INDIAN J DERMATOL VENEREOL LEPROL 1986; 52 : 155-157

METHOTREXATE THERAPY FOR PSORIASIS
(A preliminary report)

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Fourteen patients, 9 males and 5 females, with chronic severe intractable psoriasis resistant to conventional therapies were treated with methotrexate. Five had psoriatic erythroderma while 9 had extensive disease. Methotrexate therapy given orally in weekly single doses of 20-30 mg was effective in all cases. The side effects observed included nausea and vomiting, headache, pain abdomen, diffuse alopecia and loss of appetite.

Key words : Psoriasis, Methotrexate, Treatment.

Methotrexate has been used for the treatment of intractable and crippling psoriasis for the past over 20 years.[1-3] According to the guidelines of Psoriasis Task Force of National Programme for Dermatology,[4] the use of methotrexate is advised for psoriatic erythroderma, psoriatic arthritis, acute generalised pustular psoriasis, psoriasis in areas of body preventing employment and extensive disease. The decision to administer methotrexate must be individualised. If the disease is ruining the life physically, mentally and economically, methotrexate administration is advised.

Despite the fact that methotrexate has been in use for over two decades in many centres in India and abroad, we are not aware of any published Indian study. The present is a preliminary report of a continuing study conducted at our centre.

Materials and Methods

Fourteen patients not responding to conventional therapies were selected. Pretreatment assessment included complete haematologic profile, renal and hepatic function tests, needle biopsy of the liver and X-ray of chest. Continuing evaluation was done weekly for haematologic parameters for the first 2 months and subsequently at 2-3 month intervals. Liver and renal function tests were done at 3 and 6 months respectively after the initial monthly tests for first 3 months. Liver biopsy was done annually and graded into 4 grades[5] : Grade I, normal, mild fatty infiltration, mild nuclear variability, mild inflammation; Grade II, moderate-severe nuclear variability, moderate-severe portal tract expansion, portal inflammation and focal necrosis; Grade III, portal fibrosis (septum formation); and Grade IV, cirrhosis.

All patients were hospitalised for the initiation of therapy. Drug was administered in a single weekly oral dose of 5 mg and stepped up by 5 mg each week till the clearance of lesions started. The optimum dose was maintained till there was 90-95% clearance. The parameters used for therapeutic response were clinical, such as degree of erythema,scaling and infiltration graded as + to +++. The dose of methotrexate was gradually reduced by 2.5 to 5 mg/month to a maintenance level, when only 4-5 small lesions remained.

Results

Out of the 14 patients, 9 were males and 5 females. The age ranged from 18 to 56 years and the duration of disease varied from 4/12 to 20 years. Five patients had extensive erythroderma and 9 had extensive disease in whom psoriasis was estimated to cover nearly 80% of the body surface area. The laboratory investigations carried out before methotrexate administration ranged between : haemoglobin 10.5-

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14.75 gm%, total leucocyte count 4600-10800/cmm, platelet count 1,50,000-2,60,000, SGOT/SGPT 9/10-23/10 IU, alkaline phosphatase 4-14 KA°, serum bilirubin 0.5-1.0 mg, blood urea 20-39 mg, serum creatinine 1-1.5 mg. All investigations were within normal limits. The risk factors present were diabetes mellitus in one patient, 6 patients were clinically obese and one was addicted to alcohol which he discontinued on starting methotrexate. The pre-MTX liver biopsies showed mild fatty change (grade I) in 2 patients, lipogranulomatous hepatitis (grade I) and idiopathic hepatitis (grade I) in one patient each, ann non-specific changes (grade I) in 5 patients. Two patients were excluded from the study due to unreliability of compliance on account of poor economic status, and chronic active hepatitis in one patient.

Only one patient required 35 mg of MTX for clearing, the optimum dose for the others varied between 20-30 mg weekly. The optimum time required for clearance varied from 3-20 weeks. The maintenance dose of MTX varied between 15-20 mg weekly.

The main side effects encountered were nausea, vomiting, and mild to moderate headache experienced by 7 patients each on the day of MTX administration. Three patients each experienced pain in the abdomen, diffuse alopecia, loss of appetite and giddiness. Two patients had loose motions and another 2 had ulceration of the mouth and glossitis. One patient had bleeding from gums and a female patient developed endogenous depression, probably unrelated. Three patients developed hyperpigmentation over the exposed areas of body. Three male patients had no side effects. During a follow up of 3 years, the drug did not have to be discontinued in any patient due to side effects. Weekly intramuscular administration was temporarily started in one female patient due to intolerable nausea and vomiting. No treatment failures were noted.

The post-methotrexate laboratory investigations revealed the range of values as under : haemoglobin 11.2—14.10 gm%, total leucocyte count 4600—11,000/cmm, platelet count 1,50,000-2,40,000, SGOT/SGPT 4/7-23/12 IU, alkaline phosphatase 8-20 KA°, serum bilirubin 0.5-0.6 mg, serum creatinine 1.0-1.7 mg. None of the laboratory parameters were found to be abnormal. From typed manuscript, the post-methotrexate liver changes did not exceed grade I-II in any patient.

One-yearly post-MTX biopsy done in 8 patients showed, mild fatty change (grade I) in 2 patients, granulomatous hepatitis (grade I) and lipogranulomatous hepatitis (grade I) in one patient each, doubtful fibrosis (grade II) in one patient and non-specific reactive hepatitis (grade I) in 3 patients. In 2 patients liver biopsies done at the end of 2nd and 3rd year also showed mild fatty change (grade I) and non-specific hepatitis (grade I) respectively.

Out of 14 patients included in the study 3 were lost to follow up. All the patients had experienced more than 75% clearance and it is being maintained on the maintenance dose in all of them.

Comments

Methotrexate acts by inhibiting the enzyme dihydrofolate reductase and blocking the synthesis of thymidylate, one of the four precursors of DNA, thereby arresting the cell division. Besides the direct action on the rapidly proliferative epidermal cells,[6,7] methotrexate depresses the motility of neutrophils in chamber membranes, but does not interfere with the random motility in tubes.[8] The near absolute contra-indications for methotrexate therapy are, significant hepatic and renal damage, pregnancy, fibrosis or cirrhosis of liver, severe anemia, leucopenia, thrombocytopenia, active peptic ulcer, excessive alcohol intake, acute infectious diseases and an unreliable patient. A relative contra-indication in both sexes is the fertile period of life.

Continuing evaluation for haematologic, renal and hepatic parameters is essential because bone marrow depression, nephro and hepatotoxicity are serious complications. The liver biopsy is required to be repeated annually.[9]

Methotrexate should be avoided in grade III and IV damage, while its administration can be continued with grade I and II changes where the damage is reversible. Post-methotrexate studies did not warrant discontinuation of methotrexate therapy in any of our patients. The weekly oral schedule seems to be the best for MTX administration.

Conflicting views of MTX induced hepatic injury have been reported.[9,10-13] No significant fibrosis or cirrhosis was found in the post-MTX liver biopsies in studies reported by the International Co-operative Group.[14] The cumulative dosage of methotrexate should be calculated after every six months and liver biopsies performed annually or when the cumulative dose exceeds 1.5 gm. Liver function tests alone are not a reliable indicator of methotrexate induced hepatic fibrosis/cirrhosis.

Our study indicates that methotrexate is effective and safe for the treatment of intractable, crippling and severe psoriasis, not responding to conventional therapy. The goal should not necessarily be total clearing, but achievement of adequate control at the lowest possible MTX dosage.

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