3:00

COMPARISON OF LOW *VERSUS* HIGH DOSE ENALAPRIL THERAPY FOR PATIENTS WITH SEVERE CONGESTIVE HEART FAILURE (CHF).

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Angiotensin-converting enzyme inhibitor (ACEI) therapy is useful in the management of CHF, but optimal dosing regimens are not well established. Response to ACEI therapy and clinical course may be predicted by plasma norepinephrine (NE) levels. We attempted to assess the relative safety and efficacy of low versus high dose enalapril in patients with severe CHF, and to determine the association of NE levels with clinical outcome.

Methods: 27 outpatients with severe CHF (mean EF=15% [4-30%]; mean VO2max=14.5ml/kg/min [8.3-25.1 ml/kg/min]) being evaluated for cardiac transplantation were randomized to either 2.5 mg bid or 15 mg b.i.d. of enalapril. High dose therapy was initiated at 2.5 mg b.i.d. and increased to 15 mg b.i.d. over 6 weeks. Patients were initially evaluated with 2-D echo, MUGA, V02 max, 24 hr Holter, electrolytes, BUN/Cr, and plasma NE levels, and followed monthly. There was no significant difference in clinical parameters at baseline between the two groups. Major clinical events included death or hospitalization, and minor events included significant intensification of outpatient medical regimens.

Results: All 27 patients tolerated the 2.5mg b.i.d. dose. Only 2/14 patients on high dose therapy were intolerant of the full dose, both due to hypotension; one of these had amyloid. A total of 9 major events and 15 minor events occurred in this population whose mean follow-up was 4.3 months. Only two major events and four minor events occurred in patients on high-dose therapy. 8/9 major events and 12/15 minor events occurred when the patients' most recent NE levels were greater than 900 pg/ml (normal <400 pg/ml).

Conclusions: Both high and low dose enalapril were well tolerated in these patients with severe CHF. Fewer clinical events occurred in patients on high dose enalapril. These data also suggest that high plasma NE levels predict clinical events.

3:15

PLACEBO-CONTROLLED, CROSS-OVER TRIAL OF PHYSICAL TRAINING, LISINOPRIL AND THE COMBINATION IN MODERATE TO SEVERE HEART FAILURE

Theo E. Meyer, Barbara Casadei, Andrew J. S. Coats, Alberto Radaelli, Patrick P. Davey, Stamatis Adamapolous, James Conway, Peter Sleight. Oxford University, Oxford, United Kingdom.

To establish whether physical training(Tr) has comparable/additive effects to Lisinopril (Lis) 10 mg/day, we entered 12 male Pts(aged: 67±4 yrs) with moderate to severe heart failure(EF=16±5%), all of whom were considered by independant clinicians to require converting enzyme inhibitors, into a placebo-controlled, cross-over trial. After a 4 week run-in phase during which 3 baseline exercise tests were obtained, Pts were randomly allocated to 4 cross-over periods of 6 weeks each. These included: placebo (Pl) and Tr, Pl and detraining (DTr), Lis and Tr, and Lis and DTr. Pts exercised at home on a bicycle ergometer for 20 min/day for 5 days/week at 60-80% of their maximal workload. Compliance to Tr was 85±15%. Results are shown in the table(HR submax=Heart Rate at submaximal workload; Max O_2=maximal O_2 consumption; SBP,DBP = systolic and diastolic blood pressure; Vi=minute ventilation; *p< 0.05 and **p<0.01 vs Pl&DTr; #p< 0.05 and ##p<0.01 vs Pl&Tr; ¶p< 0.05 and ¶¶p<0.01 vs Lis&DTr).

Results(mean±SD)	Pl&DTr	Pl&Tr	Lis&DTr	Lis&Tr
HR submax(bpm)	119±24	110±20	115±25	111±22
SBP(mmHg)	117±11	115±98	97±6**	96±8##
DBP(mmHg)	76±12	81±16	65±6**	63±7##
Max O_2 (ml/min/Kg)	13.4±2	14.1±3*	13.2±2	14.4±3¶¶
Exercise Time(min)	13.3±3	14.6±3*	14±2	15.8±2¶¶
Vi/50Watts(l/min)	24.7±6	25±5	24±4	22±4#¶¶

We conclude: 1. Exercise performance in these Pts with moderate to severe heart failure was enhanced by Tr whether or not they were on Lis. 2. While there was no clear benefit from Lis alone, a non significant trend was shown for the combination of Lis and Tr to be better than Tr alone. 3. Tr may be a useful adjunct to the existing medical therapy for heart failure.

Wednesday, March 6, 1991
2:00PM–3:30PM, Room 260, West Concourse
Reperfusion Therapy: Catheterization Laboratory Observations

2:00

Does Arterial Patency 90 Minutes Following Thrombolytic Therapy Predict 42 Day Survival?

Bjorn P. Flygenring, Florence H. Sheehan, J. Ward Kennedy, Harold T. Dodge, Eugene Braunwald for the TIMI Investigators, University of Washington, Seattle, WA.

Data from patients (pts) treated with tissue plasminogen activator in the Thrombolysis in Myocardial Infarction Trial (TIMI) phase I were analyzed to determine if 90 min patency of the infarct related vessel predicts 42 day survival. Patency (TIMI grade 0-3) was evaluated visually by the core laboratory. The centerline method was used to calculate the circumferential extent of hypokinesis more severe than 2SD below normal (hypolength). Mortality for normal perfusion (TIMI grade 3) was compared with abnormal perfusion (TIMI grade 0-2).

Results: Univariate analysis showed lower mortality in pts with TIMI grade 3 (normal) flow:

Grade	N	% Mortality		p
0	90	11.1	8.8	
1	33	9.1		
2	115	7.0		<0.005
3	150	4.7	4.7	

Mortality was less well predicted by separating pts into flow grade 0 or 1 (10.6%) vs grade 2 or 3 (5.7%), p=0.08. On multivariate analysis of clinical and angiographic parameters, the strongest predictor of survival was LV function. Cox regression summary:

	Chi Square	p
Hypo-length	9.1	0.003
Age	6.9	0.01

Conclusion: Although LV function remains as the single most prognostic indicator, achievement of normal perfusion (TIMI grade 3) following thrombolytic therapy may be important for improved survival.

2:15

THE IMPORTANCE OF TEMPORARY REPERFUSION AFTER THROMBOLYTIC THERAPY FOR ACUTE MYOCARDIAL INFARCTION.

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This study was designed to analyze the presence of benefit from temporary reperfusion after rt - PA infusion. 120 patients with AMI (< 5 hours) were submitted to coronary angiograms to document total occlusion of the infarct related artery (IRA) followed by rt - PA infusion. IRA patency was assessed every 15' for 90' and the angiograms were repeated 24 hours later. The patients were divided in 3 groups after the coronariographies: A. reperfusion of the IRA (e.g. patency in at least one of the angiograms but not in the last one); B. maintained reperfusion; C. maintained occlusion of the IRA. Mortality was 7.1% (2 / 28), 7.0% (4 / 57) and 22.9% (8 / 35) for A, B, and C (p = 0.05). In our sample, some patients with temporary reperfusion represented a special set of patients with a better short term prognosis. We may hypothesize that despite having an occluded IRA they have benefited from temporary reperfusion.

GROUP	N	Age	Delay	IRA	Death
A	28	53.6	234	12 LAD 15 RCA 1 CFX	2 (7.1%)
B	57	54.7	233	29 LAD 26 RCA 2 CFX	4 (7.0%)
C	35	54.2	230	12 LAD 18 RCA 5 CFX	8 (22.9%)
p		NS	NS	NS	p = 0.05