11:15

707-4 The Randomized Aldactone Evaluation Study (RALES): Parallel Dose Finding Trial

Bertram Pitt, RALES Investigators. *Ann Arbor, MI*

Aldactone (AL), an aldosterone (A) receptor antagonist, causes diuresis and symptomatic improvement in patients with heart failure (HF) maintained on an angiotensin converting enzyme-inhibitor (ACE-I). The effective dose and safety of AL in patients with HF on an ACE-I and loop diuretic was determined in a multicenter, randomized, double-blind study of placebo (P) (n = 40); AL 12.5 mg (n = 41), 25 mg (n = 45), 50 mg (n = 47) and 75 mg (n = 41) over 12 weeks. Left ventricular ejection fraction was ≤35%; 80% males; mean age 62 years; with 50% in NYHA Class II and 50% in III–IV. The mean dose of captopril was 62.0 mg, enalapril 14.3 mg and furosemide 73.9 mg. Digitalis and Potassium (K) supplements were given in approximately 80% and 30% of patients, respectively. Efficacy was assessed by measuring changes in N-terminal plasma atrial natriuretic factor (ANF) pmol/L and systolic (S)/diastolic (D) blood pressure (BP) mmHg from baseline to 12 weeks (Δ). Safety by Δ in serum K mmol/L, creatinine (Cr) μmol/L and incidence of hyperkalemia (HK) ≥6.0 mmol/L.

	P	AL12.5	AL25	AL50	AL75	p
ΔANF	+55	−287*	−295	−351*	−371*	**
ΔS/D BP	+2.6/+1.9	−1.4/−2.3	−4.8/−3.2*	−5.9/−5.3*	−7.6/−5.3*	**
ΔK	−0.1	+0.2*	+0.4*	+0.5*	+0.6*	**
ΔCr	0	+0.1*	+0.1	+0.2*	+0.3*	**
HK (%)	0	2	7	11	12	**

*p < 0.05 vs. placebo; **significant treatment effect, p < 0.05

There were no deaths during the drug administration period of the study, and no significant changes in NYHA class among treatment groups. Thus, in patients with HF on an ACE-I and loop diuretic, AL at a dose ≥12.5 mg is effective, with a dose response relationship to 75 mg. There was an increased incidence of HK with AL ≥50 mg. The effect of AL on hospitalization and death will be determined in the RALES-Survival Trial.

11:30

707-5 Functional Correlates and Prognostic Importance of Chronic Atrial Fibrillation in Patients with Dilated Cardiomyopathy and CHF

Prakash C. Deedwania, Steven Singh, Ross Fletcher, Susan Fisher, Bramah Singh, CHF STAT Investigators. *VAMC/Fresno & Washington*

Although atrial fibrillation (A. fib) has been labeled as a marker of relatively advanced LV dysfunction and increased mortality in patients with CHF, the available data provide conflicting findings. Accordingly, we evaluated the relationship of chronic A. fib with several important clinical and objective parameters in the Congestive Heart Failure Survival Trial of Antiarrhythmic Therapy (CHF STAT). A total of 633 patients with LVEF < 40%, dilated cardiomyopathy and chronic CHF were evaluated. Ninety-six percent were receiving ACE inhibitors. *Baseline characteristics:* 97 (15%) had A. fib. Comparison of baseline characteristics (mean values) between patients with A. fib (n = 97) and those without A. fib (n = 536) is shown:

	Mean Age	Etiology IHD NIHD	LVEF <30%	LVIDd >55 mm	XRay CT > 0.5	Avg PVCs/h	% on Dig
A. fib (+)	65 ±	58% 42%*	63%	97%	98%*	228	96%*
A. fib (−)	67 ±	73% 27%	66%	96%	84%	188	66%

* = P < 0.01

The analyses of above data showed that significantly greater number of patients with CHF and A. fib had CT ratio > 0.5 on chest X-ray as well as a larger percent of A. fib patients had nonischemic cardiomyopathy. As expected, a significantly greater proportion of A. fib patients were receiving digoxin therapy.

Follow-up: All patients were followed on a regular basis at 3 mo intervals. During the median follow-up period of 25 months, Kaplan-Meier survival estimates of the overall cardiac mortality and the risk of sudden cardiac death did not reveal significant difference between patients with chronic atrial fibrillation and those without A. fibrillation.

Conclusion: These results demonstrate that in patients with dilated cardiomyopathy, systolic LV dysfunction and chronic CHF, the presence of A. fib is not a marker of more advanced heart failure nor an increased risk of cardiac mortality and sudden cardiac death.

11:45

707-6 Amiodarone Decreases Ability of Baseline Ventricular Arrhythmia Severity to Predict Mortality

Ross D. Fletcher, Steve Singh, CHF-STAT Investigators. *Veterans Affairs Washington, D.C.*

The Congestive Heart Failure Survival Trial of Antiarrhythmic Therapy (CHF-STAT) entered 633 high risk patients (pts) with ejection fraction (EF) ≤40%, PVCs/hr ≥ 10 on 24 hour Holter recording and on active vasodilator therapy. Pts were randomized to amiodarone or placebo. Despite marked ventricular arrhythmia suppression, overall mortality was the same for amiodarone and placebo treated pts. An analysis to identify groups at risk based on frequency or severity of ventricular arrhythmia at baseline for both placebo and amiodarone is as follows:

	Placebo		Amiodarone	
	M1	p	M1	p
PVCs < 30/hr	4%		14%	
> 30/hr	19%	<0.002	19%	NS (0.47)
PVCs < median*	11%		16%	
> median	21%	<0.0003	19%	NS (0.54)
High EF, Low PVC*	11%		13%	
High PVC	13%	NS	14%	NS (0.48)
Low EF, Low PVC*	14%		17%)	
High PVC	28%	<0.05	23%)	NS (0.48)
VT ≤3 events/24hr	13%		16%	
≥4	21%	<0.003	20%	NS (0.43)

*High, Low = >, <, median, EF (26%) & PVCs/hr (128)
M1 = first year mortality

While increased arrhythmia severity predicted increased mortality on placebo, it did not in patients subsequently assigned to amiodarone treatment. Amiodarone appears to counter the effect of increased arrhythmia severity on mortality.

708 Prognostic Implications of Radionuclide Imaging

Monday, March 20, 1995, 10:30 a.m.–Noon
Ernest N. Morial Convention Center, Room 26

10:30

708-1 Defect Size with IV Dipyridamole Tc-99m Sestamibi SPECT Imaging Predicts Both Future Cardiac Events and Other Cardiac Hospitalizations

Joseph R. McClellan, Steven D. Herman, Mark I. Travin, Rhonda M. Jenkins, Gary V. Heller. *Memorial Hospital and Roger Williams Hospital, Brown University, Providence, RI; Hospital of the University of Pennsylvania, Philadelphia, PA*

Optimal management of patients with coronary artery disease requires identification of those at greatest risk of future adverse cardiac events. The relationship between defect size after IV dipyridamole with Tc-99m Sestamibi SPECT imaging and cardiac events (death, MI) or need for other cardiac hospitalizations for CHF, unstable angina (UA) or late revascularization (REV) (>6 months after imaging) was evaluated in 512 pts followed for 12.8 ± 9.8 months. Defects were classified as small (Sml), moderate (Mod) or large (Lrg). Of 216 pts with normal scans, there were 3 cardiac events and 11 other cardiac hospitalizations. Of the 296 pts with abnormal scans, there were 22 cardiac events (Sml 1.5%, Mod 6.9%, Lrg 12.5%) and 51 other cardiac hospitalizations (Sml 6%, Mod 12%, Lrg 20%). An abnormal scan was a