Injection

MITOCIN

Mitomycin USP

Antineoplastic

Action and Clinical Pharmacology: Mitomycin was first investigated as an antibiotic in Japan. It was then found to be active as an antineoplastic agent. It selectively inhibits the synthesis of deoxyribonucleic acid (DNA). The exact point of mitomycin attachment to DNA remains unknown. There is a correlation between the guanine and cytosine content of DNA and the degree of mitomycin-induced cross-linking. At high concentrations of the drug, cellular RNA and protein synthesis are also suppressed.

Pharmacokinetics: In humans, mitomycin is rapidly cleared from the plasma after i.v. administration with a biphasic plasma elimination curve. Time required to reduce the serum concentration by 50% after a 30 mg bolus injection is 17 minutes. After injection of 30 mg, 20 mg or 10 mg i.v., the maximal serum concentrations were 2.4 µg/mL, respectively. Approximately 10% of a dose of mitomycin is excreted unchanged in the urine. Since metabolic pathways are saturated at relatively low doses, the percent of a dose excreted in urine increases with increasing doses. In children, excretion of i.v. administered mitomycin is similar. Mitomycin is not appreciably absorbed from the urinary bladder, following intravesical administration. Serial plasma samples from 55 patients treated with doses of 20 to 40 mg of mitomycin by increasing doses instillation were assayed. There was no mitomycin detectable (assay limit 10 to 100 µg/mL) in any plasma samples collected during and 30 minutes post-therapy at any dose.

Indications and Clinical uses: In the palliative treatment as an adjunct to surgery, radiation or chemotherapy for adenocarcinoma of the stomach and colon. Mitomycin as a single agent is indicated as topical therapy for superficial (no invasion beyond the lamina propria) transitional cell carcinoma of the urinary bladder. Efficacy has been demonstrated both in patients who have had no prior intravesical chemotherapy and in those who have failed such therapy with thiotepa or other antineoplastic agents.

Contra-Indications: Patients who have demonstrated a hypersensitivity to it in the past, patients with thrombocytopenia, leukopenia, coagulation disorder, or an increased bleeding tendency due to other causes. Mitomycin is contraindicated for intravesical administration in patients who have demonstrated a hypersensitive or idiosyncratic reaction to it in the past.

Warnings in clinical states: Mitomycin is a potent drug and should be used only by physicians experienced with cancer chemotherapeutic drugs. Blood counts should be taken weekly. Mitomycin must be discontinued or dosage reduced upon evidence of abnormal depression of the bone marrow or the development of significant renal or pulmonary toxicity. Mitomycin should not be administered to any patient with a white blood cell count below 4000 mm and a platelet count below 150000 mm or to those with potentially serious infection. Bone marrow depression, notably thrombocytopenia and leukopenia, is the most severe toxicity. This may contribute to overwhelming infection in an already compromised, poor risk patient and may result in death.

Pregnancy: Safety use of mitomycin in pregnant women has not been established. Mitomycin has known teratogenic properties in animals, therefore, the benefits derived from the use of mitomycin in pregnancy must be weighed against the hazards involved.

Precautions: Mitomycin should be administered, preferably, to patients who are hospitalized and who can be observed carefully and frequently during and after therapy. It should be used with extreme caution in patients with significant impairment of renal function.

Adverse Reactions: Bone Marrow Toxicity: The most serious and most common toxicity of mitomycin is thrombocytopenia and leukopenia which occur any time within 8 weeks after onset of therapy. In a recent study, at a dose of 20mg/every 6 to 8 weeks, by itself or in combination with 5-fluorouracil, leukopenia accured in 74 of 94 patients, with 10 being in the life-threatening category, and thrombocytopenia occured in 68 to 94 patients, with 18 being in the life-threatening category. In a previous study, at doses of 0.5 mg/kg/day for 5 days and repeating once monthly, or 0.25 mg/kg every 2 weeks, leukopenia and/or thrombocytopenia occured in 605 of 937 patients. The return to normal counts after cessation of therapy was within 10 weeks. Mitomycin produces cumulative myelosuppression.

Integument and Mucous Membrane Toxicity: This has occurred in approximately 4% of patients treated with mitomycin. Cellulitis at the injection site has been reported and is occasionally severe. Stomatitis and alopecia also occur frequently. Rashes are rarely reported. The most important dermatological problem with this drug, however, is the necrosis and consequent sloughing of tissue which results if the drug is extravasated during injection.

Hemolytic Uremic Syndrome (HUS): A serious and often fatal syndrome consisting of microangiopathic hemolytic anemia, thrombocytopenia, renal failure, and hypertension has been reported in patients receiving mitomycin. Most of these patients received long-term therapy (6 to 12 months) with mitomycin in combination with fluorouracil and doxorubicin; however, some patients received mitomycin in combination with other drugs or were treated for less than 6 months.

Acute side effects: Fever, hemolytic anemia, anorexia, stomatitis, hypoglycemia, mucositis and diarrhea have occurred.

Genitourinary Irritation: Genitourinary irritation following intravasical administration indicated dysuria, cystitis, nocturia and increased frequency of micturition, hematuria, and other symptoms of local irritation. Approximately 25% of the patients treated experienced irritative symptoms, but not all were unequivocally drug-related and may have been symptoms of the disease.

Dermatitis: Dermatitis occured in approximately 10% of the patients treated. It was commonly manifested as plamar rash with desquamation, generally appearing on the extremities and less often on the trunk, and also as genital rash. Topical steroids have been employed but their therapeutic value has not been determined.

Symptoms and treatment of overdose: No specific antidote for mitomycin is known. Management of overdosage would include general supportive measures to sustain the patient through any period of toxicity that might occur.

Dosage and administration: Mitomycin should be given with care to avoid extraversion of the compound into the tissue. If extravasation occurs, cellulitis, ulceration and slough may result. Shake well until dissolved. If the product does not dissolve immediately, shake under warm tap water for approximately 2 minutes until a solution is obtained. I.V.: After full hematological recovery from any previous chemotherapy, may be used at 6 to 8 weeks intervals. Because of cumulative myelosuppression, patients should be re-evaluated after each course of mitomycin and the dose reduced if the patient has experienced any toxicities. No repeat dosage should be given until leukocite count has returned to 3000 and plateelet count to 75000. When mitomycin is used in combination with other myelosuppressive agents, the doses should be adjusted accordingly. If the disease continues to progress after 2 courses of mitomycin, the drug shoukl be stopped since chances of response are minimal.

Stability: Reconstituted with sterile water for injection to a concentration of 0.5 mg/mL, mitomycin is stable for 14 days refrigerated or 7 days at controlled room temperature (15 to 30°C). The reconstituted and diluted solutions should be inspected for discoloration, haziness, particulate matter and leakage prior to administration. Discard unused portion.

Availability and storage: Each vial contains: Mitomycin USP 10mg. Non-medicinal ingredients: mannitol, sodium chloride for pH adjustment. Single use vials packaged individually.

Store below 25°C. Protect from direct sunlight. Keep out of the reach of children.

مائیٹوسین انجکشن

مائیٹو مائی سین 10 ملی گرام

25° سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ دھوپ، گرمی اور نمی سے محفوظ رکھیں۔

تمام ادویات بچوں کی پہنچ سے دور رکھیں۔ ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

Revised: Jan.2017

Manufactured by :

Pharmedic Laboratories (Pvt) Limited.

16 Km. Multan Road, Lahore - Pakistan

Phone : (92-42) 37511861 - 65, Fax : (92-42) 37511396