

THERAPEUTIC APPROACHES IN ANKYLOSING SPONDYLITIS: CHALLENGES AND EVOLVING TREATMENT PARADIGMS

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Introduction. Ankylosing spondylitis (AS) is a chronic autoimmune disorder that primarily affects the spine and the lumbosacral joints, leading to their ankylosis and, eventually, disability. Characterized by inflammation and progressive damage, AS predominantly impacts individuals under 40 years of age, with a higher prevalence in men. The disease is associated with the human leukocyte antigen HLA-B27, a genetic marker that plays a crucial role in its pathogenesis. AS is recognized for its significant societal impact, as it often leads to early disability in the younger population, affecting their quality of life and productivity. Recent updates in therapeutic guidelines emphasize the combination of non-pharmacological and pharmacological interventions to manage disease progression and alleviate symptoms. This paper explores the current treatment options for AS, focusing on the effectiveness and safety of non-steroidal anti-inflammatory drugs (NSAIDs), biologic therapies, and newer immunomodulatory agents, as well as the need for updated treatment guidelines.

Materials and Methods. The research for this mini-thesis is based on an extensive review of current literature and clinical studies surrounding the treatment of AS. Studies were selected from internationally recognized medical journals, focusing on the therapeutic strategies employed in managing AS, including pharmacological treatments such as NSAIDs, disease-modifying antirheumatic drugs (DMARDs), biologic therapies, and the newer targeted drugs, such as Janus kinase (JAK) inhibitors and IL-17 inhibitors. The review methodology included an analysis of clinical trials and meta-analyses, with particular attention given to the efficacy and safety profiles of these treatment modalities. Research from the Spondyloarthritis International Society (ASAS), European League Against Rheumatism (EULAR), and American College of Rheumatology (ACR) guidelines were incorporated to assess the evolution of therapeutic recommendations. This paper also synthesizes expert opinions and emerging data on the use of biological therapies and the potential need for more individualized treatment plans in light of patient response variability.

Results. The findings from the review of current literature reveal a shift in the management paradigm of AS, highlighting the growing role of biologic therapies and targeted immunomodulation. NSAIDs remain the first-line treatment for AS, helping to alleviate pain and inflammation. However, their long-term use raises concerns due to serious side effects such as gastric ulcers, liver toxicity, and cardiovascular issues. Despite these risks, NSAIDs continue to be a cornerstone of initial treatment, often prescribed on a long-term, daily basis to manage disease activity.

For patients who do not respond to NSAIDs, second-line therapies include biologic agents, such as TNF- α inhibitors (e.g., adalimumab, infliximab) and IL-17 inhibitors (e.g., secukinumab, ixekizumab). These biologics have shown significant efficacy in reducing disease activity, improving mobility, and slowing disease progression. The introduction of IL-17 inhibitors has been particularly noteworthy, as these agents target a key pro-inflammatory cytokine involved in the pathogenesis of AS. Studies have demonstrated that IL-17 inhibitors can reduce the activity of AS, as well as prevent radiological damage to the spine and joints, with favorable safety profiles.

Janus kinase (JAK) inhibitors, such as tofacitinib, filgotinib, and upadacitinib, represent a new class of drugs that have shown promising results in treating refractory AS. A 12-week study on filgotinib demonstrated a 33% reduction in AS disease activity among NSAID-refractory patients. However, concerns regarding the safety of JAK inhibitors remain, with adverse events reported in clinical trials, although no major safety concerns have been identified.

The effectiveness of sulfasalazine, a traditional DMARD, remains under debate. While some studies suggest its moderate efficacy in treating the peripheral form of AS, other evidence points to its effectiveness in both axial and peripheral forms of the disease. However, its role as a second-line therapy is less pronounced compared to biologics and JAK inhibitors.

The most striking recent development is the dual inhibition of IL-17A and IL-17F through bimekizumab, which has shown rapid and sustained improvements in key AS indicators, with over 60% of patients achieving an ASAS40 response at 320 mg. These results underscore the growing importance of IL-17 inhibitors in the therapeutic landscape of AS.

Conclusion. In conclusion, the management of ankylosing spondylitis has evolved significantly over the past decades, with considerable advancements in pharmacological therapies. The updated treatment guidelines emphasize a



combination of non-pharmacological approaches, such as exercise therapy, and pharmacological treatments, including NSAIDs, DMARDs, and biologic therapies. While biologics such as TNF- α inhibitors and IL-17 inhibitors have revolutionized AS treatment, there remain concerns about the safety profiles of long-term NSAID use and the emerging data on newer agents like JAK inhibitors.

Given the complexity and variability of treatment responses, it is crucial that treatment plans be tailored to individual patients, considering both efficacy and safety. Furthermore, the evolving evidence calls for the modernization of international treatment guidelines to incorporate the latest therapeutic advancements. Future research should focus on optimizing drug regimens, assessing the long-term effects of new therapies, and investigating the impact of AS treatments during the COVID-19 pandemic. As the understanding of AS continues to deepen, more personalized and effective treatment options are expected to emerge, improving the quality of life for patients with this debilitating condition.

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