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A Review On Naproxen, Methotrexate and Mannitol for the treatment of Rheumatoid Arthritis Disease

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Abstract: *Nonsteroidal anti-inflammatory drugs (NSAIDs), methotrexate (MTX), and mannitol are widely employed therapeutic agents in the management of pain, autoimmune diseases, and intracranial pressure, respectively. Naproxen, a traditional NSAID, remains a benchmark for analgesic and anti-inflammatory therapy owing to its efficacy in rheumatologic and musculoskeletal disorders, though it carries risks of gastrointestinal injury, renal impairment, and cardiovascular complications .In contrast, MTX is the anchor disease-modifying antirheumatic drug (DMARD) for rheumatoid arthritis (RA), exerting dual mechanisms of action: inhibition of dihydrofolate reductase at high doses (anticancer use) and enhancement of adenosine-mediated anti-inflammatory pathways at low doses . Despite its therapeutic utility, MTX toxicity, including hepatotoxicity, myelosuppression, and pulmonary injury, necessitates close monitoring and folate supplementation .*

Mannitol, a potent osmotic diuretic, is extensively used in neurocritical care to reduce intracranial and intraocular pressure. Its mechanism centre's on increasing tubular osmolarity to induce osmotic diuresis and create osmotic gradients across the blood–brain barrier. However, excessive or repeated dosing predisposes to osmotic nephrosis and acute kidney injury (AKI), particularly in vulnerable patients . Drug–drug interactions pose additional challenges: NSAIDs with anticoagulants or SSRIs heighten bleeding risks, while NSAIDs and PPIs can impair MTX clearance, amplifying toxicity .Similarly, co-administration of mannitol with other nephrotoxic drugs (e.g., aminoglycosides, cisplatin) aggravates renal injury .

Taken together, balancing efficacy with safety represents the central clinical challenge in the use of these agents. Naproxen remains effective with comparatively lower thrombotic risk than other NSAIDs, MTX provides durable remission in RA when optimally dosed and monitored, and mannitol continues as a mainstay for acute osmotherapy under strict biochemical surveillance. Future directions should emphasize safer regimens, early toxicity detection, and individualized therapeutic strategies integrating pharmacokinetics, pharmacodynamics, and patient comorbidities.

Keywords: Naproxen, Methotrexate, Mannitol, NSAIDs, Rheumatoid arthritis, Osmotic nephrosis, Adverse effects, Pharmacology

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