High-Dose Methotrexate: Nursing Considerations for Administration and Supportive Care

Breanne Roche, DNP, APRN, CPNP-PC, CPHON®, Patricia A. Clarke, DNP, APRN, CPNP-PC, CPHON®, Danielle Ford, BSN, RN, OCN®, Shannon Collins Shaver, BSN, RN, OCN®, and Joanna Thompson, RN, BSN

BACKGROUND: High-dose methotrexate (HDMTX) is the backbone of many pediatric and adult oncology treatment protocols. It requires appropriate monitoring and supportive care because delayed elimination of MTX can lead to serious toxicities. No reviews specifically addressing nursing management regarding standard treatment protocols and delayed MTX elimination exist.

OBJECTIVES: This article provides an overview of HDMTX treatment and nursing considerations, including toxicities, components of supportive care management, and strategies to manage administration and delayed elimination of MTX.

METHODS: A review of published literature and guidelines was performed to evaluate nursing considerations for patients receiving HDMTX.

FINDINGS: Using existing and novel tools, nurses can closely monitor patients and provide supportive care to mitigate HDMTX toxicity. Early identification of delayed MTX elimination and subsequent treatment with glucarpidase, if appropriate, has been associated with shorter length of hospital stay and decreased incidence of grade 4 toxicities and mortality.

KEYWORDS
high-dose methotrexate; acute kidney injury; glucarpidase; leucovorin; toxicity

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IN 1948, SYDNEY FARBER DISCOVERED THAT AMINOPTERIN, a precursor to modern methotrexate (MTX), effectively led to remission in acute leukemias (Chabner & Allegra, 2019). Further research with antifolates led to the development of MTX, a folate inhibitor that is administered as low-dose MTX for immunoinflammatory diseases and high-dose MTX (HDMTX) for other malignancies (Malaviya, 2016). An HDMTX protocol involves any MTX dose of 500 mg/m² or greater (LaCasce, 2022), leading to high initial plasma concentrations (10–1,000 micromole/L) and sustained plasma concentrations of more than 1 micromolar for 12–30 hours, and requiring rescue with leucovorin. Leucovorin replaces folates to prevent dangerously low levels of folate (Chabner & Allegra, 2019; LaCasce, 2022). HDMTX is the backbone of many chemotherapy protocols and is used primarily in pediatric patients with acute lymphoblastic leukemia, osteosarcoma, lymphoma, or certain brain tumors, and in adult patients with primary central nervous system lymphoma and other B-cell lymphomas. HDMTX therapy is recommended in several published cancer guidelines, including Children's Oncology Group protocols AALL0232 and POG 9404 (Asselin et al., 2011; Larsen et al., 2016).

The purpose of this article is to provide an overview of HDMTX treatment and nursing considerations, including HDMTX toxicities, components of supportive care, and strategies to manage HDMTX administration and delayed elimination. Two case studies are presented to illustrate HDMTX treatment and highlight key aspects of clinical care.

Methods

This article was based on a structured literature search. The literature reviewed included scholarly publications, clinical websites, and data from pivotal clinical trials.

MTX Treatment and Toxicities

Mechanism of Action of MTX

MTX disrupts DNA synthesis during cell division. After MTX enters the cell, it is polyglutamated, rendering it trapped inside the cell. It then binds the enzyme dihydrofolate reductase, which is necessary to convert folates to their active form (tetrahydrofolate). Without tetrahydrofolate, DNA synthesis is interrupted, leading to cell damage or death (Chabner & Allegra, 2019).