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MANAGEMENT OF PSORIATIC ARTHRITIS WITH PHARMACOLOGICAL THERAPIES: AN INTEGRATIVE REVIEW

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Abstract: The treatment of psoriatic arthritis (PsA) involves a multifaceted approach, with an emphasis on modulating the immune response to reduce joint and skin inflammation. Pharmacological management includes the use of non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying drugs (DMARDs), biological therapies and targeted synthetic drugs. NSAIDs are generally indicated for symptomatic relief, but do not affect the progression of the disease. Conventional DMARDs, such as methotrexate and leflunomide, play an important role in modulating the immune response, while biologics, which act specifically on inflammatory cytokines such as TNF-α, IL-17 and IL-23, offer effective options for patients with severe or refractory forms. The evolution of therapies, including new classes of targeted synthetic drugs, has contributed significantly to the control of PsA, but treatment remains challenging due to the variability in individual responses to drugs. An integrative review on the treatment of PsA is essential to consolidate current knowledge on the efficacy and safety of the various therapeutic options. By integrating data from different studies and systematically comparing them, it is possible to identify the most effective therapies, as well as better understand adverse effects, the impact on comorbidities and the improvement in patients' quality of life. This also makes it possible to analyze the effectiveness of different therapeutic classes in specific scenarios, such as in patients refractory to methotrexate or those with comorbidities such as obesity and cardiovascular disease. Integrating this evidence can provide a clearer vision of how to adapt treatment to the individual needs of each patient, taking into account responses to treatment, adverse effects and the presence of other health conditions. In addition, an integrative review on the topic is crucial to explore the gaps in knowledge and highlight areas that need further investigation, such as personalizing treatment

based on biomarkers and directly comparing different biological therapies. The treatment of PsA is dynamic and requires continuous adjustments, and it is crucial that new research explores how to improve efficacy, reduce side effects and optimize access to treatments, especially in contexts of health systems with limited resources. Therefore, by bringing together a comprehensive overview of the available evidence, an integrative review can be a valuable guide to guide future research and improve therapeutic strategies in the management of psoriatic arthritis.

Keywords: "Psoriatic Arthritis", "Treatment", "Biologic Therapy", "DMARDs", "IL-17", "TNF-α"

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease that affects the joints and is closely related to psoriasis, a dermatological condition characterized by erythematous and scaly patches on the skin [1,2]. In recent years, there have been significant advances in the understanding of PsA, including the importance of early diagnosis and the existence of a "pre-PsA" phase, in which patients present with non-specific symptoms before the full development of the disease [1,2]. In addition, the need to define therapeutic goals and address associated comorbidities such as obesity, diabetes and cardiovascular disease has been emphasized [1,2].

PsA belongs to the group of seronegative spondyloarthritides, i.e. it does not show rheumatoid factor (RF) in blood tests, unlike rheumatoid arthritis [1,2]. This characteristic helps in the differential diagnosis with other rheumatological diseases [1,2]. The disease can affect any joint in the body, including the hands, feet, spine and sacroiliac joints [1,2]. In some cases, joint inflammation can lead to severe deformities and loss of function, significantly impacting patients' quality of life [1,2].

Psoriatic arthritis is considered an autoimmune disease, in which the immune system mistakenly attacks its own joints and surrounding tissues [1,2]. T lymphocytes, a type of defense cell, play a crucial role in activating inflammation [1,2]. This inflammatory response is mediated by cytokines such as IL-17, IL-23 and TNF-α, which contribute to the destruction of bone and, paradoxically, to the formation of new disorganized bone tissue [1,2]. This process leads to the development of bone erosions and bone neoformation, resulting in joint deformities [1,2].

PsA can present in different clinical forms [1,2]. Asymmetric oligoarthritis is the most common manifestation, affecting a few joints unevenly on each side of the body [1,2]. Symmetrical polyarthritis affects multiple joints, in a similar way to rheumatoid arthritis, but without the presence of rheumatoid factor [1,2]. In more severe cases, mutilating arthritis can cause severe bone destruction, leading to irreversible deformities [1,2]. The disease can also affect the spine, characterizing spondylitis, which causes stiffness and low back pain [1,2]. Other manifestations include dactylitis, a painful swelling of the fingers or toes that leaves them looking like "sausage fingers", and enthesitis, which is inflammation of the tendon insertions, and is common in the Achilles tendon and plantar fascia [1,2].

The diagnosis of PsA is clinical, based on the patient's history, physical examination and complementary tests [1,2]. As there is no specific laboratory test, the doctor assesses the presence of joint and skin symptoms, as well as ruling out other rheumatological diseases [1,2]. In blood tests, the rheumatoid factor (RF) is usually negative, while inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) can be elevated [1,2]. Imaging tests help diagnose and monitor the disease: X-rays can reveal bone erosions and new bone formation with a characteristic "pencil in a cup" appearance,

while MRI and ultrasound are useful for detecting early inflammation in the joints [1,2].

The treatment of psoriatic arthritis (PsA) involves a multifaceted approach, with an emphasis on modulating the immune response to reduce joint and skin inflammation [1,2]. Pharmacological management includes the use of non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying drugs (DMARDs), biological therapies and targeted synthetic drugs [1,2]. NSAIDs are generally indicated for symptomatic relief, but do not affect the progression of the disease [1,2]. Conventional DMARDs, such as methotrexate and leflunomide, play an important role in modulating the immune response, while biologics, which act specifically on inflammatory cytokines such as TNF-α, IL-17 and IL-23, offer effective options for patients with severe or refractory forms [1,2]. The evolution of therapies, including new classes of targeted synthetic drugs, has contributed significantly to the control of PsA, but treatment remains challenging due to the variability in individual responses to drugs [1,2].

An integrative review on the treatment of PsA is essential to consolidate current knowledge on the efficacy and safety of the various therapeutic options [1,2,3]. By integrating data from different studies and systematically comparing them, it is possible to identify the most effective therapies, as well as better understand adverse effects, the impact on comorbidities and the improvement in patients' quality of life [1,2,3]. This also makes it possible to analyze the effectiveness of different therapeutic classes in specific scenarios, such as in patients refractory to methotrexate or those with comorbidities such as obesity and cardiovascular disease [1,2,3]. Integrating this evidence can provide a clearer view of how to adapt treatment to the individual needs of each patient, taking into account responses to treatment, adverse effects and the presence of other health conditions [1,2,3].

In addition, an integrative review on the topic is crucial to explore gaps in knowledge and highlight areas that need further investigation, such as personalizing treatment based on biomarkers and directly comparing different biological therapies [1,2,3]. The treatment of PsA is dynamic and requires continuous adjustments, and it is essential that new research explores how to improve efficacy, reduce side effects and optimize access to treatments, especially in contexts of health systems with limited resources [1,2,3]. Therefore, by bringing together a comprehensive view of the available evidence, an integrative review can be a valuable guide to direct future research and improve therapeutic strategies in the management of psoriatic arthritis [1,2,3].

OBJECTIVES

The aim of this research is to present a comprehensive analysis of the treatments available for psoriatic arthritis (PsA), highlighting the most commonly used therapies and their results in terms of efficacy, safety, adverse effects and impact on patients' quality of life [3,4,5]. The analysis includes both traditional drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs) and conventional DMARDs, and more advanced options, such as targeted biological and synthetic DMARDs [3,4,5]. The comparison of efficacy between different therapeutic classes is also addressed, considering the response of patients to the different approaches and the implications of each therapy in terms of safety, with special attention to the comorbidities often associated with PsA [3,4,5].

In addition, the study aims to discuss future prospects for the treatment of PsA, emphasizing the importance of early diagnosis and a treat-to-target approach to optimize clinical outcomes and prevent irreversible joint damage [3,4,5]. The transition from traditional therapies to early biologics and the development of targeted therapies, such as JAK and IL-23

inhibitors, are discussed as promising advances [4,5]. However, the text also acknowledges existing challenges, such as the lack of validated biomarkers for treatment personalization and the need for direct comparative studies between biologics, as well as highlighting the importance of real-world data and pharmacoeconomics to make therapies more accessible and effective [4,5].

METHODOLOGY

This integrative review analyzed the best available evidence on the treatment of psoriatic arthritis (PsA), focusing on the different therapeutic classes and their efficacy, safety, adverse effects and impact on patients' quality of life [4,5,6]. To this end, the PUBMED, VHL and MEDLINE databases were consulted, covering publications between 2018 and 2024 [4,5,6]. The search was conducted using keywords such as "Psoriatic Arthritis", "Treatment", "Biologic Therapy", "DMARDs", "IL-17", "TNF-α", combined by Boolean operators (AND, OR) to maximize the relevance of the results [4,5,6].

Additional filters were applied to limit the selection of studies to the English language and to exclude narrative review articles and non-peer-reviewed studies [4,5,6]. The inclusion of articles followed strict criteria, prioritizing studies that addressed the different therapeutic classes for PsA, such as NSAIDs, conventional, biological and synthetic targeted DMARDs, and that compared the efficacy and safety of these therapies [4,5,6]. We excluded articles that dealt with other autoimmune diseases or that did not detail the implications of therapies in the treatment of PsA, such as the impact on comorbidities and adverse effects [5,6].

The article selection process was carried out in two stages [4,5,6]. In the first phase, 89 titles and abstracts were analyzed to identify relevant studies within the initial set of retrieved articles [4,5,6]. In the second phase, 24 full papers from the selected articles were evaluated in detail, extracting data on the efficacy of therapies, safety, adverse effects and impact on the quality of life of PsA patients [4,5,6]. In addition, the impact of comorbidities such as obesity, diabetes and cardiovascular disease on the choice of therapy was considered [5,6].

The data was organized systematically, allowing for a comparison between the different therapeutic approaches and their implications in the treatment of PsA [5,6]. The final analysis was conducted based on criteria of therapeutic efficacy, safety profile, and impact on patients' comorbidities and quality of life [5,6]. This integrative approach enabled a synthesis of the best available evidence, providing a comprehensive overview to guide future research and contribute to the development of more effective and personalized therapeutic strategies in the management of psoriatic arthritis [5,6].

RESULTS

THERAPEUTIC CLASSES

The therapeutic classes for the management of psoriatic arthritis (PsA) include different types of drugs, each with its own mechanism of action and specific indication [5,6,7]. **Non-steroidal anti-inflammatory drugs (NSAIDs)** are often used for the symptomatic relief of inflammation and pain [5,6,7]. They act by blocking the production of prostaglandins, which are responsible for the inflammatory process [6,7]. Although they are useful for controlling symptoms in mild cases, they do not prevent the disease from progressing [6,7]. Among the most commonly used NSAIDs are ibuprofen, naproxen and diclofenac, which should be prescribed with caution due to the risk of gastrointestinal and cardiovascular side effects [6,7].

Synthetic disease-modifying drugs (conventional DMARDs) represent the next therapeutic step for moderate to severe cases of PsA [6,7,8]. These drugs work by modulating the immune system, reducing inflammation and slowing down the progression of the disease [6,7,8]. Methotrexate, Leflunomide and Sulfasalazine are the main representatives of this class, and are especially effective in treating peripheral joint involvement [6,7,8]. However, their therapeutic response varies between patients, and the effects can take weeks or months to become noticeable [6,7,8]. In addition, close monitoring is required due to the risk of liver and hematological toxicity [6,7,8].

For more severe cases or those refractory to conventional treatment, **biological DMARDs** offer a more specific approach [6,7,8]. These drugs block specific targets of the immune system, such as the cytokines TNF-α, IL-17 and IL-23, which play a central role in the inflammation of PsA [6,7,8]. TNF-α inhibitors, such as Adalimumab, Infliximab and Etanercept, were the first biologics used and continue to be widely prescribed [6,7,8]. Alternatively, IL-17 (Secukinumab, Ixekizumab) and IL-23 (Guselkumab, Risankizumab) inhibitors have demonstrated significant efficacy, especially in patients with skin and joint involvement [6,7,8]. However, the high cost and increased risk of infections are major challenges in the use of these therapies [6,7,8].

Another promising class are **targeted synthetic DMARDs**, which act on specific intracellular pathways of inflammation [7,8]. JAK inhibitors, such as Tofacitinib and Upadacitinib, block the action of Janus kinases, preventing the activation of the inflammatory immune system [7,8]. Apremilast, a PDE-4 inhibitor, reduces inflammation by modulating the cellular response [7,8]. These options are indicated for patients who do not respond to conventional or biological treatments, offering a new therapeutic path [7,8]. However, adverse effects, such as cardiovascular risk and hematological changes, require continuous monitoring [7,8].

Choosing the ideal treatment for each patient must take into account the severity of PsA, the profile of comorbidities and the individual therapeutic response [7,8]. Follow-up by a rheumatologist is essential to adjust therapy, assess possible side effects and ensure the long-term effectiveness of treatment [7,8,9]. In addition, a multidisciplinary approach, including physiotherapy and psychological support, can contribute significantly to improving patients' quality of life [7,8,9].

EFFECTIVENESS COMPARISON

IL-17 inhibitors and TNF-α inhibitors are two classes of biological drugs used to treat psoriatic arthritis (PsA) [7,8,9]. Both act by reducing inflammation, but their mechanisms of action are different [7,8,9]. TNF-α inhibitors block tumor necrosis factor alpha (TNF-α), a pro-inflammatory cytokine involved in various autoimmune diseases [7,8,9]. IL-17 inhibitors, on the other hand, act specifically on interleukin 17, a key cytokine in the inflammatory response of psoriasis and psoriatic arthritis [7,8,9]. This difference in action can influence the choice of treatment according to the patient's clinical manifestations [8,9].

Studies indicate that IL-17 inhibitors may be more effective than TNF-α inhibitors in treating specific manifestations of PsA, such as dactylitis and enthesitis [8,9]. Dactylitis is characterized by painful swelling of the fingers and toes, giving a "sausage finger" appearance [8,9]. Enthesitis involves inflammation where tendons and ligaments attach to bones, such as the heel (Achilles tendon) or the plantar fascia [8,9]. Patients with these manifestations may benefit most from the use of IL-17 inhibitors, such as Secukinumab and Ixekizumab [8,9].

Another relevant aspect in the treatment of PsA is the response to methotrexate, one of the most widely used drugs in the initial management of the disease [8,9]. However, a proportion of patients do not respond adequately to methotrexate or experience intolerable adverse effects [8,9]. When this occurs, the early introduction of a biological drug can improve disease control and prevent the progression of joint damage [8,9,10]. Thus, the identification of patients refractory to methotrexate should lead to a rapid change in therapeutic strategy, avoiding prolonged periods of uncontrolled inflammation [8,9,10].

With the advance of biological treatment, there has been a need to understand drug switching within this class [8,9,10]. Some patients may lose their response to the initial biologic over time due to mechanisms such as the formation of antibodies against the drug or the adaptation of the immune system [8,9,10]. In these cases, there are two therapeutic options: switching to another drug in the same class (for example, replacing one TNF-α inhibitor with another) or switching to a different class (for example, from a TNF-α inhibitor to an IL-17 inhibitor) [8,9,10]. Evidence suggests that switching to a different therapeutic class may offer better results in patients who have lost their response to the initial treatment [9,10,11].

These therapeutic decisions must be individualized, taking into account not only the effectiveness of the drug, but also the possible adverse effects and the characteristics of the patient [9,10,11]. Continuous monitoring by the rheumatologist is essential to assess the progression of the disease and adjust the therapeutic strategy as necessary [9,10,11]. In addition, regular follow-up makes it possible to identify early signs of therapeutic failure and the need for additional interventions [9,10,11].

In summary, the management of PsA with biological drugs requires a personalized approach, taking into account factors such as the type of clinical manifestation, the response to methotrexate and the need to change therapies over time [9,10,11]. Advances in therapeutic options have made it possible to control the disease more effectively, reducing inflammation and preventing joint deformities, significantly improving patients' quality of life [9,10,11].

SAFETY AND ADVERSE EFFECTS

TNF-α inhibitors (such as Adalimumab, Infliximab and Etanercept) are biological drugs widely used in the treatment of psoriatic arthritis [12,13,14,15]. They act by blocking tumor necrosis factor alpha (TNF-α), an inflammatory cytokine involved in the development of the disease [12,13,14,15]. However, these drugs can weaken the immune system, making the body more susceptible to opportunistic infections [12,13,14,15]. Therefore, before starting treatment with these drugs, it is essential to test for latent tuberculosis, since TNF-α can reactivate the disease [12,13,14,15]. In addition, there is an increased risk of respiratory infections, skin infections and, in some cases, lymphoma, although this risk is considered low [12,13,14,15].

JAK inhibitors (Tofacitinib, Upadacitinib) represent a different class of drugs that act by blocking Janus kinases (JAKs), which play a key role in inflammation [14,15,16,17]. These drugs have been associated with an increased risk of serious cardiovascular events, such as heart attack and stroke, especially in patients with cardiovascular risk factors [14,15,16,17]. In addition, JAK inhibitors increase the risk of deep vein thrombosis (DVT) and pulmonary embolism (PE), which are blood clots in the veins [15,16,17]. There is also an increased risk of infections, including herpes zoster, and cancer [16,17]. Therefore, its use should be carefully monitored, taking into account the patient's risk factors [16,17].

IL-17 inhibitors (Secukinumab, Ixekizumab) and IL-23 inhibitors (Guselkumab, Risankizumab) have a more favorable safety profile compared to TNF-α and JAK inhibitors [15,16,17]. These drugs are generally well tolerated and have a lower risk of causing serious adverse events [15,16,17,18]. However, infections can still occur, especially skin and upper respiratory tract infections [15,16,17,18]. In addition, there is a potential risk of increased inflammatory bowel disease (IBD) in predisposed individuals [15,16,17,18]. Although these drugs represent an effective option for the treatment of psoriatic arthritis, it is important that patients are monitored to identify any adverse effects over time [16,17,18].

It is essential that treatment with any of these biological drugs is carefully monitored by a doctor [16,17,18]. The rheumatologist should monitor the response to treatment, adjust the dose as necessary and be aware of possible side effects [16,17,18]. The decision on which drug to use should be based on a thorough assessment of the patient, considering both the benefits and risks involved, as well as individual risk factors [16,17,18,19,20].

Before starting treatment with biological drugs, it is important for the doctor to carry out a detailed analysis of the patient's medical history, taking into account pre-existing diseases, risk factors and possible comorbidities [20,21,22]. Regular follow-up and monitoring of side effects are essential to ensure patient safety during treatment. Thus, the choice of the most appropriate drug should be personalized, based on the specific characteristics of each patient [20,21,22].

IMPACT ON COMORBIDITIES

Arthritic psoriasis (PsA) is a condition that often coexists with several other comorbidities, including **obesity**, **diabetes** and **cardiovascular disease** [20,21,22]. Studies show that patients with PsA are at greater risk of developing these conditions, which can complicate the treatment and management of the disease [20,21,22]. Obesity, for example, is associated with an increase in systemic inflammation, which can aggravate PsA [20,21,22]. In addition, the coexistence of diabetes and cardiovascular disease can influence the course of the disease and the effects of prescribed treatments [21,22,23]. It is therefore crucial that healthcare professionals are aware of these comorbidities when planning treatment for patients with PsA [21,22,23].

The impact of comorbidities on the choice of treatment for **PsA** is significant, as certain drugs used to treat psoriatic arthritis can exacerbate these conditions [21,22,23]. For example, **TNF-α inhibitors**, which are widely used to control inflammation in PsA, can increase the risk of infections [21,22,23]. This is particularly worrying for patients with **diabetes** or **cardiovascular disease**, who already have a compromised immune system or a high risk of complications [21,22,23]. Similarly, **JAK inhibitors** can increase the risk of serious cardiovascular events and thrombosis, which requires a cautious approach in patients with a history of heart problems or a predisposition to blood clots [21,22,23]. These interactions between treatment and comorbidities make a careful assessment of risk and benefit essential [21,22,23].

Furthermore, not all the drugs used to treat PsA present significant risks for associated comorbidities [21,22,23]. Some treatments, such as **IL-23 inhibitors**, have shown a **neutral** or even **beneficial effect** on cardiovascular risk [21,22,23]. This means that, unlike other therapies that can increase the risk of heart disea-

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se, IL-23 inhibitors can not only not aggravate it, but also reduce the risk in certain patients [21,22,23]. This characteristic makes these drugs an attractive option for patients with **PsA** and cardiovascular comorbidities, as they can offer control of the disease without adding an additional risk to cardiovascular health [21,22,23].

The choice of treatment for PsA must therefore be highly **individualized**, taking into account the specific comorbidities of each patient [21,22,23]. The presence of conditions such as diabetes, heart disease and obesity can influence the choice of drug, dosage and monitoring of treatment [22,23,24]. The **doctor must carefully weigh up the benefits and risks**, adjusting the treatment according to each patient's needs [22,23,24]. In some cases, it may be necessary to try different therapies until the most effective and safe one is found, always taking the patient's general health into account [22,23,24].

To ensure that treatment is as safe and effective as possible, it is essential that patients **inform the doctor of all their health conditions** [22,23,24]. This will allow the doctor to make informed decisions about the best therapeutic approach [22,23,24]. **Regular** medical follow-up is also essential to monitor not only PsA but also comorbidities, ensuring that any complications are treated appropriately [22,23,24]. Adjustments in treatment may be necessary over time, according to the evolution of PsA and the patient's associated conditions [22,23,24].

DISCUSSION

IMPORTANCE OF EARLY DIAGNOSIS AND TREATMENT

The **pre-clinical phase of** psoriatic arthritis (PsA) refers to the period before the classic symptoms of the disease appear, such as pain and swelling in the joints [16,17,18,19,20]. During this stage, subtle changes can occur in the immune system and joints, but these changes are usually imperceptible to the patient [16,17,18,19,20]. However, diagnostic imaging techniques, such as magnetic resonance imaging, and other sensitive methods can detect these early changes [16,17,18,19,20]. Recognizing PsA in the preclinical phase is fundamental because it can allow intervention before the disease causes irreversible damage to the joints [16,17,18,19,20].

Early recognition of PsA, even before the appearance of typical symptoms, has a significant positive impact on the prognosis of the disease [22,23,24]. Starting treatment in the preclinical phase can prevent or delay the progression of joint damage, such as bone erosions and deformities, which are common in more advanced stages [22,23,24]. With early treatment, the risk of physical disability and loss of joint function is substantially reduced, which improves long-term quality of life [22,23,24]. This demonstrates the importance of early detection to avoid serious complications in the future [22,23,24].

The **"Treat-to-Target"** concept is an approach aimed at defining specific goals in the treatment of PsA, such as achieving remission of the disease or reducing its activity to a low level [14,15,16,17]. In this model, treatment is adjusted regularly according to the patient's response, with the aim of achieving and maintaining these goals over time [14,15,16,17]. This approach allows for personalization of treatment, as targets are adjusted according to the progress and individual needs of each patient, which optimizes clinical results [11,12,13,14,15,16,17].

The **Treat-to-Target** strategy aims to improve clinical outcomes by preventing joint damage and improving patients' physical function [11,12,13,14,15,16,17]. By continuously monitoring disease activity and adjusting treatment as necessary, it is possible to avoid long-term complications and provide patients with a better quality of life [11,12,13,14,15,16,17]. This treatment model also helps to personalize care according

to the evolution of the disease and individual responses to treatment, which is crucial for therapeutic success [11,12,13,14,15,16,17]. In simple terms, diagnosing and treating PsA early, with a goal-oriented approach, may be the key to achieving the best possible results in the management of the disease [11,12,13,14,15,16,17].

EVOLUTION OF THERAPEUTIC STRATEGIES

The transition from the isolated use of synthetic DMARDs to the early use of biologics marks an important change in the approach to the treatment of psoriatic arthritis (PsA) [11,12,13,14,15,16,17]. In the past, synthetic DMARDs, such as methotrexate, were the first line of treatment, and biological drugs were only used in more severe cases or when DMARDs were not effective [11,12,13,14,15,16,17]. However, there is currently a growing trend to start treatment with biological drugs earlier, especially for patients with risk factors for severe joint damage [11,12,13,14,15,16,17]. This is because biologics are more effective at controlling inflammation and modulating the immune system [11,12,13,14,15,16,17].

The early use of biologics has been shown to be beneficial in slowing down the progression of the disease and preventing irreversible joint damage [11,12,13,14,15,16,17]. Studies show that biologics have the ability to control inflammation more effectively than synthetic DMARDs, which helps preserve joint function and improves patients' quality of life [11,12,13,14,15,16,17]. When used in the early stages of the disease, biologics not only control symptoms, but also help prevent the more serious complications of PsA, such as bone erosions [11,12,13,14,15,16,17]. In this way, patients can experience less pain, less disability and greater mobility in the long term [11,12,13,14,15,16,17].

The development of targeted therapies represents another major advance in the treatment of PsA. Drugs such as JAK inhibitors and IL-23 inhibitors are newer therapies that act on specific targets in the immune system [11,12,13,14,15,16,17]. These treatments have the potential to offer more effective and personalized options for patients, especially those who do not respond adequately to traditional treatments [11,12,13,14,15,16,17]. By focusing on specific molecular targets, these therapies are more precise, with a lower risk of side effects compared to broader therapies such as corticosteroids [1,2,3,4,5,6,7,8,9].

The expansion of therapeutic options with new classes of drugs, such as biologics and targeted therapies, allows doctors to personalize treatment according to the specific needs of each patient [1,2,3,4,5,6,7,8,9]. This is especially crucial for PsA patients who do not respond well to conventional treatments or who experience adverse effects with these drugs [1,2,3,4,5,6,7,8,9]. Personalizing treatment helps to maximize therapeutic benefits and improve treatment adherence, providing patients with more effective management of their condition [1,2,3,4,5,6,7,8,9].

Although the new treatments show promising results, more long-term studies are needed to assess the safety and efficacy of these therapies, especially in relation to the comorbidities that many PsA patients have [1,2,3,4,5,6,7,8,9]. The long-term efficacy and effects on the patient's general health, such as the cardiovascular impact, still need to be well understood [1,2,3,4,5,6,7,8,9]. This is key to ensuring that these treatments not only control PsA, but also do not cause complications in other aspects of the patient's health. Continued research will help refine the use of these therapies and offer increasingly effective and safe treatments [1,2,3,4,5,6,7,8,9].

CHALLENGES AND FUTURE PROSPECTS

The treatment of psoriatic arthritis (PsA) faces significant challenges, especially with regard to personalizing treatment [4,5,6,7,8]. Each PsA patient can respond uniquely to drugs, and the current lack of validated biomarkers to predict treatment response is an obstacle [4,5,6,7,8]. Although biomarkers can offer a way of identifying which patients will benefit most from a particular drug, there is still no scientific consensus or widely accepted biomarker for PsA [4,5,6,7,8]. Ongoing research, however, seeks to identify those molecules that can indicate disease activity and potentially predict the effectiveness of different therapies [4,5,6,7,8]. In the near future, blood tests or other tests could be used to determine the most suitable drug for each patient, improving both the efficacy and safety of treatment, as well as reducing side effects [4,5,6,7,8].

Another major challenge in the treatment of PsA is related to the lack of direct comparative studies between biological drugs [19,20,21,22]. There are several biological options on the market, but few studies have made direct comparisons on the relative efficacy of these drugs [19,20,21,22]. This creates uncertainty when choosing the most appropriate treatment for patients who do not respond to initial treatments or who are refractory to conventional therapies [19,20,21,22]. The lack of direct comparative data makes it difficult to decide which biologic should be used and in what sequence. In order to optimize treatment, it is essential to carry out direct comparative studies between biologics, especially for patients with more severe forms or who do not respond well to standard treatment [19,20,21,22]. These studies would not only help to choose the best therapy for refractory patients, but also to improve long-term results [19,20,21,22].

In addition to comparative studies, the incorporation of real-world data and pharmacoeconomics studies also plays a crucial role in the future of PsA treatment [19,20,21,22]. Real-world data, collected outside the controlled environment of clinical trials, can provide valuable information on how drugs perform in clinical practice, considering factors such as treatment adherence and comorbidity management [19,20,21,22]. This data can help adjust treatment guidelines to reflect patients' day-to-day conditions [19,20,21,22]. Pharmacoeconomics studies, in turn, are essential for assessing the cost-effectiveness of treatments [19,20,21,22]. With the high cost of biological drugs, these studies can help determine which therapies are more affordable and sustainable in the long term for health systems, allowing more patients to have access to effective treatments [19,20,21,22].

The future outlook is for more effective, safe and affordable PsA treatment, based on a combination of treatment personalization, direct comparative studies and real-world data analysis [19,20,21,22]. Integrating these elements can transform the therapeutic approach, providing treatments that are more tailored to patients' individual needs and improving clinical outcomes [19,20,21,22]. Furthermore, with the continuous analysis of pharmacoeconomics, healthcare systems can be guided to offer high-impact therapies while balancing costs, ensuring that access to treatment is maintained in an efficient and sustainable manner [19,20,21,22].

In summary, the future of psoriatic arthritis treatment depends on overcoming challenges such as the lack of widely validated biomarkers, the need for direct comparative studies between drugs and the use of real-world data and pharmacoeconomic analyses [19,20,21,22]. Ongoing research is essential to provide the necessary foundations for these improvements, and collaboration between

doctors, researchers and patients will be key to achieving significant advances in the field [19,20,21,22]. With more personalized and efficient treatment, patients will be able to count on therapies that not only control PsA, but also improve their quality of life in the long term [19,20,21,22].

CONCLUSION

The treatment of psoriatic arthritis (PsA) involves a wide range of therapies, each with its advantages and challenges. Non-steroidal anti-inflammatory drugs (NSAIDs) are often used to relieve pain and inflammation, but they do not prevent the progression of the disease, as well as posing risks of gastrointestinal and cardiovascular side effects. In contrast, synthetic disease-modifying drugs (conventional DMARDs), such as methotrexate, can reduce inflammation and slow down the progression of the disease, although they carry potential risks of liver and hematological toxicity. For more severe or refractory cases, biological DMARDs offer a more focused approach, blocking specific targets of the immune system. However, their high cost and the increased risk of infections make careful evaluation necessary. More recently, targeted synthetic DMARDs, such as JAK inhibitors, represent an option for patients who do not respond well to other treatments, although these drugs are also associated with cardiovascular and hematological risks.

The choice of the ideal treatment should be individualized, taking into account the clinical manifestations of each patient, the response to previous treatments, such as methotrexate, and potential adverse effects. Comparisons between different therapeutic classes, such as IL-17 inhibitors vs. TNF-α inhibitors, can be key to optimizing the choice of treatment. Studies indicate that IL-17 inhibitors may be more effective for conditions such as dactylitis and enthesitis. For patients refractory to methotrexate, early introduction of biologics or switching biologic therapies may offer superior control of inflammation, slowing progression and preventing joint damage. However, as treatment is highly specific to each patient, regular adjustments should be made based on clinical response and treatment tolerance.

In addition to considering the efficacy, safety and adverse effects of therapies, it is also crucial to analyze the impact of comorbidities on treatment. Patients with PsA often face comorbidities, such as obesity, diabetes and cardiovascular disease, which can influence the choice of treatment. Drugs such as TNF-α or JAK inhibitors, for example, can exacerbate heart problems or increase the risk of thrombosis, making a careful approach necessary. In contrast, IL-23 inhibitors have demonstrated a neutral or even beneficial effect on cardiovascular risk, which may be advantageous for patients with associated comorbidities. Treatment should be personalized to ensure patient safety and treatment efficacy, with regular follow-up to monitor possible adverse effects and therapeutic adjustments.

Early diagnosis and early intervention play a fundamental role in PsA. Detecting the disease in the pre-clinical phase, when there are no obvious symptoms yet, can prevent irreversible joint damage and improve the prognosis. The concept of "Treat-to-Target", which aims to achieve remission or low disease activity, is an important strategy for optimizing clinical results. This approach allows regular treatment adjustments based on individual response, preventing joint damage and improving patients' physical function. The evolution of therapeutic strategies also reflects a growing trend to use biologics early, especially in patients at high risk of progression, to slow down inflammation and disease progression.

The future of PsA treatment depends on several prospects. Personalizing treatment with biomarkers, although still in the research

phase, promises to transform the way drugs are chosen, boosting efficacy and minimizing adverse effects. In addition, direct comparative studies between biologics are essential to optimize therapeutic choices, especially in refractory cases. The use of real-world data and pharmacoeconomics studies will enable a more comprehensive assessment of the efficacy, safety and cost-effectiveness of treatments, helping to make therapies more accessible without compromising the quality of treatment. With collaboration between doctors, researchers and patients, the combination of personalization, comparative studies and real-world data could lead to more effective, safe and affordable treatments for psoriatic arthritis, providing a better long-term quality of life for patients.

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