

945-20 In Vivo Human Major Histocompatibility Complex (MHC) α -Chain Gene Transfer into Pig Hearts by Intracoronary Delivery

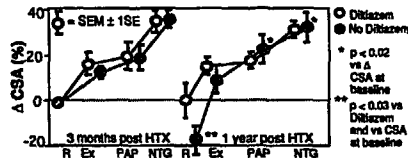
Alexander Popov, Ivan Aleksic, Meina Ren, Elliot Corday, Peter Barath. Cedars-Sinai Medical Center, Los Angeles, CA

We hypothesized that transfection of the recipient's MHC genes into the donor heart results in the expression of the MHC gene product on the donor organ cell surface, which might facilitate the acceptance of both allo- and xenografts. *Methods:* To demonstrate the feasibility and determine the optimal characteristics of the human MHC gene transfer into an animal organ in vivo, the isolated and purified gene was incubated in ratios 1:1 to 1:10 with lipofectin for 10 min. Then we superselectively cannulated the apical segment of the LAD of normal pigs with a non-occlusive PE catheter and delivered the gene/lipofectin complex (500 μ g DNA/animal) over 30 min. The animals were sacrificed in 4, 24, 48 and 72 hours (4 animals/group). We detected the gene product by immunohistochemical staining using monoclonal antibody to human α chain. Negative controls: lipofectin delivery alone, deletion of primary antibody. Positive control: human tonsils. *Results:* In the carrier positive areas (oil red O detection), the endothelial cells of the capillaries, arterioles and small arteries revealed a strong confluent immunohistochemical α chain positivity. At 48 h moderately α chain positive mononuclear cells appeared in the areas where the endothelial cells were also α chain positive. The myocardial cells remained negative. The gene expression reached its maximum at 24 h but was still present at 72 h. The optimal DNA/lipofectin ratio was 1:4. *Conclusion:* 1. Intracoronary delivery of human MHC gene results in the expression of this gene in the endothelial cells of the pig hearts. 2. The efficiency of the transfection depends on the DNA/lipofectin ratio and the timing.

945-21 Prevention of Graft Atherosclerosis by Diltiazem in Heart Transplantation: A Pure Vasodilatory Effect?

Barbara K. Julius, Giuseppe Vassalli, Marko Turina, Wolfgang Kiowski, Otto M. Hess. Cardiology and Cardiovascular Surgery, University Hospital, Zurich, Switzerland

Background: Diltiazem has been shown to prevent the occurrence of graft atherosclerosis after heart transplantation (HTX). *Patients and Methods:* 23 patients (pts) were studied 3 and 12 months after HTX. At baseline examination pts were randomized to receive either Diltiazem (D) or no calcium antagonist (C). Coronary cross-sectional area (CSA) was determined by bi-plane quantitative coronary angiography at rest (R), during supine bicycle exercise (Ex), after 10 mg intracoronary papaverin (PAP) as well as 1.6 mg sublingual nitroglycerin (NTG). *Results:* There was a significant reduction in CSA at 12 months follow-up in C but not in Diltiazem-treated pts. However, PAP- (18 vs 40%) as well as NTG-induced vasodilation (31 vs 49%) was reduced at follow-up examination in Diltiazem-treated pts when compared to C.



Conclusions: The decrease in coronary artery dimensions is prevented by Diltiazem in HTX pts during short-term follow-up. However, this effect is due to coronary vasodilation rather than to prevention of graft atherosclerosis.

946 Neurally-Mediated Syncope

Tuesday, March 26, 1996, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall E
Presentation Hour: 9:00 a.m.-10:00 a.m.

946-73 Response to Treatment Directed at Neurally Mediated Hypotension Among Patients With Chronic Fatigue Syndrome: Can it Be Predicted?

Issam Bou-Halajig, Peter Rowe, Jean S. Kan, Hugh Calkins. The Johns Hopkins Medical Institutions, Baltimore, MD

Recent studies have reported a close association between chronic fatigue syndrome (CFS) and neurally mediated hypotension (NMH) with treatment directed at NMH resulting in near complete resolution of symptoms in a subset of patients with chronic fatigue syndrome (CFS). The purpose of this

study was to compare the clinical characteristics and response to upright tilt (tilt) of those CFS patients with and without a favorable response to treatment. Nineteen patients with CFS and a positive response to tilt were treated (16 F, 3 M, 32 ± 13 yrs). The mean duration of follow-up was 24 ± 5 weeks. Nine patients experienced near total resolution of symptoms. Clinical characteristics evaluated included age, sex, duration and severity of symptoms, and stage of positive response to tilt. Severity of symptoms was based on a 5 point scale (5 = most severe).

Results: Patients with a favorable response to treatment had a shorter duration of symptoms (40 ± 28 vs 87 ± 52 m, p = 0.03), and less severe symptoms (3.8 ± 0.8 vs 4.8 ± 0.4, p < 0.01). There was no difference in age (33 ± 13 vs 31 ± 14, p = 0.8), number of prior failed rx (2.2 ± 1.9 vs 4.0 ± 3.6, p = 0.2), male sex (2/9 vs 1/10, p = 0.14) or the proportion of patients who had a positive response during phase I of tilt (5/9 vs 9/10, p = 0.14).

Conclusions: Patients with chronic fatigue syndrome who demonstrate a favorable response to treatment directed at NMH are characterized by less severe symptoms of shorter duration.

946-74 Diagnostic Utility of Mechanical, Pharmacological and Orthostatic Stimulation of the Carotid Sinus in Patients With Unexplained Syncope

Carlos A. Morillo, Mark A. Wood, David M. Gilligan, Dwain L. Eckberg, Kenneth A. Ellenbogen. McGuire VA Medical Center, Medical College of Virginia, Richmond, VA

Carotid sinus hypersensitivity (CSH) is a frequently unrecognized cause of unexplained syncope usually diagnosed by eliciting significant bradycardia/hypotension during carotid sinus massage (CSM) in the supine position. The diagnostic utility of mechanical, pharmacological and orthostatic stimulation of the carotid sinus was assessed in 37 consecutive patients (mean age 63 ± 2.3 yr) with unexplained syncope. ECG and blood pressure were continuously recorded; a 100 μ g bolus of nitroprusside (N) was administered and followed after 60 seconds by 150 μ g of phenylephrine (P). After 10 minutes of recovery CSM was performed in the supine position, and 2 minutes after assuming a 60° upright position. A 60° low-dose isoproterenol head-up tilt (HUT) was performed in all patients.

	HRb	Δ HRN	Δ HRP	Δ HR0°	Δ HR60°	Δ SP0°	Δ SP60°	n
CSH[-]	72	18	21	6	8	8	10	16
CSH[+]	70	14	13	15	25*	17	58*	21

HRb: baseline heart rate, Δ HR: heart rate change, beats/min, Δ SP: systolic blood pressure change, mmHg. *p < 0.05 between groups.

CSH was diagnosed in only 3 (8%) patients in the supine position, and in 18 (48%) in the upright position increasing the diagnostic yield by 40%. HUT was positive in 4 (19%) patients with CSH.

Conclusions: Assessment of CSM during orthostatic stress identifies an additional 40% of patients with CSH otherwise unrecognized by CSM performed in the supine position. Pharmacologic assessment does not add any additional information.

946-75 Influence on Autonomic Balance During Head-Up Tilt of Endoscopic Transthoracic Sympathicotomy

Satoru Sakagami, Takeo Tedoriya, Manabu Fujimoto, Yukio Nakamura, Takeshi Ueyama. Kanazawa National Hospital, Kanazawa, Japan

Endoscopic transthoracic sympathicotomy (ETS) is a minimal invasive procedure of thoracic sympathetic block. ETS is done under general anesthesia, and after carbon dioxide insufflation of the pleural cavity, the upper thoracic sympathetic chain is electrocoagulated. ETS has been used successfully in the treatment of primary palmar hyperhidrosis. To investigate the influence of ETS on cardiac autonomic function, we analyzed heart rate variability during head-up tilt test before and after ETS in 12 patients with primary palmar hyperhidrosis. The inclination of the table was varied at the following angle: 0°, 30°, 60°, 90°, and maintained for 10 minutes at each angle. From the continuous ECG, sympathovagal balance was determined with power spectral analysis of heart rate variability using a maximal entropy method.

	RR (msec)	LF (ms ²)	HF (ms ²)	LF/HF
0° (before)	944 ± 94	642 ± 235	1072 ± 1260	1.0 ± 0.6
0° (after)	917 ± 156	437 ± 290	623 ± 487	1.1 ± 0.9
30° (before)	821 ± 119	504 ± 221*	286 ± 203	3.1 ± 2.9*
30° (after)	840 ± 169	277 ± 245*	272 ± 207	1.3 ± 1.0*
60° (before)	735 ± 91	606 ± 404*	219 ± 281	6.7 ± 8.1*
60° (after)	765 ± 128	241 ± 173*	192 ± 170	3.6 ± 2.4*
90° (before)	671 ± 95*	568 ± 440*	82 ± 50	9.4 ± 9.1*
90° (after)	736 ± 136*	259 ± 197*	82 ± 71	5.3 ± 4.7*

*p < 0.05, LF: low frequency, HF: high frequency

These data suggest that ETS suppress the excitation of the sympathetic

TUESDAY POSTER