Influence of betamethasone on concentrations of digoxin in rat serum, liver and heart

P. ATKINSON & J. JACKSON
(introduced by W. C. BOWMAN)

Pharmacia Diagnostics, Hounslow, Middlesex, and Department of Physiology and Pharmacology, University of Strathclyde, Glasgow

It has been demonstrated (Atkinson & Jackson, 1979) that methyl prednisolone can elevate concentrations of digoxin in rat serum and heart. In these experiments bethamethasone, another synthetic glucocorticoid, was administered together with digoxin. The digoxin concentration in the liver was assayed together with the serum and the heart by R.I.A.

Male Sprague-Dawley rats (200 g) were given an intra-muscular injection of digoxin (5 μg) and either betamethasone or saline (the solvent vehicle for betamethasone). After 1 h the animals were killed by a blow on the head and exsanguinated. The blood was centrifuged and the serum was assayed for digoxin. The hearts and livers were dissected out. The organs were sliced and washed three times in Krebs' solution, so that serum would be removed. The organs were then macerated, digoxin was extracted three times with chloroform. The chloroform for each group was pooled and evaporated to dryness. The digoxin was re-dissolved in 6 ml of rat serum, which contained no digoxin. Serial dilutions of this serum were made, so that the assay value would fall on the standard curve.

There were six animals in each treatment group.

The digoxin values for serum, liver and heart are expressed in nM/l and are shown on Table 1.

These results show that betamethasone elevated concentrations of digoxin in rat serum and heart. Betamethasone also lowered concentrations of digoxin in rat liver. This may have been because of competition at non-specific binding sites. This competition may have resulted in the elevated serum concentrations, which would have in turn elevated the concentration in the heart. This study involved serum concentrations greatly in excess of those found in humans undergoing digoxin therapy. The concentrations of betamethasone were also well above those used in therapeutics. This probably means that this interaction would not normally cause problems in patients receiving digoxin (Doherty, 1973).

Table 1 Digoxin concentrations in rats treated with betamethasone

Dose of Betamethasone (mg)	*Concentration of digoxin* (nM/l) ($n = 6$)		
	Serum ± *s.d.*	*Heart*	*Liver*
0	12.1 ± 0.8	5.1	72.3
0.1	12.3 ± 0.9	7.2	63.4
0.5	13.3 ± 1.3	11.2	42.7
1.0	14.6 ± 2.0	16.5	35.4
5.0	15.7 ± 3.2	22.7	36.2

References

ATKINSON, P. & JACKSON, J. (1979). Elevation of serum and heart digoxin levels in rat by methyl prednisolone. *J. Pharm. Pharmac.* (in press).

DOHERTY, J.E. (1973). Digitalis glycosides: Pharmacokinetics and their clinical implications. *Ann. Intern. Med.* **79**, 229–238.

Comparison of individual and cumulative dose-response curves

A. DUNNE (introduced by P.J. CANNON)

Department of Pharmacology, University College Dublin, Belfield, Dublin, 4

The individual dose (I.D.) and cumulative dose (C.D.) techniques for determination of the dose-response curve for histamine on guinea pig ileum are compared. The C.D. determinations were made with 15 s, 30 s and 45 s between doses. Each of four strips of ileum was exposed to all four methods (three C.D. and one I.D.) in a 4 × 4 Latin square arrangement. The resulting sixteen dose-response curves were fitted singly to the equation

$$y = \alpha.\left[1 - \left(1 + \left(\frac{x}{\gamma}\right)^{\beta}\right)^{-1}\right]$$

where

- y = response in arbitrary units.
- x = concentration of histamine in organ bath (0.3 μM to 80 μM).
- α = response at infinite dose.
- β = exponent or 'slope factor'.
- γ = dose corresponding to 50% of the response at infinite dose.