

LETTER TO THE EDITOR

Methotrexate Therapy for Psoriasis in Elderly Patients with Impaired Renal Function

Methotrexate is still a valuable drug in selected cases of recalcitrant psoriasis. The risk of side effects, especially liver damage (4), demands a careful medication and continuous laboratory monitoring of the patients. As methotrexate (MTX) is excreted mainly by the kidneys (1), an optimal drug dosage should take the renal function into consideration. It is a well-known fact that serum creatinine is a poor indicator of renal function which should be determined as endogenous creatinine clearance (Cl_{creat}) or as ^{51}Cr -EDTA clearance. For a rapid bedside evaluation a practical nomogram based on sex, weight, age, and serum creatinine is available (2).

In a pharmacokinetic study on MTX, using 3H -labelled MTX (5), we demonstrated a significant inverse relation between the renal function, measured as Cl_{creat} , and the early serum disappearance of MTX, expressed as serum MTX half-life ($MTX-T_{1/2}$), following intravenous administration:

$$\log MTX-T_{1/2} \text{ min} = -0.601 \times \log Cl_{creat} \text{ ml/min} + 3.361$$

In the treatment of psoriasis, MTX is usually given orally once a week at 12 h intervals for a total of three partial doses (3). The purpose is to maintain a therapeutical MTX concentration for about 37 h, which is the estimated life cycle time of psoriatic epidermic cells (3). This triple dose schedule, however, does not allow for differences in the patients' renal function, for example due to age (2). As seen from the equation, this means that patients with an impaired renal function, including all elderly patients, tend to accumulate the drug and have prolonged high serum levels beyond the intended 37 h, if the partial doses are not reduced appropriately. It should be noted that blood levels following small MTX doses routinely used in clinical practice are similar, whether the administration is by oral or intravenous route (1). In order to deal with this basic problem, it might be advantageous to introduce different intervals between the partial doses which would be correlated to the patients' renal function, for example about four times the $MTX-T_{1/2}$ in hours. This value can easily be calcu-

lated from the equation given above, when the patient's Cl_{creat} is known. For practical clinical use, this modification would imply three partial doses (each of about 50 $\mu g/kg$ body weight, for example) at 12 h intervals to patients having a Cl_{creat} above 60 ml/min; and two partial doses with a 16 h interval to those with a Cl_{creat} between 40 and 60 ml/min. Patients with a Cl_{creat} of 20-40 ml/min should receive only a single partial dose, if ever given MTX at all. In the case of rapidly changing renal function, MTX should of course never be used.

By this procedure, patients with psoriasis and receiving MTX in fractionated doses once a week tend to achieve identical mean MTX serum levels during therapy. Furthermore, the cumulative dose of MTX, a factor which is correlated significantly with late side effects (4), is thus reduced in patients with impaired renal function, as generally seen in the elderly.

The dose schedule does not deal with the prolonged MTX elimination from serum at very small serum concentrations, occurring 10 to 20 h after ingestion (5). The significance of this phenomenon is still uncertain.

References

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K. Weismann, M.D.
Department of Dermatology
Rigshospitalet
DK-2100 Copenhagen
Denmark

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