Digoxin-Like Immunoreactive Substance in Renal Failure

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Table 1. Characteristics of patients and controls

Table 2. Correlation of serum digoxin and digitoxin levels with urea, Cr, Ccr, blood pressure, heart failure and edema

analysis by RIA (kit: Coat-A-Count Diagnostic Products Corporation, Los Angeles, Calif., USA). Student's *t*-test and Pearson correlation were used for statistical evaluation.

Table 1 shows the characteristics of patients and controls. There was no significant difference in the mean serum digoxin level between the patients and healthy controls, but the mean serum digitoxin values were found

Dear Sir,

The cardiac glycosides digoxin and digi-toxin are important drugs in the management of heart failure and arrhythmias, and can be measured by radioimmunoassay (RIA) in serum and urine. It is known that cardiac glycosides have a high toxicity and narrow therapeutic ranges (usually 0.8-2.0 ng/ml) [1]. It has recently been reported that detectable levels of digoxin-like immunoreactive substance (DLIS) are found in third trimester pregnant women, neonates, patients with liver disease, patients with acute and chronic renal failure, hemodialysis patients and normal subjects [2-7]. These studies show that monitoring cardiac glycoside concentrations in serum is an important and useful measurement in patients with renal failure. We measured DLIS in the serum of renal failure patients and normal subjects.

Patients, Methods and Results

Serum samples were obtained from 51 patients (23 males, 28 females) and from 25 healthy controls (13 males, 12 females). None of the patients or controls were receiving any cardiac glycosides. Patients had various ne-phropathies: essential hypertension 38 cases; chronic glomerulonephritis 4 cases; chronic tubulointerstitial nephropathy 5 cases; diabetic nephropathy 3 cases, and amyloidosis 1 case. We assessed hematocrit, white blood cell, sedimentation, blood urea nitrogen, serum creatinine (Cr) and creatinine clearance (Ccr) in patients and healthy controls. We recorded whether patients had heart failure or not. Blood samples were stored at -20°C until

Urea, mg/dl Cr, mg/dl Ccr, ml/min Systolic blood

pressure, mm Hg Diastolic blood

pressure, mm Hg

0.3847 $p < 0.01$ 0.2010 $p > 0.05$

0.3620 $p < 0.01$ 0.1853 $p > 0.05$

-0.3167 $p < 0.05$ -0.4525 $p > 0.01$

0.2802 $p < 0.05$ 0.2104 $p > 0.05$

0.2444 $p < 0.05$ 0.1966 $p > 0.05$

Edema and heart failure 0.2275 $p < 0.05$ 0.0877 $p > 0.05$

to be significantly higher in the patients than those in the healthy controls (table 2).

Heart failure and edema were detected in 17 patients. Six patients had a Ccr of under 20 ml/min, and the remaining patients more than 50 ml/min. In patients digoxin correlated directly with blood pressure, urea, Cr and edema, and digoxin and digitoxin correlated inversely with Ccr (table 2).

Discussion

DLIS, causing falsely raised plasma di-goxin concentrations, has been reported in pregnant women, neonates, patients with liver disease and patients with acute and chronic renal failure (2-7). Our study shows that DLIS correlated directly with blood pressure, urea, Cr and inversely with Ccr. DLIS is believed to be water-soluble and heat-stable, with a molecular weight of less

than 1,000 daltons. DLIS is present in serum and carried in plasma by albumin [2]. Some authors reported that DLIS represents a volume-sensitive factor like atrial natriuretic factor [8-10]. However, the exact structure and physiological importance of DLIS is still unknown. Cardiovascular disease often affects patients with renal failure and leads to mortality in these patients. The presence of DLIS in this population may pose serious problems in interpreting the plasma digoxin concentrations [11]. Our observations indicate that digoxin pharmacokinetics are altered minimally in renal failure patients.

In conclusion, we found high plasma levels of DLIS in patients with edema, hypertension and lower Ccr. Therefore DLIS was considered as a volume-sensitive factor.

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