Characteristics and Outcomes of Methotrexate Toxicity: A Descriptive Retrospective Study

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Background: Methotrexate (MTX) is commonly used in many medical conditions such as rheumatoid arthritis, psoriasis, malignancy. MTX toxicity is resulting in mucositis, dermatitis, marrow suppression, hepatitis, and renal failure. The standard treatment, especially for chronic supra-therapeutic dose ingestion, is not well established.

Objective: To describe clinical characteristics, clinical effects, treatment, and outcomes of methotrexate toxicity.

Methods: This was a retrospective case series of adult (>18 years) patients with MTX toxicity reported to Ramathibodi Poison Center (RPC) from 2011 to 2015. Patient characteristics, circumstance of exposure, clinical effects, laboratory results, treatment, and outcome were described. Severity of bone marrow suppression were categorized based on leukocyte count into 5 grades (0 – 4) according to CTCAE. Empiric and total dose of folinic acid were reported.

Results: There were 24 patients with MTX toxicity reported to RPC. Median age was 64.5 years (range 25 – 92 years). Common diseases related to MTX use were rheumatoid arthritis 50%, psoriasis 25%, systemic sclerosis 4%, and other 17%. Common comorbidities were CKD 25%, DM 8.3% and cirrhosis 8.3%. Circumstance of exposure was unintentional ingestion 12.5%, medical error 41.7%, and therapeutic dose 45.8%. Clinical manifestations were mucositis 91.7%, leukopenia 91.7%, thrombocytopenia 87.5%, anemia 91.7%, hepatitis 62.5%, and renal insufficient 45.8%. There were 16.7% patients were categorized to grade 0 initial leukocyte (>4000), 12.5% in grade 1 (3000 – 4000), 25% in grade 2 (2000 – 3000), 25% in grade 3 (1000 – 2000), and 16.7% in grade 4 (<1000). Treatment to patients was folinic acid 95.8%, blood transfusion 70.8%, and inotropic drug 16.7%. There were 4 deaths, including 2 patients with initial leukopenia grade 4, one with septic shock and initial leukopenia grade 3, and last one with initial leukopenia grade 0 with septic shock and DKA. Of the 4 cases presented with grade 4 leukopenia, 2 cases received higher total dose of folinic acid (>400 mg/m²/day) and 2 cases received lower total dose (<200 mg/m²/day). Thus, these patients were dead.

Conclusion: Patients presented with initial leukopenia grade 4 are high morbid and mortality. Receiving high dose of folinic acid is survival achievable.

Keywords: Methotrexate toxicity, Leucovorin, Folinic acid, Leukopenia