Methotrexate

Methotrexate (MTX) is an antimetabolite and disease-modifying antirheumatic drug (DMARD) that acts by inhibiting dihydrofolate reductase. This results in stopping production of dTMP (thymidine), which is necessary for DNA, RNA and protein synthesis, thus resulting in cell death.Adverse effects of MTX administration include myelosuppression (though this can be treated with leucovorin), macrocytic anemia, hepatitis, teratogenic effects and oral mucositis.



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Indications

Rheumatoid Arthritis

Roman King-Arthur

MTX is indicated as the first-line therapy for moderate to severe rheumatoid arthritis (RA). The mechanism for how it decreases the severity of arthritis is not clear. Prior to treatment with MTX, several pre-treatment interventions should be undertaken including laboratory assessment of CBC, serum creatinine, AST and ALT.

Cancer

Tumor-guy

MTX is effective in cancer because of its ability to result in cell death of rapidly dividing cancer cells. It is used in the treatment of various cancers including leukemias, lymphomas, choriocarcinoma and sarcomas.

Medical Abortion

Aborting Fetus

MTX followed by vaginal misoprostol can be used for elective medical abortion, which is typically performed up to 49 days gestational age. This regimen (MTX + misoprostol) is considered inferior to mifepristone + misoprostol because the interval between treatment and complete abortion is longer. MTX is also used for treatment of small, unruptured ectopic pregnancies.

Mechanism

Folic Acid Analog

Flicking Acidic-lemon On-a-log

MTX is a chemical analog of folic acid. It prevents folic acid metabolism and thus thymidine production because it has a much higher affinity for dihydrofolate reductase than folic acid.

Inhibits Dihydrofolate Reductase

Inhibiting-chains on Di-hydryl-foliage Red-duck

Without dihydrofolate reductase, which MTX binds and competitively inhibits, the biologically active form of folic acid, tetrahydrofolate, cannot be formed.

Side Effects

Pulmonary Fibrosis

Fiber-ball hitting Lungs

Pulmonary toxicity is associated with methotrexate use, and patients can develop irreversible pulmonary fibrosis. Other pulmonary side effects of this drug include hypersensitivity pneumonitis and bronchitis.

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Myelosuppression is Treated with Leucovorin Rescue (Folinic Acid)

Suppressed red and white blood cells Rescued by Luke-vulture

MTX can lead to myelosuppression, and thus a low white blood cell count. This can be reversed with administration of Leucovorin, which has vitamin activity equivalent to that of folic acid but does not require dihydrofolate reductase to be converted to its biologically active form. This quickly allows thymidine levels to be restored so that DNA, RNA and protein synthesis can occur.

Macrocytic Anemia

Macaroni Anemone

Because MTX results in a functional deficiency of folic acid, macrocytic anemia can result. Macrocytic anemia is described by the mean corpuscular volume being greater than 100 (MCV > 100 fL).

Hepatitis

Happy-tie-liver

MTX can result in liver toxicity due to unknown causes. AST and ALT should be obtained to assess for liver damage prior to initiation of MTX therapy.

Teratogenic

Tarantula-gem

MTX leads to cell death, especially of rapidly dividing fetal cells. Pregnant women must not take this drug during pregnancy.

Mucositis

Mucous-on-fire

MTX leads to cell death of GI tract epithelial cells leading to inflammation and ulceration of these mucus membranes, particularly in the oral region.

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