POSTER SESSION

1097 Pediatric Pulmonary Hypertension and Transplantation

Monday, March 18, 2002, 9:00 a.m.-11:00 a.m.
Georgia World Congress Center, Hall G
Presentation Hour: 10:00 a.m.-11:00 a.m.

1097-97 Treatment of Pulmonary Arterial Hypertension Associated With Congenital Heart Disease With Intravenous Epoprostenol: Impact of Therapy on Timing of Transplantation

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Introduction: Intravenous epoprostenol (EPO) improves exercise tolerance, hemodynamics, and survival in primary pulmonary hypertension (PPH). Patients with pulmonary hypertension (PH) associated with congenital heart disease (CHD) demonstrate improved hemodynamics with EPO over the short term. The objective of this study was to determine the long-term effects of EPO in CHD and implications for timing of lung or heart-lung transplantation.
Methods: The Rush database of 264 patients with PH treated with EPO since 1991 was queried for patients with CHD. The sixteen patients with CHD were matched in a 2:1 fashion with 32 PPH patients for age, gender, and functional class (FC) at the time of EPO initiation. Hemodynamics and exercise time at time of EPO initiation and at one year was compared using students paired t-test. Survival over 5 years was analyzed using Kaplan-Meier analysis.
Results: EPO resulted in similar improvements in hemodynamics and treadmill times in both PPH and CHD at 1 year. In CHD the PVR declined by 30% from 17 to 12 Wood units ($p<0.001$), the systemic arterial O2 saturation improved from 88 to 91% ($p=0.024$), and the treadmill time improved 118% from 226 to 492 seconds ($p=0.023$). The 1, 3, and 5 year survivals were 93%, 83%, and 81% for CHD versus 84%, 66%, and 62% for PPH respectively.
Conclusion: The favorable response of CHD to EPO is similar to that of PPH. The survival of CHD with EPO exceed that of PPH and that of lung or heart-lung transplantation which has a 1, 3, and 5 year survival of 60%, 48%, and 40%. The treatment of patients with PH associated with CHD with EPO may delay or avoid need for transplantation.

1097-98 Sildenafil (Viagra) in Childhood and Neonatal Pulmonary Hypertension

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Bacground: Cyclic guanosine monosphate (cGMP) mediates vasodilation induced by nitric oxide (NO). Inhibition of type 5 phosphodiesterase (present in high concentration in pulmonary vasculature) elevates cGMP and promotes vasodilation. Therefore, we investigated the effect of oral sildenafil in pulmonary hypertension. Methods: We administered oral sildenafil (0.25 -0.5 mg/kg) to 16 patients (median age 6 years, range 3 days to 18 years, gender 7M,9F). All patients had pulmonary hypertension defined by echocardiography or catheter measurement. During cardiac catheterisation (n=6) we measured hemodynamics before and 20 minutes after administration of sildenafil. We administered sildenafil to 5 patients with refractory suprasystemic pulmonary hypertension after gradual withdrawal of inhaled NO, despite alkanilisation, (diagnoses included repair of congenital diaphragmatic hernia n=3, and pulmonary vein stenosis n=2). Five patients received chronic sildenafil therapy, given 4 times a day (primary pulmonary hypertension n=3, secondary pulmonary hypertension n=2). Subsequent evaluation was by echocardiography and distance walked in 6 minutes . Results:During cardiac catheterisation mean pulmonary artery pressure decreased from 50±8 to 38±12 mmHg ($p<0.05$) and indexed pulmonary vascular resistance decreased from10.5±4.9 to 7.6±4.6 Wood Units m2 ($p<0.05$). There were no changes in mean systemic pressure 64±4 to 65±8 mmHg, systemic vascular resistance 17.1±4.6 to 17.6±5.2 Wood Units m2 or cardiac index 4.0±1.2 to 4.0 ±1.2 l/min/m2. In 5 patients sildenafil attenuated the rise in pulmonary artery pressure and permitted discontinuation of NO without hemodynamic instability 4-6 hours after oral sildenafil. In the chronic therapy group 3/ 5 patients followed for a median of 12 weeks had improvements in 6 minute walk distance of 200%. Conclusion: Our results suggest that oral sildenafil selectively decreases pulmonary vascular resistance, attenuates rebound pulmonary hypertension and facilitates weaning of prolonged inhaled NO therapy and improves distance walked in 6 minutes. Sildenafil offers promise in the treatement of acute and chronic pulmonary hypertension.

1097-99 Basal Pulmonary Vascular Resistance and Its Response to Exogenous Nitric Oxide Late After Fontan Operation

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Background: The pulsatile nature of pulmonary blood flow is important for shear-stress mediated release of endothelium-derived nitric oxide (NO) and lowering pulmonary vascular resistance (PVR) by passive recruitment of capillaries. Normal pulsatile flow is lost or markedly attenuated after Fontan-type operations, but to date, there are no data on basal pulmonary vascular resistance and its responsiveness to exogenous nitric oxide, at late follow up in these patients.
Methods: We measured indexed pulmonary vascular resistance (PVRI), using Fick principle to calculate pulmonary blood flow, with respiratory mass spectrometry to measure oxygen consumption, in 10 patients (median age 11.2yr, range 8- 17 yrs, 7 male, 3 female) at mean 5 yrs after a Fontan-type operation (4 atriopulmonary connections, 2 lateral tunnels, 3 extracardiac conduits, 1 intraatrial tube). Ventilation under general anaesthesia during cardiac catheterisation was adjusted to avoid alveolar hypoxemia or hypoventilation. Measurements were made before and after NO inhalation at 20 ppm for 10 minutes.
Results: The baseline cardiac index was 2.5 ± 0.64 L/min/m2. The basal PVRI was 2.07 ± 0.89 Wood units/m2 (mean ± SD) and showed a significant reduction to 1.46 ± 0.37 ($p=0.03$) after NO inhalation. 6 patients showed pulsatility on the pulmonary arterial pressure trace (4 atriopulmonary connections, 2 lateral tunnels), however, they did not differ significantly from those with a non-pulsatile waveform, either in terms of basal PVR (2.11 ± 1.19 and 2.02 ± 0.05, $p=0.8$) or response to NO (1.37 ± 0.33 and 1.63 ± 0.40, $p = 0.11$), respectively.
Conclusion: PVR falls with exogenous nitric oxide late after Fontan-type operation. These data suggest that endogenous NO production may be reduced late after Fontan-type operation, even in patients with some pulsatility in the pulmonary circulation. Therapeutic strategies to enhance pulmonary endothelial NO release may have a role in these patients.

1097-100 Presenting Features and Clinical Outcomes for Children With Metabolic Cardiomyopathies

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Background: Metabolic diseases are an important cause of childhood cardiomyopathy. This review examines the presenting features and clinical outcomes for children with these conditions enrolled in the National Australian Childhood Cardiomyopathy Study (NACCS).
Methods: NACCS is a population-based study including all children in Australia with CM presenting <10 years of age from 1987-97. Cases were collected from all paediatric cardiologists and paediatric cardiac centres, as well as from adult cardiologists, regional paediatricians, cardiac transplant centres and coronial records. Cases were classified according to accepted WHO guidelines. Metabolic diseases were defined as those with a biochemical abnormality aetiologically linked to the cardiomyopathy. Children with progressive neuromuscular diseases and those with dominant systemic or neurological symptoms were excluded.
Results: There were 28 children with metabolic conditions (8.9% of study population) including 6.5% of patients with DCM, 2.5% with HCM and 32.6% of patients with unclassified cardiomyopathy. Congestive heart failure at presentation occurred in 21/28 (75%). Commonest diagnoses were respiratory chain enzyme deficiencies (10), Barth syndrome (8), carnitine deficiency syndromes (4) and fatty acid oxidation defects (4). Children with respiratory chain enzyme deficiencies had variable cardiomyopathies including DCM, HCM and mixed hypertrophy with systolic dysfunction. 7/8 (87.5%) children with Barth syndrome had LV non-compaction (LVNC) and the other had DCM. Barth syndrome was present in 7/29 (24%) patients with LVNC. 6 of 8 with unclassified cardiomyopathy (increased LV wall thickness with systolic dysfunction) had metabolic disease. Overall mortality was 17/28 (60.7%). In 6/10 the diagnosis of a respiratory chain defect was not made until after death.
Conclusions: There is considerable clinical heterogeneity among children with metabolic cardiomyopathies. They should be suspected in children with atypical cardiac features. Barth syndrome should be excluded in males with LVNC. Routine assay of respiratory chain enzymes on postmortem or explanted hearts may improve the diagnostic yield.

1097-101 Risk Factors Associated With Posttransplant Coronary Artery Disease in Pediatric Cardiac Transplant Recipients

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Background: Post-transplant coronary artery disease (PTCAD) is associated with a high mortality and a significant risk of graft failure. A number of associated factors have been postulated including ischemic time, gender mismatch, cytomegalovirus (CMV) infection, and rejection history. However, to date, the cause of PTCAD is not currently known.
Purpose: The purpose of the current study is to examine possible factors associated with PTCAD in a pediatric transplant population.
Methods: All pediatric patients less than 18 years of age who had undergone cardiac transplantation at Loma Linda University Children's Hospital during the years 1985-2001 were retrospectively reviewed.
Results: A total of 338 infants and children underwent orthotopic cardiac transplantation. Overall survival is 70%. Forty-three patients (12.1%) developed PTCAD. The average time to PTCAD was 5.96 yrs (range 1.14 - 14.45). Mortality within the PTCAD group was significantly higher that the remaining transplant population (57% vs. 26%, $p<0.001$). Patients who developed PTCAD had a higher number of rejection episodes per year (1.06 vs 0.49, $p=0.001$) There was a lower incidence of CMV found in the donors of those patients who went on to develop PTCAD (40% vs 60%, $p=0.008$). Patients who developed PTCAD had a shorter overall dopamine requirement in the post-operative period (3.87 vs 5.10 days, $p<0.05$). Factors not associated with PTCAD included: ischemic time of the graft, gender, gender mismatch, blood type, donor to recipient weight ratio, right and left ventricular end-diastolic pressure, days on mechanical ventilation in the post-operative period, CMV status of the recipients, or HLA tissue typing mismatch.
Conclusion: PTCAD among pediatric cardiac transplant recipients significantly increases mortality. PTCAD is associated with the number of rejection episodes. The role of CMV infection remains unclear. PTCAD is not associated with ischemic times, as has been previously suggested. Early and frequent coronary artery evaluation in children with frequent rejection episodes may be warranted.