Mezlocillin Pharmacokinetics in Renal Impairment

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ABSTRACT

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Mezlocillin is an acylureidopenicillin that is active against clinically important bacteria. Although some investigators have evaluated mezlocillin elimination with compartmental linear kinetics, studies in animals and man suggest that mezlocillin excretion follows nonlinear dose dependency. Such behavior may complicate dosimetry in patients with renal insufficiency.

To establish mezlocillin kinetics in patients with renal impairment, we gave 27 adult subjects with various levels of renal function mezlocillin, 3 gm, over 30 minutes. A significant relationship between the rate of mezlocillin elimination and renal function was observed. The elimination half-life increased from 0.96 hours in normal subjects to 3.60 hours in anuric patients. Similarly, the area under the plasma concentration versus time curve increased from 243 mg-hr/l to 728 mg-hr/l. This relationship was used to establish dosage guidelines. In addition, graphical non-linearity of the plasma concentrations was observered in patients with impaired renal function.

To determine the effects of dose on the elimination kinetics of mezlocillin, six subjects with normal renal function and six anuric subjects were given mezlocillin in

1, 3, and 5 gm doses by intravenous bolus injection. Each dose was separated by one week. Although the rate of elimination was not prolonged by increasing the dose in patients with normal renal function, the half-life increased from 1.67 hours after the 1 gm dose to 2.25 hours after the 5 gm dose in anuric patients. This study shows that mezlocillin elimination is dose dependent in anuric patients, and that the capacity limited process involves the non-renal elimination of the drug.