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Physical activity as part of therapy of spondyloarthropathy - review

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Abstract

Spondyloarthropathy is a group of chronic inflammatory diseases involving the sacroiliac joints and spine. Due to the prevalence of spinal pain, its diagnosis is often delayed for up to several years. If left untreated, it leads to a significant deterioration of the patient's quality of

life, disability, and eventually premature death. At present, there are drugs with which the disease activity can be effectively controlled, although some of them are not widely used due to their high cost. Despite the development of modern technology and the increasing spectrum of available therapies, rehabilitation and exercise still remain one of the basic elements of treatment. This article discusses and evaluates various forms of physical activity in terms of their effects on disease activity, joint and non-joint complaints, inflammatory markers and patient well-being. The most important conclusion of the analysis is that physical activity is safe for patients and it is never too late to start.

Keywords
spondyloarthropathy, physical activity, exercise therapy, rheumatological diseases

1. Introduction

Spondyloarthropathies are a group of chronic inflammatory diseases involving the sacroiliac joints and spine [1, 2]. Statistically, the problem affects 0.1% - 0.4% of the population [3]. The disease occurs with varying frequency in different regions of the world - most often in the Northern Arctic, least often in Southeast Asia [4]. It includes ankylosing spondylitis, psoriatic arthritis, spinal involvement in the course of inflammatory diseases of the gastrointestinal tract, reactive arthritis and undifferentiated spondyloarthropathy [4, 5]. Depending on the presence of changes in the sacroiliac joints visualized on X-ray, spondyloarthropathies can be divided into radiographic and non-radiographic - the risk of progression of non-radiographic spondyloarthropathy into radiographic spondyloarthropathy is about 50% [3, 6]. Another test used for imaging the sacroiliac joints is MR, which can detect lesions at a lower stage of progression than X-ray [7]. Its main symptoms include spinal pain of an inflammatory nature, morning stiffness, and fatigue [1]. Extra-articular symptoms may also be present [8]. Based on the 2010 Assessment of SpondyloArthritis international Society (ASAS) criteria, axial spondyloarthropathy can be diagnosed when a patient meets the following criteria:

visualization of sacroiliac arthritis on MR or X-ray in combination with one of the characteristic features of spondyloarthropathy, or the presence of HLA B27 antigen in combination with 2 features of spondyloarthropathy [9]. The hallmarks of spondyloarthropathy are: sacroiliac pain of an inflammatory nature, peripheral arthritis, tendinitis, toe inflammation, uveitis, psoriasis, Crohn's disease or ulcerative colitis, positive HLA B27 antigen, elevated blood CRP levels, positive family history, good response to NSAID treatment defined as a significant reduction or resolution of pain within 48 hours of taking the full dose [9]. These criteria can only be applied to patients whose low back pain occurred before the age of 45 and has persisted for a minimum of 3 months [9]. Some patients may present with a peripheral form, in which symptoms such as peripheral arthritis, tendonitis or toe inflammation predominate [10].

Unfortunately, due to the prevalence of spinal pain and the late referral of patients to specialists, its diagnosis is often delayed by up to 6-8 years [3, 11]. Left untreated, it significantly reduces quality of life, often leads to disability due to structural damage to the spine, which in turn results in inability to work and increases healthcare costs [1, 11]. Therefore, early diagnosis and the inclusion of appropriate therapy is so important. In this article, we will present methods of treating spondyloarthropathy with particular emphasis on the importance of non-pharmacological methods such as exercise.

2 Methods

A literature analysis was performed using the PubMed database. Only publications from the last 10 years were included. The keywords used were spondyloarthritis searched alone or in combination with physical activity or exercise. Articles classified as review, systemic review, randomized controlled trial and meta-analysis were analyzed. Only publications in English were used. Articles cited in the publication were selected by 3 independent researchers. Reference was also made to Drug Program B82 “Treatment of patients with severe active spondyloarthropathy without radiographic changes characteristic of AS”.

3 Treatment

The main goal of spondyloarthropathy treatment is to achieve remission or low disease activity [8]. Assessment of disease activity is performed using standardized questionnaires such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) or the Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) [8]. A BASDAI value of less than 2 and ASADAS-CRP of 1.3 are considered to be in remission, while high disease

activity is expressed by a BASDAI of more than 4 or ASDAS-CRP of more than 2.1 [8]. An acceptable response to treatment is considered a reduction in BASDAI of 50% or 2 units and a reduction in ASDAS-CRP of more than 1.1 points [8]. Sometimes the assessment of activity can be hindered by comorbidities, e.g.: fibromyalgia [8].

3.1 Non-steroidal anti-inflammatory drugs (NSAIDs)

The first line of treatment is NSAIDs [10]. We can divide them into classic, non-selective NSAIDs that inhibit COX-1 (cyclooxygenase 1) and COX-2 (cyclooxygenase 2), e.g. diclofenac, and selective COX-2 inhibitors, e.g.: celecoxib [10, 12]. Cyclooxygenases are enzymes whose function is to convert arachidonic acid into prostaglandins [10]. COX-1 is mainly found in platelets, stomach, renal collecting ducts and vascular endothelial cells [10]. COX-2 activity, on the other hand, increases mainly during inflammation [10].

Initially, the highest recommended dose of NSAIDs should be used if there are no contraindications [8]. Significant improvement should occur within the first 3 months of using the drug, and it should take no more than 6 months to reach the goal of therapy [8]. Studies have shown that NSAIDs, especially selective NSAIDs, in addition to their symptomatic and anti-inflammatory effects, can also inhibit disease progression especially in patients with baseline significantly elevated CRP, although not all authors agree on this point [12].

3.2 TNFα inhibitors

When treatment with NSAIDs is ineffective, there is the possibility of using modern biological therapy [13]. One of the main groups of biological drugs are tumor necrosis factor (TNFα) inhibitors. TNFα is a pro-inflammatory cytokine that, among other things: inhibits osteoblast function, stimulates osteoclast formation, stimulates the production of metalloproteinases, and increases angiopoietin 1 expression in synovial membrane fibroblasts increasing angiogenesis, which in turn increases the influx of cytokines into the joint [5]. TNFα inhibitors are divided by chemical structure into monoclonal antibodies (adalimumab, infliximab, golimumab, certolizumab) and soluble receptors (etanercept) [5]. These drugs are effective and safe in the treatment of axial spondyloarthropathy [13, 14, 15]. They have a beneficial effect not only on joint complaints, but also on reducing feelings of chronic fatigue, as well as the sleep problems often seen in patients, with greater improvement reported by those who initially had more severe symptoms [16]. In addition, they reduce the risk of uveitis [17]. They have also been shown to improve sleep quality [18]. However, like any drugs, they have some drawbacks, such as: high cost and

increased risk of infection during their use [14]. These can range from mild upper respiratory tract infections caused by viruses, fungal infections of the mucous membranes, HPV infections, to serious infections such as tuberculosis [19, 20]. It is now believed that once long-term remission is achieved, one can proceed with dose reduction or even complete withdrawal of therapy, which, however, carries the risk of exacerbation [14]. In addition, it should be considered that long-term use of TNFα inhibitors may have a beneficial effect on the progression of radiographic changes in the spine, although this thesis is subject to further research [7]. Unfortunately, about one in four or one in five patients will not achieve a satisfactory response to therapy [5]. This may be partly due to TNFα promoter gene polymorphisms [5]. In Poland, these drugs are reimbursed only in drug programs of the National Health Fund.

3.3 Interleukin 17 inhibitors

Another group of modern drugs that are monoclonal antibodies are interleukin 17 (Il-17) inhibitors [21]. They are divided into selective interleukin 17A (Il-17A) inhibitors - e.g., ixekizumab and secukinumab - and Il-17A inhibitors and interleukin 17F inhibitors - e.g., bimekizumab [21, 22]. These interleukins are important mediators of inflammation that exacerbate bone damage, so inhibiting them plays a key role in reducing inflammation, which in turn reduces the severity of subjective and physical symptoms [22]. According to the recommendations of the Assessment of SpondyloArthritis International Society and European League Against Rheumatism (ASAS-EULAR) and the American College of Rheumatology, Spondyloarthritis Research and Treatment Network and Spondylitis Association of America (ACR-SPARTAN-SAA) should be used in patients who achieve no or satisfactory improvement after TNFα inhibitors [3, 15, 23]. They have been effective in both early and advanced stages of the disease [3]. A significant effect of ixekizumab treatment was observed on laboratory parameters of inflammation and active inflammatory changes observed on MRI of the sacroiliac joints [21]. Predictive factors for the efficacy of these drugs are baseline elevated CRP, active inflammatory lesions of the sacroiliac joints as visualized by MRI, and male gender [23]. On the other hand, the presence of the HLA-B27 antigen is a weak predictor - treatment outcomes were not significantly different between HLA-B27 negative and HLA-B27 positive patients [23]. The downside of using secukinumab, on the other hand, was an increased risk of uveitis compared to TNFα inhibitors, which are monoclonal antibodies [15]. The most common side effects were upper respiratory tract infections,

nasopharyngitis, diarrhea and headaches [3]. In Poland, these drugs are reimbursed only in drug programs of the National Health Fund.

3.4 Janus kinase inhibitors

Janus kinase inhibitors (JAKs) are selective, synthetic, oral disease-modifying drugs [22, 24]. Their mechanism of action involves blocking JAK-STAT interaction, which is involved in inflammatory processes, among other things, by inhibiting one of the 4 enzymes that are janus kinases (JAK1, JAK2, JAK3, TYK2) [25]. Their group includes, for example: upadacitinib, tofacitinib [24, 25]. Studies have shown that JAK inhibitors were associated with a slightly higher risk of cancer compared to TNFα inhibitors, although malignant processes were rare in either group [25]. Nonetheless, it has a similar level of efficacy and safety to the previously mentioned therapies [22]. In Poland, these drugs are reimbursed only in drug programs of the National Health Fund.

It should be remembered that if one biologic drug is ineffective, it is possible to switch to another drug that is either an antibody or a synthetic [22]. Patients who have already been treated with these types of substances may have worse results than patients starting treatment with the first drug [22].

3.5 Physical activity

As important as pharmacotherapy is non-pharmacological treatment [26]. Physical activity plays a special role [27, 28]. It is included in the 2021 EULAR and 2022 ASAS-EULAR recommendations. [27, 29]. Physiotherapy and exercise in a structured form can be an effective part of therapy, especially in patients who are unable or unwilling to exercise independently [26, 27]. Yet even simple exercises performed at home are better than no exercise [30]. Exercises performed under the supervision of an expert have been shown to be more effective than exercises performed independently by patients [27, 28]. Exercises performed in a group have been shown to be slightly more effective than exercises performed alone [29]. Regular exercise improves muscle strength, cardiorespiratory fitness, spinal mobility, thoracic expansion, reduces inflammation, and even has the effect of reducing symptoms of depression [28, 29]. They also improve sleep quality [18]. Benefits are noted both by objective indicators and reported by patients themselves [28]. To date, it has not been possible to determine whether any of the exercises are more effective than others [27].

An example procedure whose effectiveness has been tested in patients with spondyloarthropathy (and rheumatoid arthritis) and the presence of varying degrees of

disability is long-term active exercise therapy [31, 32]. It was applied for 52 weeks in the study group, while the control group received usual care. Participants were evaluated during the study after 12, 26, 52, 104, 156 and 208 weeks [31]. During the 52-week period, each participant completed 64 half-hour exercise sessions, which included functional exercise (i.e., focused on improving activities of daily living, such as carrying objects, dressing, washing, etc., as well as improving motor functions such as motor coordination or balance), aerobic exercise (e.g., walking, running, cycling, rowing), muscle strengthening and range of motion extension (using the patient's body weight and other equipment), as well as elements of education and health promotion [31]. In addition, patients were encouraged to engage in physical activity between sessions [31]. Each participant received exercises individually tailored to his or her abilities [31]. Patients in the control group, on the other hand, were initially under the care of only their attending physician [31]. After 52 weeks, those in the control group were offered coverage of long-term active exercise therapy [31]. After 52 weeks, those in the control group were offered coverage of long-term active exercise therapy [31]. When evaluated after 52 weeks, long-term active exercise therapy appeared to be more effective, although the study is still ongoing [32].

Another study tested the effect of high-intensity physical activity [33]. It proved that performing aerobic and strength exercises of this type of intensity resulted in lower ASDAS and BASDAI, inflammation parameters, and reduced pain, feelings of stiffness and fatigue in patients [33]. This type of exercise also had short-term beneficial effects on improving mood and sleep quality [34]. In addition, they contributed to reducing patients' feelings of psychological distress and improving functioning in daily life [35]. Performing strength and endurance exercises also showed positive effects on reducing cardiovascular risk in participants - the study group showed reduced arterial stiffness, pulse wave velocity, improved cardiorespiratory fitness and body composition [36]. Exercises performed in water may also prove beneficial [37]. The program included both stretching, aerobic and strength exercises, as well as relaxation and breathing techniques [37]. These have been shown to be associated with reductions in scores, BASDAI, BASFI, pain, swelling and joint stiffness [37].

Patients can also be offered exercises to achieve improvement in a particular body part, for example: the cervical spine [38]. The research group used a progressive program of exercises performed at home aimed at improving the stability of this part of the spine [38].

Educational content was delivered to patients via a multimedia platform [38]. Patients were assessed using the BASDAI, BASFI and Bath Ankylosing Spondylitis Metrology Index (BASMI) scales [38]. Flexion, lateral flexion, extension and rotation of the spine were also assessed [38]. There was an obvious improvement in spinal mobility after 6 weeks in the exercise group [38].

It is important to remember to select exercises from different groups, as for example: the use of aerobic exercises alone had no significant effect on reducing disease activity as measured by BASDAI and Bath Ankylosing Spondylitis Functional Index (BASFI), CRP, ESR [39]. Nor did they significantly improve patients' function [39].

However, it is not only the type of exercise itself that is important, but also the patients' health beliefs and attitudes toward performing physical activity [40]. It has been shown that these beliefs can be modified by incorporating physical activity into a patient's life [40]. One study included participants in an intensive aerobic and strength exercise program containing a total of three sessions per week [40]. Using the Exercise Health Beliefs questionnaire, patients' sense of the impact of exercise on their health before, during and after the intervention was measured [40]. There was a significant effect of the experiment on participants' health beliefs, which translated into a greater chance that they would continue physical activity [40]. Also, another study found that patients in the group that actively exercised were more likely to engage in leisure-time physical activity after the experiment than those in the non-exercise group, although due to the low intensity of exercise, no significant differences were observed between the groups in terms of disease activity as measured by the ASDAS [41].

An interesting approach is the use of special wearable devices to measure physical activity [42]. These can be pedometers, accelerometers or inertial measurement units [42]. They provide information on the number of steps taken per day, the number, intensity and duration of activities undertaken, time spent sitting, and energy expenditure [42] The three most common locations where trackers have been worn are the wrist, lower back and hip [42]. For most patients, wearing these types of devices is an acceptable way to collect data [42]. They can be a valuable aid not only to researchers and physicians managing patients, but also to the patients themselves by motivating exercise [42].

In contrast, excessive work-related physical activity can have adverse effects [30]. It has been shown that patients in more physically demanding occupations have a faster progression observed in imaging studies and a greater severity of complaints [30].

4. Conclusion

In conclusion, exercise and physiotherapy are recognized, effective and safe therapies for spondyloarthropathy [29, 43]. They have the greatest effect on reducing disease activity and lowering inflammatory parameters, with a slightly smaller effect on the severity of subjective symptoms such as pain and stiffness [44]. In addition, the addition of aerobic exercise improves cardiorespiratory fitness [44]. The most common side effect reported by patients was pain [45]. To date, it has not been possible to design a single exercise plan that is effective for all patients with spondyloarthropathy, so personalization of treatment is necessary. Patients should be reminded that it is never too late to start regular physical activity. It is beneficial in patients with all rheumatologic diseases, but it is patients with spondyloarthropathy who may experience a particularly positive effect on disease activity.

Author's Contribution

Conceptualization, Karolina Mikołajczak; methodology, Hanna Ćwirko; software, Urszula Garlak; check, Karolina Mikołajczak, Hanna Ćwirko and Urszula Garlak; formal analysis, Karolina Mikołajczak; investigation, Hanna Ćwirko, Urszula Garlak; resources, Karolina Mikołajczak; data curation, Urszula Garlak; writing - rough preparation, Karolina Mikołajczak; writing - review and editing, Hanna Ćwirko, Urszula Garlak; visualization, Hanna Ćwirko; supervision, Karolina Mikołajczak; project administration, Karolina Mikołajczak;

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