Bone resorption is suppressed at the maximum level approximately 3 months after the start of oral bisphosphonate therapy. This effect remains stable throughout the pharmacotherapy [27].

Despite the fact that this class of medicines demonstrates high efficacy in reducing the risk of fractures in OP [28], the use of bisphosphonates may be accompanied by frequent and serious ARs: osteonecrosis of the jaw, atrial fibrillation, atypical femoral fractures [29–31]. Parenteral administration of bisphosphonates can also cause side effects such as fever, increased fatigue, myalgia, headache [30]. In turn, the resulting ARs require additional safety control of pharmacotherapy.

Denosumab, which is included in the clinical guidelines for the treatment of various forms of OP, is currently one of the most frequently prescribed medicines, reducing the activity of osteoclasts and, unlike bisphosphonates, does not damage the intracellular structures of the osteoclast [32]. The medicine has high efficacy in the treatment of OP, in particular, positive treatment dynamics are observed in the lumbar spine, its use reduces the risk of fractures and reduces pain syndrome [33, 34], and promotes an increase in bone mineral density [35]. Safety data for denosumab are quite convincing even after many years of its use: rare ARs are observed, such as the development of erysipelas, eczema. Clinical manifestations of serious ARs are the risk of multiple fractures after discontinuation of the medicine [36].

⁵ MeSH. Medical Subject Headings 2024 [Internet]. Available from: https://meshb.nlm.nih.gov

⁶ Clinical Guidelines No. 87. Osteoporosis. Ministry of Health of the Russian Federation. Available from: https://cr.minzdrav.gov.ru/recomend/87_4

⁷ Clinical Guidelines No. 614. Pathological fractures complicating osteoporosis. Ministry of Health of the Russian Federation. Available from: https://cr.minzdrav.gov.ru/recomend/614_2



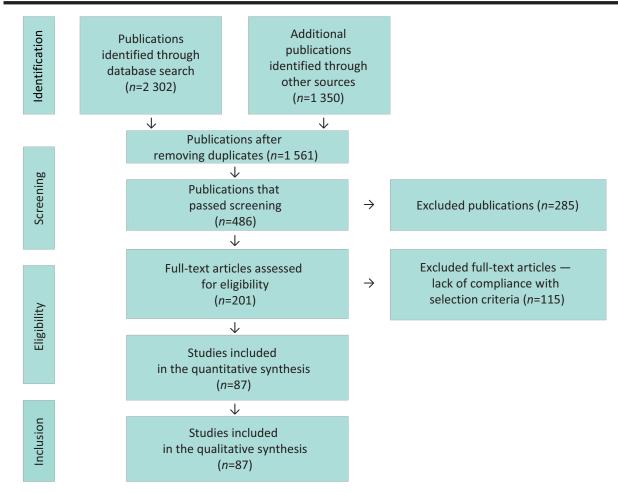


Figure 1 - Flowchart of source selection

Teriparatide remains the main medicine for the treatment of OP. It significantly reduces the risk of non-vertebral fractures, significantly stimulates bone formation, increases the mineral density of bone tissues in the lumbar spine and femoral neck in the long term [37]. The medicine is characterized by good tolerability [38] and a low frequency of severe ARs, which allows us to talk about its safe use in patients, including comorbid elderly patients [39]. Ars, caused be the medicine, are classified by researchers as nonserious, most often observed from the digestive and musculoskeletal systems [40]. The medicine can be used after the development of severe ARs, such as osteonecrosis of the jaw and atypical femoral fracture, against the background of the use of bisphosphonates as it is of the first line of treatment for OP [41]. Teriparatide may be an alternative pharmacotherapy option [42], and also demonstrates high rates of efficacy when combined with denosumab, providing an increase in bone mineral density and fracture prevention [34, 43].

Another medicine of choice in the treatment of OP is strontium ranelate. It is a first-line medicine in the treatment of postmenopausal OP in women, and can be safely used for a long time (up to 8 years) [44]. Reviews of studies evaluating pharmacotherapy for OP

with strontium ranelate demonstrate an adequate level of efficacy [45], which is shown, first of all, due to the distinctive anti-resorptive and bone-forming effect on bone remodeling, which leads to an improvement in bone density indicators [46]. However, in the periodically updated safety report of the European Medicines Agency, there were described increased risks of developing myocardial infarction with the use of strontium ranelate, in connection with which a decision was made to limit its medical use⁸, and in some countries the production of this medicine was discontinued due to concerns about its safety [47].

The combination of calcium and colecalciferol is an integral part of the pharmacotherapy of patients with OP. Increased calcium intake is required for primary and secondary prevention of OP, reducing the risk of hip fractures and maintaining bone mineral density [48]. Vitamin D deficiency can contribute to an increased risk of developing OP and its consequences, reducing the ability to physical activity in elderly people [49, 50]. Increased calcium intake is necessary

⁸ PSUR assessment report. Strontium ranelate. EMA/ PRAC/136656/2013. European medicines agency, 11 April 2013. Available from: https://www.ema.europa.eu/en/documents/ variation-report/protelos-h-c-560-psu-0031-eparassessment-reportperiodic-safety-update-report_en.pdf



throughout the treatment of OP, which is achieved by increasing the amount of food with this trace element or using calcium medicines. The use of colecalciferol is recommended when its deficiency is established. The course begins with therapeutic doses with further transfer of the patient to preventive pharmacotherapy⁹. Thus, the use of a combination of calcium and vitamin D plays a key role in the prevention and treatment of various forms of OP, primarily by preventing fractures [51].

Continuous use of these medicines can lead to the development of various ARs in patients. As a rule, researchers describe ARs that can be classified as non-serious in terms of severity: flu-like syndrome, arthralgia, nausea, epigastric pain, constipation [52], fatigue, loss of appetite, metallic taste in the mouth [53]. At the same time, there are suspicions of a possible link between high calcium intake and an increased risk of developing cardiovascular diseases, such as stroke, myocardial infarction, while other researchers refute this assumption [54]. Nevertheless, some authors studying various methods of pharmacotherapy for OP emphasize that the efficacy and results of treatment depend on their use in combination with calcium and vitamin D preparations [32, 44].

The numerous data on ARs of medicines used for the treatment of OP found in the literature sources predetermine the need to study the problem of compliance of patients with OP, since the side effects of these medicines can affect adherence rates.

Adherence to treatment in patients with osteoporosis

Recently, awareness of the importance of adhering to the treatment regimen has increased, since a low level of compliance leads to consequences both for an individual patient (a decrease in the level of efficacy of pharmacotherapy, an increase in the level of morbidity and mortality) and for the healthcare system in whole, leading to an increase in financial costs [55]. There are three key stages of adherence to treatment: initiation of treatment (taking a new medicine), adherence (the degree to which the amount of medicine taken by the patient corresponds to the prescribed one), and discontinuation of therapy (termination of MP intake for any reason). At each of these stages, there are various factors that can affect patient compliance, both negatively and positively [56]. Non-compliance with the rules of medicine intake is a universal problem of a large number of diseases of a chronic nature, an additional problem is the difficulty of assessing the level of compliance, since there is inconsistency in the studied factors that determine the deviation of patients from the prescribed therapy and, as a result, their subsequent analyzes [57]. The most common methods

of increasing the level of adherence to therapy are reducing the number of emerging ARs of medicines, simplifying the pharmacotherapy regimen, digitalization of healthcare, communication with the patient and conducting psychological consultations, however, it is additionally required to take into account the specifics of a particular disease and the characteristics of each patient [58].

The problem of adherence of patients with OP to treatment is relevant, there is a decrease in the compliance of patients over time after the fracture occurred. Only a third of patients continue to take calcium and vitamin D medicines for 3 or more years, and only half of them adhere to the medicine dosage regimen prescribed by the doctor [59]. The level of adherence in patients with OP, as in most people suffering from chronic diseases, is unstable: according to various estimates, in the first year of treatment it ranges from 34 to 75%, in subsequent years - from 18 to 75% [60]. Low adherence to treatment leads to a decrease in the increase in bone mineral density and less suppression of bone metabolism in patients with OP, which leads to a higher frequency of fractures, an increase in the number of hospitalizations and healthcare costs [60]. Healthcare professionals prescribing medicine therapy should take into account not only the characteristics of the patient, the course of the disease, but the patient's financial capabilities, which can also serve to reduce adherence to treatment. In the case of OP, factors that reduce the level of patient adherence to therapy are additionally the chronic nature of the disease, long-term pharmacotherapy, a large number of medicines prescribed simultaneously [61]. Doctors and healthcare professionals should focus on maintaining the persistence of patients, which is a fundamental factor in adherence to therapy [62], and also look for other ways to increase compliance.

Measuring adherence rates allows to analyze the profile of the use of medicines prescribed for OP, assess the presence of deviations between the prescription of medicines in medical practice and clinical guidelines outlined in the guidelines for doctors. Periodic monitoring of such indicators is an important tool for optimizing pharmacotherapy for OP and right allocation of healthcare resources [63]. Various questionnaires for patients are used to assess adherence to treatment. The most common for patients with OP are the Treatment Satisfaction Questionnaire for Medication (TSQM), the EuroQol-5 questionnaire, which assess the efficacy of the treatment, the side effects that occur, the convenience of using medicenes, the overall satisfaction of patients with the treatment, as well as their quality of life [64]. Researchers need to rationally use various methods of conducting the survey to obtain more reliable data. A modern approach to studying the level of compliance is the use of machine

⁹ Clinical Guidelines No. 87. Osteoporosis. Ministry of Health of the Russian Federation.



learning models, such as ExtraTree, SMOTE-SVM, which are used to predict adherence to treatment in patients and, therefore, adjust pharmacotherapy [65].

The use of medicines with significant time intervals between doses, such as bisphosphonates, as a rule, allows you to increase compliance and achieve the necessary treatment results [66]. Special care and frequency of taking oral dosage forms of bisphosphonates, which is necessary due to the low bioavailability of medicines are a factor reducing compliance [67]. Medicines for more convenient use and increasing the level of adherence to therapy, are being developed with the most infrequent dosing frequency, for example, ibandronic acid at a dosage of 150 mg 1 time/month [68], and the results of studies show that the prescription of medicines in a monthly or weekly regimen leads to a significant increase in the number of patients adhering to the regimen, rather than with daily use. [69]. Other researchers note that patients receiving oral forms of medicines are less likely to adhere to the treatment regimen than patients receiving them by subcutaneous or intravenous administration [70]. Therefore, the choice of the route of administration of medicines is also an important factor for increasing compliance.

However, possible manifestations of ARs of bisphosphonates, in particular, serious side effects [29–31], are factors that force the patient to abandon the prescribed therapy [71]. A possible way to solve the problem of low compliance due to developing ARs may be a transition to safer medicines, for example, to denosumab, which can be used for a long time, without requiring breaks in treatment [72]. Teriparatide also demonstrates lower risks of developing ARs compared to oral bisphosphonates, indicating a favorable safety profile of the medicine [73].

In some cases, refusal of therapy is associated with the patient's fears due to the expectation of the development of possible ARs, even if they themselves have not encountered them — fear of side effects is one of the main reasons for stopping the prescribed treatment [74]. In a study by Roh et al. it is emphasized that the level of non-compliance with the treatment regimen in patients with insufficient awareness is significantly higher (47%) than in patients with sufficient information about OP and the pharmacotherapy used (29%) [75]. In this case, increasing the patient's awareness of the disease and methods of therapy can contribute to increased compliance [76], for example, through the "Patient School" [77]. Familiarizing the patient with the features of the medical interventions carried out by the attending physician is a multi-stage process, including research, collecting a history of life and further determining the health problem, its comprehensive assessment taking into account the level of influence of the pathology on the quality of life, drawing up a treatment plan, studying the degree

of benefit of the patient's awareness for himself [78]. The use of methods to increase patient awareness allows to reduce the frequency of hospitalizations and disability rates, temporary loss of working capacity of the population [79], as well as improving the prognosis of the course of the disease and the quality of life of patients [80]. Participation of patients in the "School for Patients with Osteoporosis" contributes to increasing their awareness of the rules and duration of medicines' use, reducing the risk of developing ARs, which makes patients control the necessary level of vitamin D in the body, performing physical exercises, assessing an effective method of influencing the results of OP therapy [81]. Group consultations of patients, conducted for a long time, have a positive effect on achieving the goals of therapy: involving patients in the process of treatment, providing individual assessments of the risk of developing fractures (for example, using the FRAX*10 algorithm system) and the ability to make decisions on pharmacotherapy independently can significantly increase patient compliance [82].

An additional factor that improves the level of adherence to therapy is the involvement of caregivers or relatives of patients in the treatment process, since they, as a rule, better perceive information from a healthcare professional, help patients solve problems of a technical nature (road to the hospital, purchase of medicines, search for training materials, etc.). Researchers report that in solitary patients the number of fractures in the 3rd year of observation is higher (6.2%) than in people who are helped by caregivers and relatives (1.1%) [83].

The results of the pharmacotherapy and the level of adherence to therapy can be influenced by other factors, for example, the excessive burden on the healthcare system like the period of the coronavirus infection pandemic. Healthcare professionals reported a reduction in the number of densitometric studies (this is evidenced by 50.6% of respondents), an increase in the number of remote consultations for both new (62.3%) and regular patients (81.7%), a lower quality of medical care provided for fracture prevention (51.7%), as well as interruption of the course of injectable bisphosphonate therapy (45.4%) and denosumab (6.3%) [84]. Delaying the use of denosumab may increase the risk of developing vertebral fractures; no such AR was found on bisphosphonate therapy, which can accumulate in patients for a long time, patients could be transferred to alternative pharmacotherapy options. [85]. The International OP Foundation and the National OP Foundation also conducted a survey of medical and pharmaceutical workers and, in addition to the above factors, focused on the problem of medical supply disruptions causing difficulties in the selection of pharmacotherapy

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 $^{^{10}}$ FRAX®. Fracture Risk Assessment Tool. Available from: https://frax.shef.ac.uk/FRAX/tool.aspx?lang=rs $\,$



[86], which leads to a decrease in the efficacy of OP treatment. Coronavirus infection in patients with OP also leads to negative consequences both on the course of the underlying disease and on the therapy being carried out: the risks of hypercoagulation complications require cancellation or use with caution of raloxifene and estrogen, increasing the risk of thrombosis, metabolic disorders in bone tissue, observed in patients with OP, can exacerbate the course of coronavirus infection [87].

CONCLUSION

So, the problem of adherence to treatment in patients with OP is an important issue in modern healthcare. Compliance can be influenced by a number of factors, such as insufficient awareness of patients about the need for pharmacotherapy, ARs

and the chronic nature of the disease. Low rates of adherence of patients to the prescribed therapy lead to aggravation of the course of OP, the occurrence of fractures, and a decrease in the quality of life of patients.

One of the most effective ways to improve compliance is to increase patients' awareness of the disease, its course, methods, and the need for pharmacotherapy. Healthcare professionals can provide this information to patients through the "Patient Schools." This method demonstrates high efficacy in improving the prognosis of the course of the disease, the quality of life of patients, reducing the level of complications of the disease (the need for hospitalization, the resulting loss of working capacity, disability). There is an urgent need to develop new accessible methods to improve adherence to treatment in patients with OP.

FUNDING

This study did not have financial support from third-party organizations.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors made an equivalent and equal contribution to the preparation of the publication. All authors confirm that their authorship meets the international ICMJE criteria (all authors made a significant contribution to the development of the concept and preparation of the article, read and approved the final version before publication).

Asan M. Beitullaev — writing material on treatment adherence, graphic design, screening of publications;

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Том 12, Выпуск 5, 2024 361