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Management of osteoarthritis in the context of COVID-19

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Regular revision of the management of osteoarthritis by world associations has been performing both to the epidemiological features of the spread of the disease in 80% of the after-50-years-old population, and to the comorbidities. The group of this age has the highest risk of susceptibility and severe course of COVID–19. Objective. To reveal the features of the step-by-step algorithm for the treatment of patients with osteoarthritis in the conditions of the COVID-19 pandemic. Methods. The study is based on the analysis of the published data on the peculiarities of non-pharmacological and pharmacological means according to the step-by-step algorithm for the treatment of patients with osteoarthritis. 227 published scientific sources, from which 54 editions with a reliable evidence base were selected. Results. The treatment of patients with osteoarthritis in the conditions of a pandemic requires correction, due to the use of drugs with certain pharmacokinetic and pharmacodynamic properties that can atypically or negatively affect the systems of the body. Each of the four steps of the treatment algorithms for patients with osteoarthritis was analyzed, taking into account the pathophysiological features of the course of chronic joint disease and acute viral damage to the respiratory system. It was noted that despite the high variability of treatment methods for patients with osteoarthritis, decisions regarding the therapeutic tactic should be made taking into consideration the individual characteristics of the body and comorbidities. It was emphasized that the final decision regarding the prescription of corticosteroids and non-steroidal anti-inflammatory drugs must be properly argumented. The correction of the treatment measures set at each step of the algorithm is proposed. It would prevent the aggravation of the chronic impression of the joints in the adverse situation of the COVID-19 pandemic. Conclusions. A profound search in the scientific published sources for evidence concerning the specifics of the effect of non-pharmacological and pharmacological means of treatment for patients with osteoarthritis will allow to use their effects effectively using step-by-step algorithm especially during the dangerous pandemic situation.

Регулярний перегляд менеджменту остеоартриту світовими асоціаціями зумовлений не лише епідеміологічними особливостями поширення хвороби у 80 % населення віком понад 55 років, а й наявними в них коморбідними захворюваннями. Ця вікова група суспільства має найбільший ризик сприйнятливості та важкий перебіг COVID–19. Мета. Виявити особливості покрокового алгоритму лікування хворих на остеоартрит в умовах пандемії COVID-19. Методи. Проаналізовано інформацію про особливості нефармакологічних і фармакологічних призначень за покроковим алгоритмом лікування хворих на остеоартрит із 227 опублікованих наукових джерел, із яких обрано 54 видання з достовірною доказовою базою. Результати. Лікування хворих на остеоартрит в умовах пандемії потребує корекції, що зумовлено використанням препаратів із певними фармакокінетичними та фармакодинамічними властивостями, які можуть нетипово чи негативно вплинути на системи організму. Проаналізовано кожний із 4 кроків алгоритмів лікування пацієнтів із остеоартритом з урахуванням патофізіологічних особливостей перебігу хронічного захворювання суглобів і гострого вірусного ураження респіраторного відділу легень. Відмічено, що попри високу варіативність методів лікування хворих на остеоартрит, рішення щодо тактики слід приймати зважаючи на індивідуальні особливості організму та коморбідні захворювання. Зауважено на зваженості прийняття рішення щодо призначення кортикостероїдів та нестероїдних протизапальних препаратів. Запропоновано корекцію комплексу лікувальних заходів на кожному кроці алгоритму, що дозволить запобігти загостренню хронічного враження суглобів у несприятливій ситуації пандемії COVID-19. Висновки. Ретельний пошук в опублікованих доказових джерелах особливостей впливу нефармакологічних і фармакологічних засобів лікування хворих на остеоартрит дозволить ефективно використовувати їхню дію за покроковим алгоритмом під час небезпечної пандемічної ситуації. Ключові слова. Чотирикроковий алгоритм, лікування остеоартриту, пандемія, COVID-19.

Key words. Four-steps algorithm, osteoarthritis treatment, pandemic, COVID-19

Introduction

Regular revision of the management of osteoarthritis by international associations is due not only to the epidemiological features of the spread of the disease in 80 % of the population over the age of 55 [1], but also to the existing comorbid conditions, including: diabetes in 33% of patients, dyslipidemia in 63 %, gastro-intestinal diseases in 65 %, obesity in 57 %, peripheral vascular disease in 18 %, bronchial asthma in 16% [2].

This age group of the population has almost the greatest risk of susceptibility and severe course of COVID-19 [1]. The pandemic nature of the spread of acute respiratory disease requires the correction of step-by-step recommendations for the treatment of patients with chronic degenerative-dystrophic damage to the joints.

A variety of endo- and exogenous factors create difficulties when choosing treatment tactics for a chronic disease and negatively affect the course of an acute respiratory disease.

Considering the pathophysiological mechanisms of the development of osteoarthritis and COVID-19 (Fig. 1), it is impossible to assert the interdependence of the chronic inflammatory degenerative process, which begins with apoptosis of chondrocytes and aseptic inflammation, and acute respiratory disease with an active immunological response.

However, a decrease in physical activity in the conditions of a pandemic causes an increase in pain syndrome in patients and deterioration of the functioning of joints affected by osteoarthritis [3].

There is no information on osteoarthritis as a factor in the severe course of COVID-19. However, therapeutic agents prescribed to patients with osteoarthritis affect the development of complications after the coronavirus disease.

The four-step algorithm for the treatment of chronic inflammatory joint disease remains one of the leading one under European recommendations, proposed and scientifically substantiated by The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) in 2019 [4].

Osteoarthritis is characterized by a progressive course and ranks 11th in the frequency of causing disability, which determines the need for correction of treatment, especially in pain management, in modern pandemic conditions.

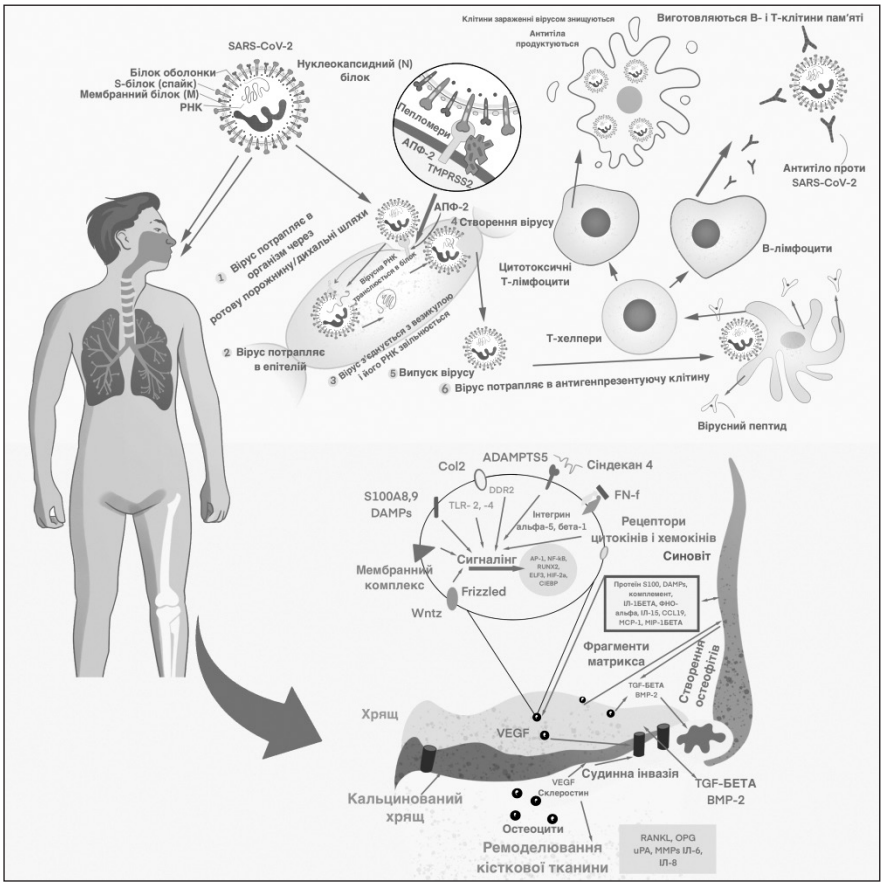

Fig. 1. Schematic presentation of pathophysiological mechanisms of osteoarthritis and COVID-19 development (adapted by the authors)

Purpose: to reveal the features of the step-by-step algorithm for the treatment of osteoarthritis patients in the conditions of the COVID-19 pandemic.

Material and methods

The study involved assessment of information on the peculiarities of non-pharmacological and pharmacological prescriptions according to the step-by-step algorithm for the treatment of osteoarthritis patients from 227 published scientific sources, from which 58 publications with a reliable evidence base were selected.

Results and their discussion

During the treatment of patients with COVID-19, the rules of the anti-epidemic regimen should be followed, taking into account the recommendations for acute respiratory disease and correction of chronic joint damage. This means close cooperation between general practitioners, orthopedists, rheumatologists, therapists, infectious disease specialists and pulmonologists to ensure continuous consultation and joint decision-making during the course of diseases in order to avoid complications [1].

Basic principles (non-pharmacological stage of treatment)

Physical therapy and counseling as the basic principles of the four-step algorithm include informing about the course of osteoarthritis, the patient's determination to reduce weight and normalize the diet not only in case of obesity, but also in case of predisposition to obesity, prescribing a complex of rehabilitation exercises (aerobics, stretching, etc.).

Under the conditions of pandemics, in particular COVID-19, it is necessary to correct management, namely:

– to create conditions for counseling patients online in order to avoid unwanted contacts and reduce the risk of transmission of a dangerous respiratory disease. Proposed and tested substantiated effective measures are not only communication with patients online, but also independent performance of elements of an objective examination by summarizing all necessary documentation [5]. Active dynamic, even remote, monitoring of the course of the disease, especially in people over 55 years of age, is absolutely necessary, because they remain in COVID-19 risk zone [1];

– general recommendations regarding rehabilitation exercises and light gymnastics remain relevant [6]. However, the lockdown makes adequate motor activity impossible, especially in older people. In the recommendations of rehabilitators, attention is focused on the need to observe 150 minutes of moderate physical activity per week or 75 minutes of intensive exercise at home [7]. It is worth avoiding rehabilitation measures that lead to a state of immunosuppression of the body and are carried out in places of mass gathering of people. Rehabilitation procedures in specialized centers should be carried out only for patients who have recently undergone surgical interventions and independent restoration of functioning is impossible, and sometimes risky;

– the diet should correspond to the level of physical activity. The World Health Organization recommends carefully planning your diet during the pandemic and giving preference to fresh fruits and vegetables, home-cooked meals, but respecting the portion size of food intake, and limiting the use of salt and sugar. The fat content in the total volume of food should not exceed 30%. Instead, it is recommended to eat foods rich enough in fiber and drink the necessary amount of liquid, which in conditions of a sedentary lifestyle increases intestinal peristalsis and improves metabolism [8].

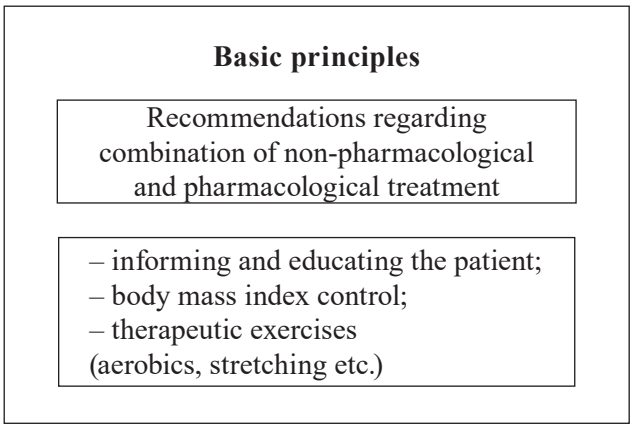

Fig. 2. Basic principles of treatment (according to [4])

Step 1 (Fig. 3) involves the prescription of clinically effective slow-acting symptomatic drugs for the treatment of patients with osteoarthritis (SYSADOA) and paracetamol (if necessary), as well as the use of insoles and braces in rehabilitation measures with unloading of the relevant areas of affected joints with existing deformations and distortions. In case of objective symptoms, it is necessary to follow general recommendations regarding the use of a support stick, walkers, and crutches, especially in muscle weakness.

Management correction

The combination of physiotherapeutic and pharmacological treatment remains important. However, patients should limit cold procedures, hydro- and manual therapy during acute respiratory disease [9].

Evidence of a negative effect of SYSADOA drugs on the body's reaction during a respiratory disease has not been found. Positive effects include anti-inflammatory action [10], reduction of COX-2 level [11], and activation of the immune response [12].

The discussion of the hypothesis about the effect of the multidrug *diacerein* (from the SYSADOA group, licensed in Europe, Latin America) on hyperinflammatory conditions by multidirectional inhibition of interleukins (IL) IL-1, -2, -6, -8, -12, -18 and necrosis factor TNF-α tumors; antiaggregation activity of platelets; viral infection and replication, is ongoing [13].

Paracetamol is considered to be an agent that can be prescribed to patients during a pandemic. Some authors recommend taking it as an analgesic for 84 days in the correct dose without harming the body [14]. However, it has been proven that it has a minimal analgesic effect for arthralgia [15], slight advantages over NSAIDs, but in people with liver diseases during the pandemic, mortality due to liver failure increases [16]. Paracetamol has an effect on respiratory symptoms: it reduces temperature and swelling of the nasal mucosa, rhinorrhea, but does not affect sore throat, dry cough [17]. The drug does not increase the risk of infection, but it affects the course of the disease of COVID-19, because it increases the risk of complications [1].

In the treatment of patients with osteoarthritis suffering from COVID-19, it is better to use *topical NSAIDs* to reduce pain, as they have a slight effect on the respiratory system of the body due to the transdermal route of administration [18].

Step 2 (Fig. 4) is started with progression of osteoarthritis symptoms. The effectiveness of NSAIDs and intra-articular injections for existing symptoms of osteoarthritis is proven (level 1A). It is known about the excellent reduction of pain syndrome when using NSAIDs, even in comparison with opioids [1]. Therefore, in Europe, NSAIDs are prescribed in 60 % of cases [19].

However, in COVID-19 symptoms, these drugs with specific pharmacodynamics and pharmacokinetics should be prescribed with caution due to the increased risk of complications of the course of the viral disease [20]. But when using NSAIDs, it is worth remembering the increased risk of developing kidney failure in patients with COVID-19, which is the cause of mortality [21]. In addition, these drugs increase the frequency of complicated pneumonia, pleural effusion, and peritonsillar abscess [22]. It is necessary to carefully prescribe and adjust the dose to those patients who have not yet been ill, because there are reports that NSAIDs increase the body's susceptibility to infections [23].

Intra-articular injections are prescribed when symptoms persist despite a high dose of NSAIDs, or when they are contraindicated due to possible risks. Hyaluronic acid is used intra-articularly mainly in elderly patients with osteoarthritis to reduce side effects of NSAIDs [24]. Some researchers claim that the pain-free period after the injection can last up to 26 months. [25]. Retrospective data demonstrate the possibility of postponing surgical intervention (endoprosthesis) for up to 2 years [26]. Information from evidentiary sources about contraindications to

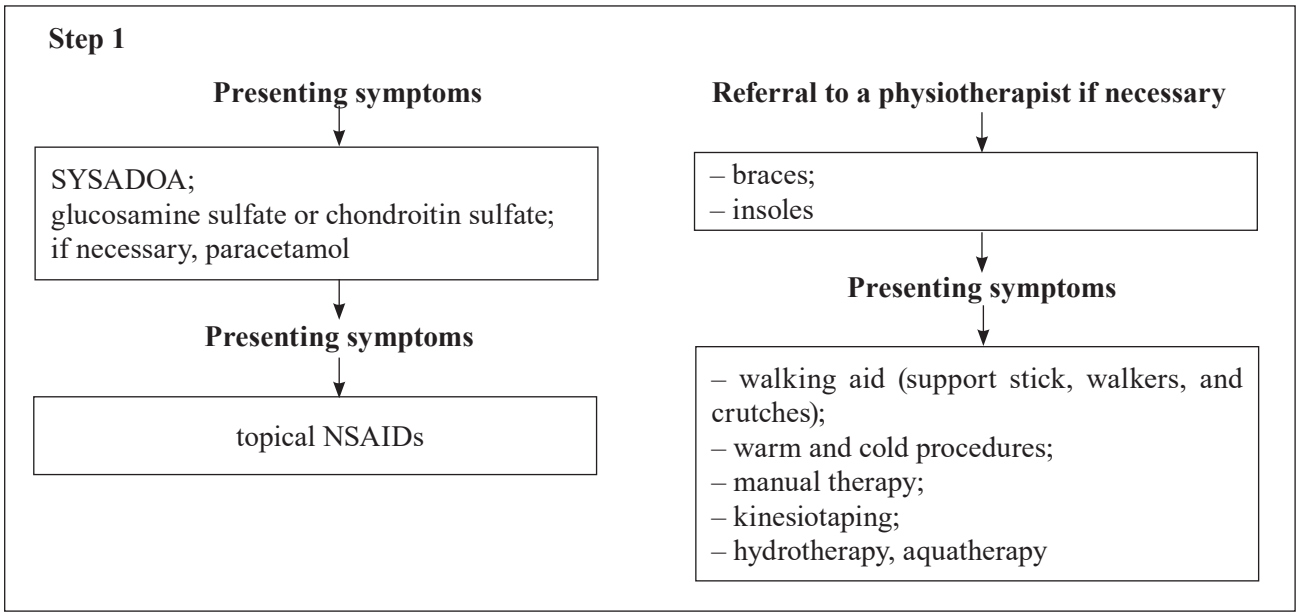

Fig. 3. Basic therapy of osteoarthritis. NSAIDs — nonsteroidal anti-inflammatory drugs (according to [4])

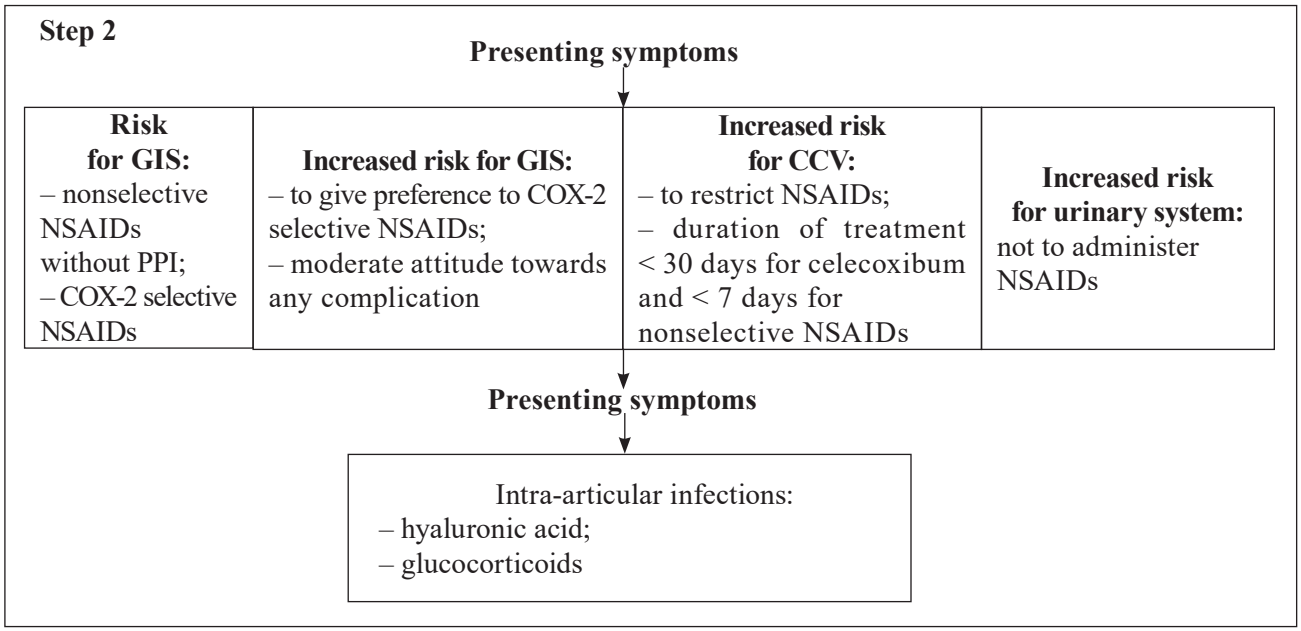

Fig. 4. Step 2 in the treatment of osteoarthritis. GIS – gastrointestinal system, CVS – cardiovascular system (according to [4])

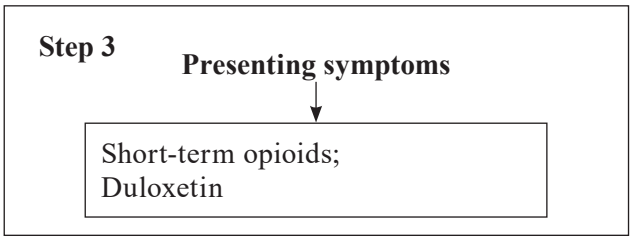

Fig. 5. Step 3 in osteoarthritis therapy (according to [4])

the introduction of hyaluronic acid during the pandemic has not been found. However, the possible risks and benefits of such treatment should be carefully evaluated [27, 28].

The effect of glucocorticosteroids (GCSs) is achieved faster compared to hyaluronic acid — within 2–4 weeks [29]. Their intramuscular administration allows to reduce pain in patients with osteoarthritis of the hip joint for up to 12 months. [30]. During the pandemic, it should be taken into account that GCSs are multi-target drugs with anti-inflammatory and immunosuppressive effects [31]. Their use in combination with an antibiotic makes it possible to reduce the mortality of patients with pneumonia. According to the WHO recommendations, GCSs should be avoided in COVID-19 management, unless they are prescribed for other reasons [32]. Intra-articular injections of GCSs can be used to reduce the pain syndrome, but it is necessary to take into account all the risks for the patient. There is still no reliable information about the occurrence of risks [33].

Step 3 (Fig. 5) involves the use of short-term opioids, which show a good result in the treatment of patients with existing pain syndrome and are considered to be «rescue therapy». Tramadol is preferred among them [34].

In COVID-19, these drugs are contraindicated!

In particular, tramadol is a weak opioid without immunosuppressive action and is included in the recommendations of the American Academy of Orthopedic Surgeons and the American College of Rheumatology in OA management [35]. However, it was found that the risk of mortality in patients with COVID-19 under the conditions of the use of opioids increases compared to NSAIDs [36]. Codeine should not be prescribed to patients during a pandemic, because due to its immunosuppressive effect, it affects the course and development of respiratory disease complications [37]. Table 1 shows a comparison of the effects of various pharmacological drugs used for the treatment of osteoarthritis in COVID-19.

Step 4 (Fig. 6) is surgical treatment (endoprosthesis for stage III–IV osteoarthritis), which is usually performed as planned, but cannot be performed due to anti-epidemic measures. Therefore, the search for scientifically proven advantages regarding the use of minimally invasive surgical measures continues due to the impossibility of performing large-scale traumatic orthopedic interventions [38].

Research is also ongoing on the possibility of using modern progressive regenerative technologies to inhibit the progression of cartilage tissue destruction, in particular: intra-articular injection of morphogenic proteins, enriched blood plasma, platelet concentrate, and mesenchymal cells. A study of the effectiveness

Table 1

Comparison of pharmacological treatment of osteoarthritis in patients with COVID-19 (adapted from [1])

Therapeutic agent	Iatrogenic effect	Respiratory tract	Interaction with COVID-19	Indications for patients with osteoarthritis
NSAIDs	Gastrointerstitial system, urinary system	Increase the risk of complications, bronchoconstriction	There are no reliable data	There are no reliable safety data. It is necessary to evaluate the harm/benefit balance
Paracetamol	Liver, kidneys in high doses	There are no risks	There are no reliable data	There are no reliable data on the safety of continuing the therapeutic agent administration
GCS	The risk of developing diabetes and hyperglycemia, immunosuppression	Increased risk of mortality in patients with pneumonia	Reduction in mortality in patients with COVID-19	There are no reliable safety data. It is necessary to evaluate the harm/benefit balance
Opioids	Nausea, vomiting, respiratory depression	Intensification of symptoms of a respiratory disease	Increased susceptibility to COVID-19, severity of presentation	It is necessary to stop administering therapeutic agents of this series in COVID-19

Table 2

Correction of management of osteoarthritis in COVID-19

BASIC PRINCIPLES	
– To provide counseling online; active condition monitoring; – Rehabilitation exercises and light therapeutic exercises in pandemic conditions, taking into account the body's reserves; – Adherence to the diet	
Step 1	
1) SYSADOA — ***there is no evidence of a negative effect***; 2) Paracetamol can be prescribed as a «painkiller» with a minimal analgesic effect; 3) Topical NSAIDs ***have an advantage*** in the treatment of patients with COVID-19	Combination of pharmacological and physiotherapeutic treatment To restrict: – cold procedures; – hydrotherapy; – manual therapy
Step 2	
1) NSAIDs should be prescribed with caution, especially in the late stages of COVID-19 due to the high rate of development of adverse reactions; 2) Intra-articular injections: – hyaluronic acid - there is no evidence of a negative effect; – glucocorticosteroids should be prescribed with caution to patients with COVID-19, taking into account all the risks	
Step 3	
Short-acting opioids are contraindicated during the COVID-19 pandemic	
Step 4	
Endoprosthetic repair should be postponed if possible, surgical intervention should be postponed in patients with acute respiratory disease of COVID-19	
Alternative methods of treatment	
– autologous platelet concentrate; – mesenchymal stromal cells; – low-frequency laser therapy; – transcutaneous neurostimulation	

of the use of cell substrates in the treatment of patients with osteoarthritis within 6 and 12 months showed their superiority over hyaluronic acid [39, 40].

Autologous platelet concentrate and platelet-rich plasma (PRP) are obtained by one- or two-stage centrifugation. The method allows the release of growth factors by activating α-granules in platelets [41]. But these technologies require standardization of both the actual method of obtaining and the approach to the treatment of patients with osteoarthritis [42].

Mesenchymal stromal cells can be isolated from bone marrow, dental pulp, umbilical cord blood and differentiate into osteocytes or chondrocytes [43]. The use of cells is a promising branch of research in

the world. Among 22 stem cell extraction methods, only 5 from two clinical centers in Iran and Korea entered the market [44]. However, only two products (Cartistem® and Stempeucell®) are approved for clinical use in the EU, and Jointstem® is in the final stage of clinical trials.

The impossibility of surgical intervention (endoprosthetic repair) during the pandemic dictates the need to find new technologies. One of the pathophysiological manifestations of osteoarthritis is a reactive local increase in the vascularization of small arteries already in the early stages of the disease due to aseptic inflammation. It has been proven that this destroys the cartilage tissue, which is unable to restore itself to an adequate state [45]. This effect is most studied in the knee joint, which is affected by osteoarthritis in 25 % of patients [46]. Embolization prevents the formation of new small vessels due to the destruction of the source of angiogenesis and, accordingly, eliminates the pain syndrome. The technique consists in the introduction of an embolic agent (imipenem and cilastatin sodium) to *a. genicularis* catheter through *a. femoralis* using a mangiograph [47]. It has been proven that knee artery embolization improves the patient's condition and reduces the level of pain sensitivity within 24 months. The duration of the surgical intervention (up to 2 hours) under local anesthesia and the minimal invasiveness of the method contribute to rapid rehabilitation and enable implementation in pandemic conditions. However, such therapy requires careful monitoring and re-introduction of the drug after 6 and 12 months. In the conducted meta-analysis, no life-threatening side effects of the indicated surgical manipulation were found [48].

It should be mentioned separately about the expansion of possibilities of physiotherapeutic influence on the affected joint during the pandemic. The effect of low-frequency laser therapy is known [49], which somewhat improves the patient's condition, reducing pain, but there is no proven reliability of the effects of this treatment method for implementation in treatment protocols [50].

Transcutaneous neurostimulation (TENS), which belongs to invasive conservative manipulations, is widely used in the management of osteoarthritis pain [51]. The technique proved to be effective for nociceptive pain, because it activates endogenous opioids, affects the growth of the pain threshold in patients with osteoarthritis [52]. Some authors report that after TENS, patients can walk longer distances without pain syndrome than those who only underwent physical rehabilitation [53]. But again, due to the insufficient level of evidence, the purpose of this method is not found in the recommendations [54].

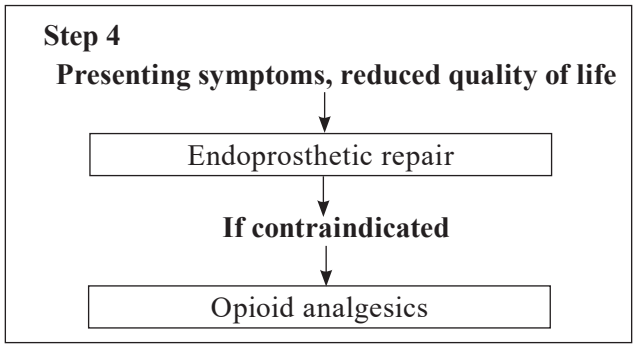

Fig. 6. Step 4 in the treatment of osteoarthritis (according to [4])

The most significant emphases in the correction of osteoarthritis management in the conditions of COVID-19 are outlined in Table. 2.

Conclusions

A thorough search in the published sources of evidence for the specifics of the effect of non-pharmacological and pharmacological means of treating patients with osteoarthritis will allow to effectively use their action according to a step-by-step algorithm during a dangerous pandemic situation.

Conflict of interest. The authors declare no conflict of interest.

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MANAGEMENT OF OSTEOARTHRITIS IN THE CONTEXT OF COVID-19

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