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Subcutaneous administration of methotrexate

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Two recent reports indicate that subcutaneous administration of methotrexate (MTX) has certain advantages over the oral and intramuscular routes.

Balis et al.[1] evaluated subcutaneous versus oral MTX in 12 children with leukemia. At a dosage of 7.5 mg/m^2 peak plasma concentrations for subcutaneous and oral administration were approximately equal. However, at a dosage of 40 mg/m^2, subcutaneous injections yielded a considerably higher peak plasma concentration. Peak MTX concentration and area under the time versus concentration curve (AUC) were four and three times higher, respectively, with the subcutaneous as compared with the oral route. The injections were well tolerated and there was no local toxicity.

Brooks et al.[2] compared the pharmacokinetics of MTX in doses up to 25 mg given by the intramuscular and subcutaneous routes in five patients with rheumatoid arthritis. Serum peak concentration values, time to peak concentration, and the AUC were not significantly different. The intramuscular and subcutaneous routes appeared to be interchangeable. Subcutaneous injections were well tolerated and less painful than intramuscular ones.

We have treated 10 patients (seven with psoriasis and three with cutaneous T-cell lymphoma [CTCL]) with subcutaneous MTX. The injections were given in the outer arm with a 25-gauge, ⅝ inch needle. Nine patients received once-weekly injections and one received them on alternate weeks. Doses of 5 mg to 87.5 mg were given for periods of 3 to 17 weeks (median 13 weeks). Six patients had previously received MTX by intramuscular administration.

All patients had a favorable clinical response to the subcutaneous injections and these appeared to be similar to those after intramuscular administration. Two patients with psoriasis experienced an increase in the serum AST level and one had a mild leukopenia. One patient with CTCL had oral mucositis. However, one patient with psoriasis stated that, although she invariably had nausea after intramuscular MTX, she had none after subcutaneous administration. The injections were well tolerated, less painful, and easier to administer than when given intramuscularly. There was no local reaction. When doses more than 50 mg were required, two injection sites were used with no greater than 50 mg (2 ml) at each site.

Subcutaneous injections can be self-administered. This can be of considerable value for patients who require parenteral administration and have difficulty in making weekly office visits. Patients should be instructed to use only 1 ml syringes so that gross errors in dosage are less likely to occur. Thus doses greater than 25 mg require the use of at least two syringes.

The cost of injectable MTX is considerably less than the tablets. In a survey of pharmacies in the San Francisco-Bay area the average cost of a 2.5 mg tablet (Lederle) was $2.87 (range $2.32 to $3.42). On the basis of the Lederle 2 ml 50 mg vial (liquid preservative protected), the average equivalent cost of 2.5 mg (0.1 ml) was $0.89 (range $0.65 to $1.24). Thus the cost of the liquid was approximately 50% to 20% that of the tablet. The injectable form is also available as a 10 ml (250 mg) vial (Lederle), which is about half as expensive per milligram as the 2 ml vial. However, this usually needs to be obtained through a hospital or clinic-based pharmacy. In addition, there are competing brands of injectable MTX. The need for syringes and needles adds to the cost of injectable MTX.

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REFERENCES

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