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ARE DMARDS BENEFICIAL IN MANAGEMENT OF PSORIASIS?

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Abstract:

Introduction:*Psoriasis is a chronic inflammatory papulosquamous skin disease with genetic predisposition and autoimmune pathogenicity. Psoriasis may also affect the joints as psoriatic arthritis and may even be associated with other conditions. Research into the pathogenesis of Psoriasis in the last few decades has given rise to several targeted therapies. Among them are Disease-modifying anti-rheumatic drugs (DMARDs), mainly used in cases of psoriatic arthritis. The article will review the various disease-modifying anti-rheumatic drugs along with strengths and weaknesses in combating Psoriasis.*

The aim of work*: An overview is aimed at describing various DMARDs and their use against Psoriasis.*

Methodology: *The review is a thorough review of PUBMED articles from the year 1984 to 2019 relating to DMARDs and Psoriasis.*

Conclusion:*Psoriasis is a chronic inflammatory skin disease that also affects other systems of the body due to inflammation. DMARDs are a group of drugs that are used to combat Psoriasis and various other inflammatory ailments. This review briefly discusses the most common examples of DMARDs, their mechanism of action, efficacy in trials, and adverse effects.*

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INTRODUCTION:

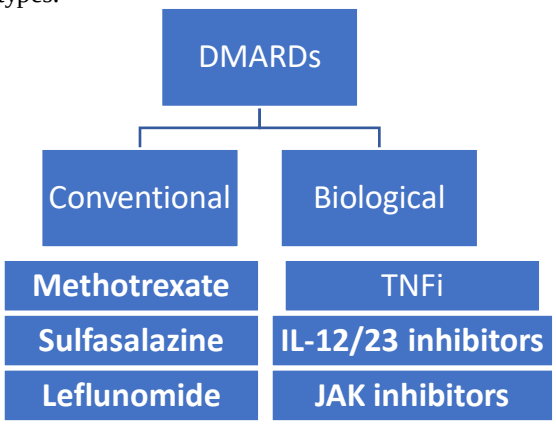
Psoriasis is a chronic inflammatory papulosquamous skin disease with genetic predisposition and autoimmune pathogenicity. Psoriasis is heterogeneously prevalent across the globe, with lower prevalence in Asian and African populations and higher in Caucasian populations. [1]

Psoriasis may also affect the joints as psoriatic arthritis and may even be associated with other conditions. People with Psoriasis are at greater risk of developing hyperlipidemia, hypertension, coronary artery disease, and type 2 diabetes. Among these, psoriatic arthritis is found in up to 40 % of psoriasis patients. Psoriatic arthritis presents with arthritis, enthesitis (inflammation of enthesis), dactylitis (inflammation of digit), and axial bone involvement. [2]

Research into the pathogenesis of Psoriasis in the last few decades has given rise to several targeted therapies. Among them are Disease-modifying anti-rheumatic drugs (DMARDs), mainly used in cases of psoriatic arthritis. The article will review the various disease-modifying anti-rheumatic drugs along with strengths and weaknesses in combating Psoriasis. [2]

DMARDs:

Disease-modifying anti-rheumatic drugs (DMARDs) are an immunosuppressive and immunomodulatory class of drugs that aim to treat not only psoriatic arthritis but also rheumatoid arthritis (RA) ankylosing spondylitis (AS), systemic sclerosis, etc. DMARDs are broadly divided into conventional and biological types. [3]



Classification of DMARDs [3]

Methotrexate:

Originally methotrexate was used as part of cancer therapy, but when used in much smaller doses, it was incorporated in the treatment of rheumatoid arthritis, psoriatic arthritis, and other inflammatory diseases. A study showed a low dose of oral methotrexate (7.5 mg or 15 mg/week) when compared with placebo showed better patient tolerance over a time of 3 months.[4] Nevertheless, the efficacy of methotrexate was questioned in other studies. Adverse effects include mouth ulcers and stomach upsets. Methotrexate may disturb the production of blood cells in the bone marrow. Considering the potential of serious side effects, proper monitoring of the patient's blood counts is essential. [5]

Sulfasalazine:

The success of sulfasalazine against rheumatoid arthritis led to its application in psoriatic arthritis. Early trials using a dose of 2 g/day over 24 weeks showed significant improvements in combating painful and stiff joints. [6] Later and larger trials also exhibited the efficacy of sulfasalazine in improving tender and swollen joints. Common adverse effects include nausea, vomiting, and changes in blood counts. Regular blood count check-ups are recommended during therapy. [7]

Leflunomide:

This drug is a selective pyrimidine synthesis inhibitor that attacks activated T cells. Leflunomide has demonstrated that it improves both joint and skin pathologies related to psoriatic arthritis. [8] It may be taken alone or in combination with methotrexate, where methotrexate alone did not suffice. Combination of methotrexate with leflunomide may be associated with liver function test abnormalities, and therefore necessitates periodic monitoring. [9]

Ciclosporin A:

Ciclosporin A is a calcineurin inhibitor, where it prevents T lymphocyte activation. Studies have shown the success of Ciclosporin A against both arthritis and cutaneous Psoriasis. Adverse effects of cyclosporin A are renal toxicity and hypertension; therefore, they must be monitored. [10]

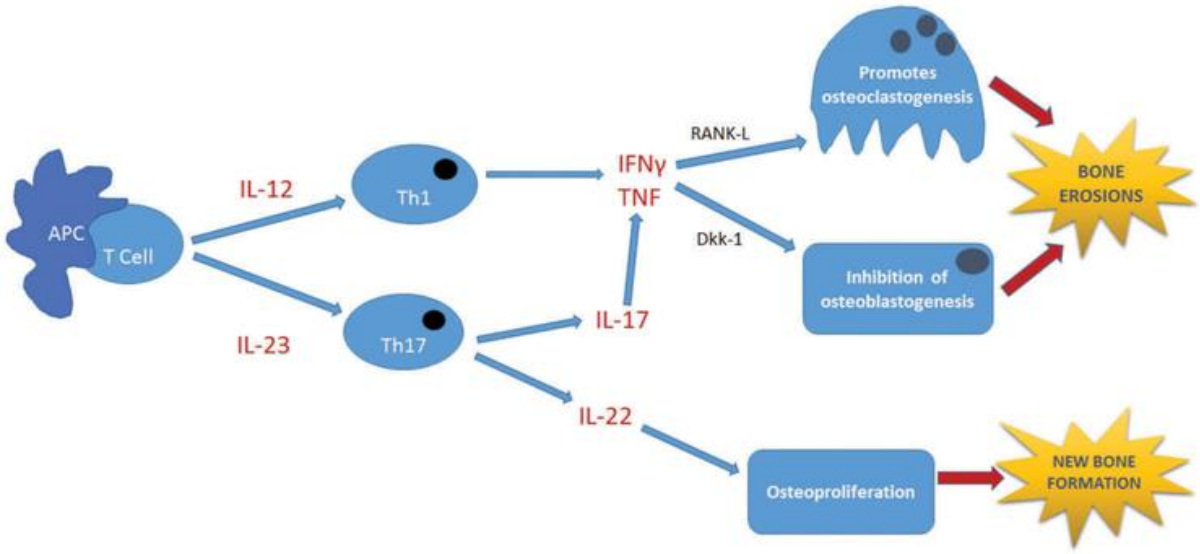


Figure: pathogenesis of Psoriasis involving IL's, TNF. [11]

TNFi

TNFi (Tumor necrosis factor inhibitor) are monoclonal antibodies that target TNF (Tumor necrosis factor). TNF is a superfamily of proteins that are essential for sustaining inflammation. Etanercept, infliximab, and adalimumab are a few approved TNFi in use. TNFi is known to diminish inflammation on both peripheral and axial joints. They also improve the symptoms of skin and nail manifestations, thereby improving the overall quality of life in Psoriasis. TNFi can also be used locally as injections into the intra-articular spaces of affected joints. Although TNFi seems to benefit all domains of Psoriasis, some patients do not respond to the treatment. [11]

IL-12/23 inhibitors

Ustekinumab is an IgG1 monoclonal antibody that attaches and neutralizes the proinflammatory IL-12 and IL-23 cytokines. Several phases of clinical trials have proven the efficacy of ustekinumab in significantly improving the Psoriasis Area and Severity Index (PASI) when compared to placebo groups. Common adverse effects found were headache, nasopharyngitis, upper respiratory tract infections (URTI), fatigue, pruritus, back pain, and injection site reactions. A very small number of subjects also developed antibodies to ustekinumab in low amounts. [12]

JAK inhibitors

Janus kinases or Jaks are intracellular tyrosine kinases and are critical for a large family of cytokines because they participate in the cytokine signaling pathway. Defects in JAK/STAT signaling pathway are thought to be involved in the pathogenesis of Psoriasis. Increased activity of STAT1 is seen in cutaneous Psoriasis. In the case of articular issues of psoriatic arthritis, an increase in JAK1/STAT3/STAT1 has been observed. Tofacitinib is a JAK (1,2,3) inhibitor which in turn blocks several inflammatory cytokines like IL (2,4,15,21) and interferon-gamma; this leads to reduced inflammatory reactions in the body. A meta-analysis found that either 5 or 10 mg of tofacitinib twice daily achieved good PASI scores but also had more adverse reactions compared to placebo. [13]

IL 17 inhibitors

Increased secretion of IL 17 leads to epidermal hyperplasia and enhanced inflammation, as seen in Psoriasis. IL 17 inhibitors directly target this group of proinflammatory mediators and suppress the inflammatory response. There are three types of IL 17 antagonists: secukinumab, ixekuzumab, and brodalumab. Several clinical trials have proven the efficacy of IL-17Antagonists in patients with Psoriatic arthritis. Recovery from functional disability, improvement in radiographic scans of joint damage, and overall disease activity for all three types of IL 17 antagonists. IL 17 antagonists have been successful in difficult to treat Psoriasis as well, such as of scalp, nails, palmoplantar, and pustular Psoriasis. With so much success and few adverse effects, additional research is undergoing to find more types of IL 17 inhibitors. [14]

CONCLUSION:

Psoriasis is a chronic inflammatory skin disease that also affects other systems of the body due to inflammation. Of which, psoriatic arthritis is pretty common and painful to psoriatic patients. A number of

anti-inflammatory drugs are used to combat this disease, and Disease-modifying anti-rheumatic drugs (DMARDs) are one of them. DMARDs are an immunosuppressive and immunomodulatory class of drugs that are used against Psoriasis and various other inflammatory diseases. In this review, we classified DMARDs into two broad groups known as conventional and biologic DMARDs. We briefly discussed the most common examples of DMARDs, their mechanism of action, efficacy in trials, and adverse effects.

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