1106 Novel Pharmacological Approaches to Congestive Heart Failure and Cardiomyopathy

Monday, March 31, 2003, Noon-2:00 p.m.
McCormick Place, Hall A
Presentation I: 1:00 p.m.-2:00 p.m.

1106-120 Immunomodulatory Effects of Growth Hormone: Administration Are Associated With Improvement in Myocardial Contractile Performance in Dilated Cardiomyopathy Patients
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Objectives: To study the immunomodulatory effects of growth hormone (GH) and to investigate whether these effects are associated with the improvement of left ventricular (LV) contractile function in dilated cardiomyopathy (DC) patients (pts).

Background: Recent studies indicate that an abnormal immune response contributes to the progression of chronic heart failure (CHF).

Methods: Plasma inflammatory cytokines TNF-α, IL-6, GM-CSF, its soluble receptor sGM-CSFR and soluble adhesion molecules ICAM-1 and VCAM-1, and anti-inflammatory cytokines IL-10 and TGF-β were measured in 12 DC pts (NYHA III; LVEF 24±3%) before and after a 3-month subcutaneous administration of GH 41U every other day (randomized crossover design). Max oxygen uptake (VO2 max), ejection systolic wall stress (EWS), mean velocity of circumferential fiber shortening (Vcf) and contractile reserve (change of Vcf/EWS after dobutamine infusion) were also determined.

Results: GH produced a significant reduction in plasma TNF-α (7.8±1.1 vs 6.0±0.9 pg/ml, p<0.05), IL-6 (4.6±0.3 vs 3.4±0.3 pg/ml, p<0.05), GM-CSF (27.2±2 vs 20.2±0.9 pg/ml, p<0.05), sGM-CSFR (4.0±0.4 vs 3.2±0.3 pg/ml, p<0.05), MCP-1 (199±55 vs 182±26 pg/ml, p<0.05), ICAM-1 (324±33 vs 274±22 ng/ml, p<0.05) and VCAM-1 (1237±88 vs 1043±77 ng/ml, p<0.05). As well as a significant increase in ratio IL-10/TNF-α (1.9±0.3 vs 3.5±0.9, p<0.05), IL-10IL-6 (2.6±0.6 vs 3.2±0.5, p<0.05) and TGF-β/TNF-α (3.1±0.6 vs 4.0±0.6, p<0.05) in DC pts. A significant reduction of EWS was observed (404±124 vs 334±41 cm², p<0.005), and a significant increase of contractile reserve (0.0005±0.00001 vs 0.003±0.0011 ccm/sec, p<0.005) and VO2 max (15.2±0.7 vs 17.1±0.9 ml/kg/min, p<0.001) was also observed. Good correlations were found between GH-induced increase in contractile reserve and the increase in VO2 max (r=-0.02, p=0.05), ratio IL-10/TNF-α (r=0.66, p<0.05) and TGF-β/VNF-α (r=0.58, p<0.05), as well as the reduction in TNF-α levels (r=-0.86, p<0.01).

Conclusions: GH modulates beneficially cytokine network in DC pts. These immunomodulatory effects may be associated with the improvement in LV contractile performance and exercise capacity of pts with CHF and DC.

1106-121 Beneficial Highs of Doses of Growth Hormone in the Optimization of Medical Treatment in Decompensated Congestive Heart Failure
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Background: Optimizing oral therapy in patients with advanced congestive heart failure (CHF) and cardiac cachexia can be a challenge.

Methods: We investigated the effects of high doses of recombinant human growth hormone (rHGH) in hospitalized patients with unstable congestive heart disease and/or decompensated heart failure (HF) on LV systolic function and mortality. We studied 10 non-consecutive patients, predominantly male (6/10), with a mean age of 73 years (range 50-89). All patients were admitted to the cardiology ICU from September 2001 to March 2002. All were treated with beta-blockers in 8/10, ACE inhibitors in 7/10, furosemide in 7/10, digoxin in 5/10 and spironolactone in 6/10. HF severity levels were NYHA class II in 4/10, class III in 4/10 and class IV in 2/10. This group was followed-up for 8 months and mortality was studied.

Results: The mean plasma concentration of GH was 137±23 ng/ml (range 45-228 ng/ml). All patients showed increments in plasma GH levels and a significant increase in LV ejection fraction (EF) of 18±6% (range 5-36%) (p<0.05). Additionally, a significant increase in systolic blood pressure (SBP) of 19±7 mmHg (range 5-49 mmHg) was observed (p<0.05). No significant adverse effects were observed. The increase in plasma GH levels was not associated with any adverse effects. One patient died during the follow-up period at 5 months due to myocardial infarction.

Conclusions: High doses of rHGH were beneficial in decompensated HF patients and were safe and well tolerated. A significant increase in EF was observed with no adverse effects. Further studies are needed to assess the impact of high doses of rHGH on the outcome of decompensated HF patients. This is the first demonstration of the use of rHGH in patients with advanced HF.