948-51 Comparison of Sodium Depletion or Repletion Effects on Aldosterone and Sodium/Potassium Excretion Characteristics in Patients with Moderate to Severe Congestive Heart Failure, in the Absence of Diuretics

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Recent studies have demonstrated that aldosterone may have a role in congestive heart failure, independent of angiotensin II, and our group and others have demonstrated that urinary sodium/potassium (Na/K) excretion may be predictive of relative changes in aldosterone secretion, including the extent of compensation during ACE inhibitor therapy. As diuretics may stimulate the renin system, and obscure patterns of Na/K excretion, we compared renin system characteristics and renal excretory patterns in patients with moderate to severe heart failure, receiving a 10 meq Na diet (n = 21), or a 100 meq Na diet (n = 18), during hospitalization, under strict matabolic diet, for a minimum of 5 days. The 100 meq group was divided into those achieving neutral Na balance (BAL, 91 ± 26 meq/24 hr; n = 8), and those persistently retaining Na (RET, 13 ± 13 meq/24 hr; n = 10).

Hemodynamic study was obtained at completion of metabolic collections. These included mean (MAP) and pulmonary wedge (PWP) pressures (mmHg), cardiac index (CI, l/min/m^2), and systemic vascular resistance (SVR, dxs/cm^5). Twenty-four hour urine collections included Na, and K (both meq/24 hr), and aldosterone excretion (UAE, mcg/24 hr) rates. Na/K is given as a ratio. Plasma renin (PRA, ng/ml/hr), and blood urea nitrogen (BUN, mg/dl) were measured. Mean values and difference between 100 meq groups (*p < 0.05) are given below:

	MAP	PWP	CI	SVR	Na/K	UAE	PRA	BUN
100 meqBAL	94	20*	2.13	1777	1.62*	6.2*	0.82*	13*
100 meqRET	82	29*	1.90	1545	0.28*	37.3*	9.6*	21*
10 meq	87	20	2.02	1732	0.26	38.0	9.9	22

Thus, Na/K ratio reflects renin system activity. Suppression of aldosterone excretion parallels increase of UNa, but occurs only in patients achieving neutral balance. We postulate that the improvement of Na/K seen with treatment interventions, is indicative of improved renal sodium handling, associated with renin system suppression.

948-52 Paradoxical Neurohumoral Axis Inhibition After Body Fluid Volume Depletion in Patients with Congestive Heart Failure and Water Retention

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Background: Hypovolemia stimulates the sympathoadrenal and renin systems and water retention. In congestive heart failure (CHF) reduction of cardiac output (CO) and, to the extent that it occurs, decrease of blood pressure (BP), have been suggested to be perceived as a state of underfilling of the arterial compartment, and to promote and perpetuate neurohumoral activation and retention of fluid. This study was aimed to probe whether intravascular volume deficit accounts for patterns that largely exceed the limits of a homeostatic response, as sometimes observed in more advanced stages of the syndrome. We reduced the body fluid mass with a non-pharmacological method, ultrafiltration (UF), in patients with CHF and water retention, and monitored the neurohumoral reaction.

Methods and Results: In 22 patients, UF was performed with a diafilter, which was part of an external venous circuit, whose flow was regulated to produce 500 ml/hour of ultrafiltrate (average total amount = 3122 ± 1199 ml) until right atrial pressure was lowered to 50% of baseline. Hemodynamics, plasma renin activity (PRA), norepinephrine (NE) and aldosterone (AL) were evaluated before and in the 48 hours after UF. Soon after the procedure, associated with a 20% reduction of plasma volume (PV) and a moderate decrease of CO and BP (consistent with a diminished degree of filling of the arterial compartment), there was an obvious fall of NE, PRA and AL. In the next 48 hours we recorded a) recovery of PV, CO and BP, b) increasing depression of the neurohumoral axis, c) striking enhancement of water and sodium excretion and resolution of peripheral edema and organ congestion. Changes of NE, PRA or AL were not related to changes of PV, CO and BP (variations in the state of arterial filling) and significantly correlated with the increase of urinary output and sodium excretion.

Conclusions: Arterial underfilling, as a the main mechanism for activation of the neurohumoral axis and retention of fluid, does not apply to the more advanced stages of CHF. The parallelism observed between fall of circulating hormones and reabsorption of extravascular fluid suggests that hypoperfusion and/or congestion of organ, like kidney and lung, may reduce the clearance of circulating norepinephrine and contribute to keep renin and aldosterone raised. A positive feedback loop between fluid retention and plasma hormone levels appears to be a mechanism of progression of the syndrome.

948-53 A New Natriuretic Factor Acting Like Loop Diuretic Drugs in Heart Failure. Relation to the Severity of Left Ventricular Dysfunction

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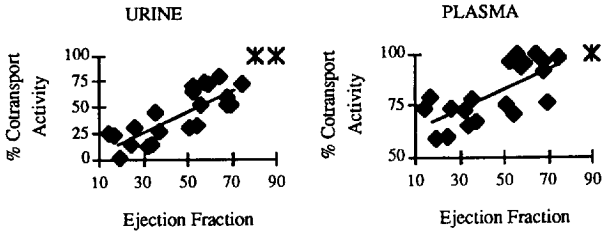
We have previously found in urine from salt-loaded rats and in patients with heart failure, a new natriuretic factor which has, in part, the biological profile of loop diuretic drugs. In patients with congestive heart failure, it is not known whether the activation of this factor is related to the impairment in systolic contractility. The aim of this study was to determine the differences in Cotransport Inhibitory Factor (C.I.F.) response between patients with or without left ventricular dysfunction. Twenty one patients were included in this study (16 men and 5 women, mean age 53, range 38 to 72). All treatments were maintained except loop diuretics. Left ventricular ejection fraction (LVEF) was measured by contrast or isotopic angiography (range 14–74%). Plasma and urine C.I.F. levels were measured by potency of the samples to inhibit cotransport fluxes in Madin and Darby canine kidney (MDCK) cells, and in human erythrocytes. Cotransport inhibition in urine and plasma was correlated with LVEF as shown in figure (* and ** = $p < 0.0002$).



This study shows that the degree of C.I.F activation is related to the level of LV dysfunction and that besides ANF, C.I.F. could play a key role in diuresis and natriuresis control in congestive heart failure.

949 Age-Related Cardiovascular Changes

Tuesday, March 21, 1995, 9:00 a.m.–11:00 a.m.
Ernest N. Morial Convention Center, Hall E
Presentation Hour: 9:00 a.m.–10:00 a.m.

949-97 The Prognostic Significance of Systolic and Diastolic Blood Pressure in the Elderly. Suggestions of a 10 Year Follow-up Study

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Nowadays the studies evaluating the relationship between blood pressure and (total and cardiovascular) mortality in the elderly have provided conflicting results.

Aim of the study was to evaluate the prognostic significance of systolic (SBP) and diastolic (DBP) blood pressure values in a cohort of 3858 elderly outpatients (mean age 72.7 ± 4.9 years, range 65–96 years, 43.5% males) enrolled in the "Study on blood pressure in the elderly-SPAA" and followed up for 10 years.

The initial assessment included two BP measurements in two visits. 90 subjects (2.3%) were lost to follow-up. There were 1546 (41%) deaths (TD), 698 from cardiovascular disease (CD). The Table shows the odds ratio (95% CI) for TD and CD according to baseline SBP and DBP (mmHg, *reference group) adjusted for main cardiovascular risk factors and diseases.

SBP	<140	140–159	160–179	≥180
TD	1*	1.1 (0.9–1.3)	1.3 (1.0–1.6)	1.5 (1.1–2.0)
CD	1*	1.2 (0.9–1.6)	1.4 (1.0–1.8)	2.0 (1.4–3.0)
DBP	<90	90–94	95–104	≥105
TD	1*	1.1 (0.9–1.3)	0.9 (0.7–1.1)	1.2 (0.8–1.7)
CD	1*	1.1 (0.9–1.4)	1.0 (0.8–1.4)	1.2 (0.8–1.9)

*reference group

In our elderly population SBP was associated with total and cardiovascular mortality while DBP was not. A similar pattern was present in both sexes, in elderly aged less or more than 75 years and in subjects with or without pre-existing cardiovascular diseases.

These data suggest that SBP should be emphasized more than DBP in the diagnosis and treatment of hypertension in the elderly.