ıfficiency on the pharmacokinetics of cyclophosphamide and some of its metabolites.

Juma, F.D; Rogers, H.J; Trounce, J.R

Abstract:

Cyclophosphamide pharmacokinetics were studied in seven patients with moderate to severe renal insufficiency (creatinine clearances 0-51 ml . min-1), and compared with a matched control group of patients with normal renal function. The mean half-life of cyclophosphamide following intravenous administration in the normal group was 8.21 +/- 2.33 (SD) h whilst that in renal failure was 10.15 +/- 1.80 h: these were significantly different. The total body clearance in the normal control group was 58.6 +/- 10.9 ml . kg-1h-1 which was significantly larger than in renal failure where it was 48.8 +/- 10.9 ml . kg-1h-1. Vd beta, Vdss and Vc were not significantly different between the two groups. A linear relationship exists between beta, the first order disposition rate constant and endogenous creatinine clearance since this drug shows a relatively small degree of compartmentalisation. The plasma half-life of phosphoramide mustard, a cytotoxic metabolite of cyclophosphamide, shows a parallel and significant increase in renal failure with the parent compound. The t1/2 in normal patients was 8.33 +/- 2.0 h, whilst in the renal failure group it was 13.37 +/- 4.23 h. Total alkylating activity as measured by the nitrobenzyl-pyridine reaction showed a significant increase in renal failure. This data suggests that in pharmacokinetic terms it may not be necessary to alter the dose of cyclophosphamide until there is severe renal impairment. Further studies correlating the efficacy and toxicity of the drug with its pharmacokinetics in renal failure are necessary.