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Digoxin dosage in patients with impaired kidney function

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Based on the so-called 'intact nephron hypothesis' (Bricker, Morrin & Kime, 1960) a linear relationship between the endogenous creatinine clearance (V_{Cr}) and the overall elimination rate constant (k_e) of many drugs can be demonstrated: $k_e = k_m + a \cdot V_{Cr}$.

In order to find the appropriate individual dose schedule of digoxin for patients with impaired kidney function, we tested this hypothesis.

Thirty-one patients with different degrees of kidney impairment (endogenous creatinine clearance ranged from 0 to 100 ml/min) were given 0·25–0·5 mg tritium labelled digoxin intravenously. The volume of distribution, the 'overall' (k_e), the renal (k_r) and extrarenal (k_m) rate constant for elimination of digoxin were determined from measurements in the plasma and in the urine. At the same time endogenous creatinine clearance (V_{Cr}) was estimated.

According to the equation $k_e = k_m + a \cdot V_{Cr}$ a linear correlation between the elimination constant and the endogenous creatinine clearance was found using the method of 'the least squares of errors'. For digoxin the following equation was calculated: $k_e = 0{\cdot}00593 + 0{\cdot}00013 \cdot V_{Cr}$; $r = 0{\cdot}91$; $S_{y/x} = \pm 0{\cdot}0019$; $P < 0{\cdot}001$. The k_e obtained from the different measurements ranged from 0·004 h^{-1} in the anurics to 0·0196 h^{-1} in normals or from 173·3 h to 35·4 h half-life respectively. The rate constant in the urine was not significantly different from the constant obtained in the plasma.

Based on this quantitative relationship between digoxin elimination and a simple clinical routine test of kidney function the individual dose schedule for patients with kidney impairment can be calculated. For practical clinical purposes, a 'bedside method' described by Dettli, Spring & Habersang (1970) is also suitable for determining the dose of digoxin.

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Plasma digoxin concentrations in children in heart failure

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Digoxin dose schedules used in paediatric units in England vary widely. We have