References


Mexiletine clearance during peritoneal dialysis

The pharmacokinetics of mexiletine in patients undergoing peritoneal dialysis have been the subject of only one case report (Jones et al., 1983). The effect of haemodialysis on mexiletine pharmacokinetics is unknown. Renal impairment itself has little effect on the pharmacokinetics of mexiletine until the creatinine clearance is reduced to less than 10 ml/min, at which point the total body clearance is slightly reduced from the 6–13 ml min⁻¹ kg⁻¹ noted in normal volunteers and patients with normal renal function (Haselbarth et al., 1981; Campbell et al., 1978) to 2.4–9.9 ml min⁻¹ kg⁻¹ (El Allaf et al., 1982). A patient requiring mexiletine therapy while admitted to the intensive care unit provided the opportunity to assess the peritoneal clearance of mexiletine.

A 70 year old Caucasian male with a past history of congestive cardiomyopathy, mitral regurgitation, hypertension, repeated bouts of peritonitis, and chronic renal failure treated with continuous ambulatory peritoneal dialysis (CAPD) was admitted from the ward into the intensive care unit after resuscitation from a cardiopulmonary arrest. The arrest was thought to be secondary to myocardial ischaemia and the hypotension secondary to sublingual nitroglycerin use. The course was complicated by congestive heart failure characterized by very high pulmonary capillary wedge pressures (30–40 mm Hg) and exquisite sensitivity to vasodilator therapy. As well, multifocal premature ventricular contractions (PVC) developed which were treated with lignocaine. Dialysis therapy consisted of 6 hourly 2 l exchanges with 1.5 and 4.25% dextrose solutions (Dianead, Baxter-Travenol). The number of exchanges of a given dextrose concentration instilled daily depended on the patient's fluid status. There was no evidence of peritonitis. As PVC continued after tapering off the lignocaine infusion, it was decided to commence long-term mexiletine therapy. Coincident with the beginning of a dialysate instillation, 200 mg of mexiletine (Boehringer-Ingelheim) was given orally. Serial serum samples were collected over the 8 h dosing interval. Urine was not produced over this period of time. Dialysate was collected over the 6 h
interval after dosing. Mexiletine was continued in a regimen of 200 mg every 8 h. In addition, dialysate was collected 6 days into therapy in order to assess steady-state dialysis drug recovery. Steady-state serum drug levels were also drawn at this time. Biological samples were analyzed for mexiletine content using a modification of the gas chromatographic method of Smith & Meffin (1980). Clearance data and amount cleared by CAPD at steady state were calculated using standard methods (Gibaldi & Perrier, 1982).

Calculated clearances (total body, dialysis, and renal) and amount cleared daily by CAPD at steady state are presented in Table 1. Samples of dialysate from this patient prior to receiving the drug demonstrated no assay interferences. The results indicate that peritoneal dialysis removes very little mexiletine. The total body clearance was similar to that reported previously in renal failure patients (Jones et al., 1983; El Allaf et al., 1982). It must be recognized that this is an apparent total body clearance since the fraction absorbed had to be estimated (88%). The minimal amount of drug removed daily by CAPD as noted by Jones et al. (1983) (5 mg) was similarly noted in our patient (17 mg).

At present, we believe that the dosage of mexiletine in a patient on peritoneal dialysis does not have to be routinely altered from that recommended for patients with severe renal impairment not on such dialysis. In most cases, this dosage regimen will be similar to that used in patients with normal renal function, although individualized dosage adjustment based upon serum concentration determinations and clinical response should be routinely performed.

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References


Effect of ranitidine on procainamide disposition

In a recent volume of the Journal, Somogyi & Bochner (1984) have provided evidence that ranitidine reduces the renal clearance of procainamide (PA) and that of its major metabolite N-acetylprocainamide (NAPA). Evidence to support their contention that ranitidine also reduces the absorption of procainamide is much less convincing.

Their evidence is based on the consideration that if all factors other than renal clearance of

Table 1 Pharmacokinetics of mexiletine in case subject

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>Total body clearance (CL)</td>
<td>4.39 ml min⁻¹ kg⁻¹</td>
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<tr>
<td>Renal clearance</td>
<td></td>
</tr>
<tr>
<td>Peritoneal dialysis (PD) clearance</td>
<td>0.13 ml min⁻¹ kg⁻¹ (3.0% of CL)</td>
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<tr>
<td>Amount cleared daily by PD at steady state</td>
<td>17.0 mg/day (2.8% of daily dose)</td>
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*No urine production during study period