Tinidazole Pharmacokinetics in Severe Renal Failure

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Summary

The single-dose pharmacokinetics of intravenously and orally administered tinidazole were studied in normal subjects and patients with severe chronic renal failure. The clearance of tinidazole was also measured in patients on regular haemodialysis.

After intravenous administration the mean elimination half-life of tinidazole was 17.1 ± 2.3 (SD) hours in the normal subjects and 16.9 ± 4.9 hours in patients with renal failure; the mean apparent volumes of distribution were 0.80 ± 0.09 L/kg and 0.69 ± 0.09 L/kg, respectively. Following oral administration the mean elimination half-life was 15.6 ± 1.6 hours in the normal subjects and 18.4 ± 3.5 hours in patients with renal failure; there were no statistically significant differences in these pharmacokinetic parameters. There was no accumulation of the major metabolite (hydroxymethyl tinidazole) in normal subjects or in patients with renal failure. Tinidazole clearance during haemodialysis was 71 ± 7.7 ml/min.

In the presence of renal failure no modification of tinidazole dosage would appear to be necessary. Tinidazole should be administered in full dosage following haemodialysis.

Tinidazole is an imidazole derivative structurally similar to metronidazole, miconazole and clotrimazole. It has been shown to be an effective agent for the treatment of trichomoniasis, giardiasis, amoebiasis and anaerobic infections (Sawyer et al., 1976). Tinidazole could be useful for treating anaerobic infections in patients with impaired renal function. In this study the single-dose pharmacokinetics of tinidazole were studied in patients with severe chronic renal failure, both on and off haemodialysis, and compared with healthy volunteers.

Methods

Patients

Three groups of patients were included in this study:

Group 1: Healthy volunteers
Group 2: Patients with severe chronic renal failure (creatinine clearance ≤ 22 ml/min) not on dialysis
Group 3: Patients with end-stage renal failure on regular haemodialysis treatment.

The patients and volunteers were aged 20 to 70
years and weighed 40 to 90kg. Patients were excluded from the study if they were pregnant, had a malignant disease, diabetes mellitus, liver disease, or if they had taken any medication in the previous 2 weeks other than those drugs routinely prescribed in renal failure. Approval for this study was given by the Ethical Committee of the North Canterbury Hospital Board. Informed consent was obtained from each patient.

Procedure

1. Three healthy male volunteers and 9 patients (5 men, 4 women) in Group 2 received 800mg of tinidazole dissolved in 400ml of dextrose monohydrate solution, and administered as a constant intravenous infusion at a rate of 60 mg/min. Blood samples were obtained for analysis before and at the end of the infusion, and 1, 3, 6, 12, 24 and 48 hours following the infusion.

2. Three healthy male volunteers and 4 patients (2 men, 2 women) in Group 3 were administered a 2g oral dose of tinidazole. All subjects were fasting and were studied during a 48-hour period between 2 haemodialysis treatments. Blood samples were taken before and at 2, 3, 6, 12, 24 and 48 hours after ingestion.

3. Four patients (2 men, 2 women) in Group 3