Acute Renal Failure after High-Dose Methotrexate Therapy

Role of Hemodialysis and Plasma Exchange in Methotrexate Removal

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Dear Sir,

High-dose regimens of methotrexate (MTX) are currently used in osteogenic sarcoma [1]. The major complications of this treatment are myelosuppression, mucositis and impairment of renal function [2]. Measures designed to accelerate MTX removal have not been carefully evaluated in man as yet. We wish to report the results of our attempts to remove MTX using hemodialysis and plasma exchange.

A 34-year-old man, with osteogenic sarcoma of the humeral head, received a first infusion of 8 g ($17.6 \cdot 10^{-3}$ M) of MTX for 4 h (4 g/m² body surface area). Renal

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Fig. 1. MTX plasma concentration versus time (A = dialysis session). Theoretical volume of distribution: 1,827 liters; area under the curve: 462 days; total clearance: 27 ml/min.

function was normal before treatment. Despite early administration of leucovorin (300 mg/day) and vigorous hydration, the patient developed acute anuric renal failure in 24 h. 2 g ($4.4 \cdot 10^{-3}$ M) of MTX were excreted during this time. On admission to the intensive care unit, serum creatinine was 4 mg/dl and plasma MTX $55 \cdot 10^{-6}$ M. Since the patient was anuric 12 hemodialysis sessions were performed for 15 days after MTX infusion (dialysis duration 6–12 h; dialyzer 1.2 m²; blood flow 300 ml/min). In an attempt to remove MTX bound to proteins, a plasma exchange was performed between the 4th and 5th dialysis sessions (plasma filtration, exchange of 60 ml/kg body weight against 4% human albumin).

Serum MTX levels [3] were measured before and after plasma exchange and dialysis, in dialysate every 2 h, in arterial and venous lines during dialysis, and in plasma exchanged. The clearance of MTX through hemodialysis was 38 ml/min. Less than 10% of the initial dose (0.7 g or 1.5 10^{-3} M) was removed during the 12 dialysis, half of which was extracted during the first session. Only 0.007 g (1.5 10^{-5} M) of MTX were removed by plasma exchange. The plasma concentration versus time is shown in figure 1.

Our present report shows that MTX is poorly cleared by hemodialysis. However, the clearance through hemodialysis is greater than through peritoneal dialysis [4]. Plasma exchange is unable to remove MTX because of the great volume of distribution and poor binding to serum albumin (60%) [2]. Removal of MTX by filtration-adsorption using charcoal filters has been proposed [5], but this procedure exposed potentially aplastic patients to thrombopenia.

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In conclusion, hemodialysis seems to be the best procedure for MTX removal in patients with acute renal failure needing dialysis. Greater efficiency could be expected if hemodialysis is initiated early after MTX infusion, before distribution of MTX in tissues. 4

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