Hemodynamic Effects of Digoxin on Congestive Heart Failure

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To assess the hemodynamic effects of digoxin (0.01 mg/kg) on congestive heart failure, we evaluated 19 patients with decreased contraction force of left ventricle (old myocardial infarction n = 9, and dilated cardiomyopathy n = 10, group 1) and 8 patients with mechanical impaired left ventricular filling (mitral stenosis n = 8, group 2). In groups 1 and 2, heart rate and pulmonary capillary pressure significantly decreased (p < 0.05). In group 1, stroke volume increased, but not significantly. In group 2, stroke volume increased significantly (p < 0.05). There were no significant changes in blood pressure and systemic vascular resistance in either group. We divided group 1 into two groups (group 1A: cardiac index increased more than 15%, group 1B: cardiac index increased less than 15%). In group 1A, cardiac index and % fractional shortening before digoxin administration were lower than in group 1B (1.97 ± 0.27 vs. 2.80 ± 0.481/min/m^2, p < 0.001, and 10.9 ± 8.0 vs. 19.5 ± 11.9%, p < 0.05, respectively). These data suggested that digoxin exerted a positive inotropic effect with decreased pulmonary capillary pressure, but cardiac index did not always increase in congestive heart failure.

DIGITALIS glycosides have been advocated as the basic inotropic agents for congestive heart failure, but their mechanisms were not clarified. The hemodynamic responses in cardiac index varied. Cardiac index after digitalization in some studies was unchanged, and in some it decreased or increased. Pulmonary capillary pressure decreased with improvement of pulmonary congestion. This study was designed to investigate the mechanism of digitalis through hemodynamic assessment in various heart diseases.

MATERIALS AND METHODS

27 patients with congestive heart failure of NYHA functional class 2–4 were studied. Group 1 consisted of 19 patients with old myocardial infarction (n = 9) and dilated cardiomyopathy (n = 10). Group 2 consisted of 8 patients with mitral stenosis. Atrial fibrillation was present in one DCM and all MS cases. None of the 27 patients had been given digitalis before.

Before the study, echocardiographic parameters such as left ventricular end-diastolic dimension (LVDd), left ventricular end-systolic dimension (LVDs) and fractional shortening (%FS) were measured. A Swan Ganz thermodilution catheter was inserted via the cubital vein. Cardiac output was measured in triplicate by thermodilution catheter. The following calculations were used: mean BP (1/3 pulse pressure + diastolic BP mmHg), stroke volume index (CI/HR ml/m^2), stroke volume-work index (SI × (SBP–PCP) × 0.0136 gmm/m^2), systemic vascular resistance (mean BP × 80/CO dynes-sec-cm^-5). After control hemodynamic measurements were obtained, digoxin 0.01 mg/kg was administered intravenously for 10 min and hemodynamic measurements were carried out at 2 and 24 hours. Values are expressed as mean and standard deviation. Statistical analysis was performed using Student’s t-test.

Key Words:
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RESULTS

In group 1, heart rate decreased significantly at 2 hours from 98.2 ± 18.8 to 85.3 ± 12.3 beats/min and at 24 hours to 85.2 ± 15.8 beats/min. In group 2, heart rate decreased significantly at 2 hours from 99.9 ± 24.7 to 80.4 ± 21.0 beats/min and at 24 hours to 84.3 ± 19 beats/min (Fig. 1). In group 1, pulmonary capillary pressure decreased significantly at 2 hours from 24.3 ± 6.1 to 18.2 ± 4.6 mmHg and at 24 hours to 16.2 ± 4.7 mmHg. In group 2, pulmonary capillary pressure decreased significantly at 2 hours from 20.9 ± 4.5 to 16.5 ± 5.6 mmHg and at 24 hours to 16.6 ± 4.8 mmHg (Fig. 2). Cardiac index showed no significant change in either group (Fig. 3). No significant change in BP and SVR were found in either group. In group 2, stroke volume index were increased significantly at 2 hours from 24.0 ± 8.9 to 29.2 ± 11.8 ml/min/m² and at 24 hours to 28.7 ± 6.9 ml/min/m². In group 1, no significant change in stroke volume was found. Therefore, we divided group 1 into two subgroups. Group 1A consisted of 7 patients in whom CI increased by 15% or more at 2 hours and group 1B consisted of 12 patients in whom CI increased by less than 15% at 2 hours. LVDe and LVDs did not change significantly in either group. %FS before digoxin administration was significantly lower in group 1A than in group 1B (Fig. 4) (10.9 ± 8.0 vs 19.5 ± 11.9%, p < 0.05). CI before digoxin administration was lower in group 1A than in group 1B (1.97 ± 0.27 vs 2.80 ± 0.48 L/min/m², p < 0.001). After digoxin, CI increased to 2.46 ± 0.8 L/min/m² in group 1A and slightly decreased to 2.52 ± 0.42 L/min/m² in group 1B. PCP levels decreased in
Fig. 3. Comparison of cardiac index in group 1 and group 2 at control state, 2 hours and 24 hours after digoxin administration.

Fig. 4. Comparison of echocardiographic parameters in group IA (CI more than 15% in group 1), group IB (CI less than 15% in group 1) and group 2 at control state before digoxin administration.

Fig. 5. Hemodynamic response in cardiac index and pulmonary capillary pressure after digoxin administration (group IA: CI more than 15% in group 1, group IB: CI less than 15% in group 1).

both groups after administration of digoxin (Fig. 5). Serum digoxin concentration was determined by radioimmunoassay in all patients. At 24 hours, S.D.L. was at therapeutic levels (0.72 ± 0.35 ng/ml).

DISCUSSION

Cardiac index rose and pulmonary capillary pressure decreased after digoxin administration. These changes occurred due to an improvement of left ventricular performance. Our data suggested that pulmonary capillary pressure declined but cardiac index did not always rise. Selzer reported that in two-thirds of 132 patients, digoxin increased CI but in the remaining one-third, no beneficial effects were demonstrated. They could not detect any difference in the
response to digoxin administration. We demonstrated a cardiac index increase with LV dysfunction, namely at control state cardiac index was low and %FS was very low. On the other hand, in mild LV dysfunction cardiac index was higher and %FS was slightly lower. Left ventricular performance in congestive heart failure was determined by three major factors (preload, afterload and contractility). So with mild LV dysfunction, cardiac index was within normal limits. The improvement of congestive heart failure after digoxin was greatly influenced by preload. It was suggested that the vasoconstrictive effects of digoxin on the veins increased blood pooling in the portal venous system. Venous pooling lowered preload.

All mitral stenosis cases exhibited atrial fibrillation. Previous reports demonstrated slowing of heart rate and prolongation of AV node. Diastolic time was prolonged. Left ventricular filling improved after digoxin administration, and venous pooling may have been partially responsible.

Although the number of patients studied was small, the main effect of digoxin with severe LV dysfunction was inotropic action. But other effects were venous pooling and slowing heart rate. Thus clinical improvement was obtained by different mechanisms.

REFERENCES
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