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Perspective

Role of Methotrexate in Systemic Lupus Erythematosus

Emma Jones*

Department of Rheumatology, University of Cambridge, Cambridge, England

DESCRIPTION

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by systemic inflammation and the production of autoantibodies that can affect multiple organs and tissues. Methotrexate, a folate antagonist and antimetabolite, has been investigated for its role in the treatment of SLE, particularly in managing certain manifestations and reducing disease activity. This article describes the mechanisms of action, clinical efficacy, safety considerations, and current guidelines regarding the use of methotrexate in SLE management. Methotrexate exerts its immunosuppressive effects through several mechanisms. Methotrexate inhibits dihydrofolate reductase, an enzyme involved in the synthesis of tetrahydrofolate, which is essential for purine and pyrimidine synthesis. This inhibition leads to reduced production of DNA and RNA precursors, thereby suppressing lymphocyte proliferation and reducing immune cell activity. Methotrexate increases the extracellular concentration of adenosine, which has anti-inflammatory properties and can inhibit pro-inflammatory cytokine production (e.g., TNF-α, IL-6). By interfering with folate metabolism, methotrexate disrupts the proliferation of rapidly dividing cells, including activated lymphocytes and synovial cells in inflammatory joints. Methotrexate has been studied primarily for its efficacy in treating specific manifestations of SLE. Methotrexate is effective in managing various forms of CLE, including Discoid Lupus Erythematosus (DLE) and Subacute Cutaneous Lupus Erythematosus (SCLE). It helps reduce skin lesions, photosensitivity, and disease flares. Methotrexate is commonly used to treat inflammatory arthritis in SLE, including polyarthritis and non-erosive arthritis. It can improve joint pain, swelling, and stiffness, often allowing for reduction in corticosteroid doses. While methotrexate is less effective in treating severe systemic manifestations such as lupus nephritis or central nervous system involvement compared to other immunosuppressant's, it may be used as an adjunctive therapy to control overall disease activity.

Safety is an essential consideration in the use of methotrexate for SLE. Methotrexate can cause liver enzyme abnormalities and hepatotoxicity, necessitating regular monitoring of Liver Function Tests (LFTs). Hematologic toxicity, including leukopenia, thrombocytopenia, and anemia, may occur with methotrexate use. Monitoring of Complete Blood Counts (CBCs) is essential. Rare cases of interstitial lung disease have been reported with methotrexate use, warranting monitoring for respiratory symptoms and imaging studies if indicated. Folic acid supplementation is often prescribed alongside methotrexate to mitigate side effects such as mucosal irritation, gastrointestinal upset, and hair loss. Methotrexate is recommended for the treatment of mild to moderate cutaneous and musculoskeletal manifestations of SLE, particularly in patients who require steroid-sparing therapies. Methotrexate may be particularly suitable for patients with predominant skin and joint involvement, where its anti-inflammatory and immunosuppressive effects can provide significant clinical benefit.

Ongoing research in SLE treatment focuses on optimizing methotrexate therapy. Tailoring methotrexate dosing and monitoring protocols based on individual patient factors, disease severity, and genetic markers. Investigating the efficacy of combining methotrexate with biologic agents or other immunosuppressant's to achieve synergistic effects and improve treatment outcomes. Assessing the long-term safety and efficacy of methotrexate in SLE, particularly its impact on disease progression, organ damage, and quality of life. As an immunosuppressant, methotrexate serves as a corticosteroid-sparing agent in SLE management. By reducing disease activity, it allows for lower doses of corticosteroids, thereby minimizing the risk of long-term steroid-related adverse effects such as osteoporosis, diabetes, and cardiovascular disease. While methotrexate is less commonly used as a primary treatment for severe manifestations like lupus nephritis, it may be employed as an adjunctive therapy to help control overall disease activity and reduce the need for higher doses of immuno suppressants like cyclophosphamide or mycophenolate mofetil. Methotrexate is utilized as maintenance therapy in SLE to prevent disease flares and maintain disease remission achieved with initial therapies. Its immunosuppressive properties help regulate the abnormal immune responses characteristic of SLE, thereby promoting long-term disease control.

Correspondence to: Emma Jones, Department of Rheumatology, University of Cambridge, Cambridge, England, E-mail: emmaj13@gmail.uk

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CONCLUSION

Methotrexate plays a significant role in the management of systemic lupus erythematosus, particularly in controlling cutaneous manifestations, arthritis, and mild systemic disease. Its mechanisms of action, clinical efficacy, safety profile, and adherence to current guidelines are essential considerations in optimizing treatment outcomes for patients with SLE. While challenges such as potential toxicity and variability in patient responses remain, ongoing research and clinical experience continue to inform best practices in methotrexate use, supporting its role as a valuable therapeutic option in the management of SLE.