Arterial Sodium Content in Experimental Congestive Heart Failure

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SUMMARY
This study sought to determine whether the electrolyte content of peripheral arteries is altered in experimental congestive heart failure (CHF) and whether such change, if present, would help to explain the abnormal vascular stiffness seen in human CHF. The concentrations of sodium (Na⁺) and potassium (K⁺) were determined in samples of aorta (Ao) and femoral arterial branches (FA) of 17 dogs. Six had ascites due to CHF produced by rapid ventricular pacing (left ventricular end-diastolic pressure [LVEDP] 26.2 mm Hg and maximal velocity of myocardial shortening [Vmax] 2.39 circumferences/sec). In the 11 animals in the control group pacing was stopped prior to the onset of CHF or the animals were not paced (LVEDP, 8.8 mm Hg and Vmax, 2.98 circumferences/sec). In CHF, mean Ao Na⁺ was 38.0 ± 2.3 mEq/100 g dry weight and FA Na⁺ was 44.2 ± 3.2 mEq/100 g. These were significantly higher than similar samples taken from the 11 normal dogs (Na⁺, 31.9 ± 1.6 [P < 0.05] and 31.9 ± 1.8 [P < 0.01] mEq/100 g, respectively). Although the water content tended to be higher and K⁺ tended to be lower in animals with CHF, these values were not significantly different from normal.

Additional Indexing Words:
Arterial electrolytes Vascular stiffness Ventricular pacing

A CHARACTERISTIC abnormality of the peripheral circulation recently reported in patients with congestive heart failure is a diminished dilator capacity of the resistance vessels.¹ Since this defect in the peripheral blood vessels improves after diuresis,¹ the possibility was considered that this abnormality was related to an excessive sodium and water content of the vasculature, which might alter the mechanical properties of the arterioles and not allow them to respond normally to dilator stimuli. To examine this hypothesis, in the present investigation it was decided to study the ionic composition of certain arterial segments of animals with experimentally induced chronic congestive heart failure.

Methods
Seventeen mongrel dogs weighing 26.1 to 46 pounds were studied. Congestive heart failure was induced in six animals by rapid ventricular stimulation by means of an implanted pacemaker at a fixed rate of 280 beats per minute over a period of 11 to 29 days.² After chronic pacing, these animals all had ascites, pleural effusions, peripheral edema, and ventricular diastolic gallops on auscultation. In the 11 animals which comprise the control group ventricular stimulation was stopped prior to the production of congestive heart failure or pacing was not carried out prior to the time of study; none had evidence of fluid accumulation. Both groups of animals were fed the same standard diet. The cardiocirculatory dynamics in both the animals with heart failure and the control group were studied in the intact animal under light sedation. The animals were sedated with morphine, 3 mg/kg, promazine, 1.5 mg/kg, and promethazine, 1.5 mg/kg, by intramuscular injection. The parameters of left
ventricular function were determined as reported in previous studies. Briefly, left ventricular pressure was obtained by percutaneous puncture. Instantaneous LV dp/dt was obtained continuously with an analog differentiating circuit.* Left ventricular transmural pressure was obtained by subtraction of the intrapleural pressure from the measured left ventricular pressure and was used in all calculations. All pressures were measured with Statham P23Db transducers and recorded with the electrocardiogram on a multi-channel oscillograph† at a paper speed of 100 mm/sec. Cardiac output was determined in duplicate by the dye-dilution technic. A rubber balloon mounted at the tip of a metal cannula was passed through the left carotid artery and placed in the ascending aorta just above the aortic valve. The balloon was rapidly inflated during diastole with 5 to 18 mm of saline by a power injector‡ triggered from the electrocardiogram. Myocardial wall tension and contractile element velocity were determined from isovolumic beats obtained during expiration as described previously. Following determination of left ventricular performance, the animals were sacrificed and samples of the aorta just above the bifurcation and tertiary branches of the femoral artery were rapidly excised. After removal of the adventitia, the samples were weighed and dried in a vacuum at room temperature to a constant weight. Water content was determined as the difference between wet weight and dry weight. The samples were then extracted with 0.1 normal nitric acid at room temperature for 1 week, and their sodium and potassium content was then determined by flame photometry. The extraction procedure and the chemical determinations were done simultaneously on all samples.

Results

The data relevant to the assessment of left ventricular function are presented in table 1. The 11 control animals were characterized by a mean left ventricular end-diastolic pressure (LVEDP) of 8.8 ± 1.1 (SEM) mm of mercury, cardiac output of 2.52 ± 0.26 L/min, and maximal velocity of contractile-element shortening (V_max) of 2.98 ± 0.21 circumferences/sec. In contrast, the six animals with congestive heart failure had mean left ventricular end-diastolic pressures of 26.2 ± 3.2 (P < 0.01), cardiac output of 2.61 ± 0.43 L/min (P > 0.5), and maximal velocity of contractile element shortening of 2.39 ± 0.11 circumferences/sec (P < 0.05).

The water content of the aorta and femoral arterial samples from the normal animals were respectively 69.2 ± 0.79 ml/100 g of tissue and 64.7 ± 0.66 ml/100 g. The values from animals with congestive heart failure were respectively 72.8 ± 1.94 ml/100 g (P > 0.5) and 66.4 ± 0.92 ml/100 g (P > 0.5). The potassium content of the arterial segments is shown in figure 1. There was no significant difference between the normal and the control animals when either the femoral artery or the aortic samples were examined. However, the sodium content of the sample of aorta for the animals with congestive heart failure was 38.0 ± 2.29 mEq/100 g and for the tertiary branches of the femoral artery, 44.2 ± 3.15 mEq/100 g. This was significantly elevated when compared with the normal values which were respectively 31.9 ± 1.55 mEq/100 g (P < 0.05) and 31.9 ± 1.83 mEq/100 g (P < 0.01) (fig. 2).

Discussion

The principal finding of this investigation is that the sodium content of peripheral arterial segments in experimental congestive heart failure was significantly elevated. This was true for the samples from both the aorta and the tertiary branches of femoral arteries. Although the water content of these samples tended to be higher and the potassium content

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†Model 350, Sanborn Co., Waltham, Massachusetts.
‡Cordis Power Injector, Cordis Corp., Miami, Florida.
in veloc of the myocardium in circumference per second.

tended to be lower with congestive heart failure, these differences were not significant. At least two possibilities emerge as explanations for the elevated arterial sodium content in congestive heart failure. First, this could be secondary to the general sodium retention characteristic of the heart failure state. Indeed, an elevated sodium content of ventricular myocardium has previously been described in congestive heart failure. Second and perhaps less likely, this elevated arterial sodium content could also represent the result of chronic stimulation of the sympathetic nervous system. Thus, it has been shown previously that when tension is elevated in isolated arterial segments by administration of catecholamines or angiotensin, there is a net uptake of sodium by the tissue.

The precise physiologic significance of the elevated arterial sodium content in congestive heart failure must remain speculative at this time. A number of important inferences can be made, however: First, since the arterial dilator capacity is reduced in patients with congestive heart failure and improved when the elevated total body sodium is lowered, it is likely that the increased arterial sodium content independently demonstrated in the present study in the animals with experimental congestive heart failure is intimately related to the increased vascular stiffness characteristic of patients in heart failure. Further credence can be given to this hypothesis by examining comparable studies of hypertension. Thus, it is well known that the arterial sodium content is elevated not only in human but in experimental hypertension as well. Furthermore, the reactive hyperemia blood flow response, a measure of the dilator capacity of the peripheral blood vessels, also is diminished in hypertension. Thus, as suggested by the observations herein, congestive heart failure appears to be another pathologic state in which diminished arterial dilator capacity and elevated arterial sodium content coexist. It is probable that this combination is not fortuitous and, indeed, the two abnormalities could be causally related.

Whatever the cause of the elevated arterial sodium content, the vascular stiffness appears to be one of the important compensatory mechanisms which allows patients with heart failure to distribute more effectively their limited cardiac output to organs with the greatest metabolic needs. An exaggerated generalized sympathetic vasoconstriction occurs in patients with heart failure at rest, which is intensified during exercise and affords a relatively greater partition of blood flow to the myocardium, brain, and exercising extremities from the nonexercising skeletal muscle and certain other organs such as the skin, kidney, and liver. Thus, the stimulus of metabolic vasodilation overrides the effects of sympathetic vasoconstriction in determining regional blood flow, as seen in the organs with high metabolic requirements. This
process termed “sympatholysis” often results in a hyperemia which may be excessive for the actual metabolic requirements of the tissue in normal subjects.\(^{29}\) Since the peripheral blood vessels in congestive heart failure dilate poorly in response to the accumulation of endogenous dilator metabolites, the excessive hyperemia which may occur in the vascular bed of active skeletal muscle is thus attenuated at least in part by the abnormal stiffness component. Therefore, this vascular stiffness abnormality thereby limits the distribution of the reduced cardiac output to exercising muscles and allows for more effective redistribution to other organs and maintenance of an adequate perfusion pressure.

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