

## Pediatric Chest Medicine 10:30 AM - 12:00 PM

### ACUTE AND CHRONIC EFFECTS OF INHALED ILOPROST THERAPY IN CHILDREN WITH PULMONARY ARTERIAL HYPERTENSION

D. D. Ivy MD<sup>\*</sup> Aimee K. Doran RN, NP Donna K. Parker RRT Lori R. Claussen RN Kelly Smith MD George Mallory MD Steven H. Abman MD University of Colorado/Children's Hospital, Denver, CO

**PURPOSE:** Inhaled iloprost is approved for the treatment of adults with pulmonary arterial hypertension (PAH); however, data in children are limited.

**METHODS:** Eleven children with PAH (age, 6.9-16.5 years; median, 12.4) were treated with inhaled iloprost (2.5 or 5.0 mcg/dose, 5-9 times daily) for 3-11 months (median, 7.8). Four had IPAH and 7 had APAH due to congenital heart disease. Pre-treatment response to iloprost vs. inhaled NO (20 ppm) during cardiac catheterization was compared. Iloprost was added to existing medications, including iv prostanooids (n = 4), bosentan (n = 8), and sildenafil (n = 11).

**RESULTS:** At cardiac catheterization, acute iloprost lowered mean PAP from 59 + 19 mmHg to 51 + 22 mmHg (p<0.05), which was identical to the response to inhaled NO. PFTs performed before and after acute iloprost treatment showed no change in FEV1 and FEF25-75% as a group; however, 3 children had a  $\geq$  than 20% decrease in airflow, and iloprost was not continued in 2 due to airways reactivity. Of 7 patients studied at 6 months, WHO functional class improved in 4 and remained stable in 3. In 5 patients evaluated at 6 months, 6-MWD (baseline mean 481m, range, 278-583m) increased by  $\geq$  10% in 2 patients, changed minimally in 2, and fell by > 10% in 1. Side effects were minimal during chronic therapy. Four patients who were receiving iv prostanooids were transitioned to iloprost without adverse effects. Two patients required transition to iv prostanooid therapy after 5 and 10 months. Three patients with a > 20% fall in mPAP to acute iloprost had a favorable long term response.

**CONCLUSION:** Inhaled iloprost was safe and well-tolerated in children with PAH, but therapy was precluded by bronchospasm in some children. Iloprost acutely lowered mPAP as effectively as inhaled NO, and acute response to iloprost was predictive of clinical response to chronic therapy.

**CLINICAL IMPLICATIONS:** Inhaled iloprost may be a useful therapy in children with PAH; however, larger clinical investigations are necessary.

**DISCLOSURE:** D Ivy, Consultant fee, speaker bureau, advisory committee, etc. Encysive, CoTherix, United Therapeutics; Product/procedure/technique that is considered research and is NOT yet approved for any purpose, Iloprost is not approved for use in children.

### AIRWAY HYPERREACTIVITY AFTER ILOPROST INHALATION IN PEDIATRIC PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

Kelly J. Smith MD<sup>\*</sup> George B. Mallory MD Steven H. Abman MD Dunbar D. Ivy MD, FCCP Texas Children's Hospital, Houston, TX

**PURPOSE:** Inhaled prostacyclin therapy is a new treatment option for patients with pulmonary arterial hypertension (PAH). Little is known about the effect of inhaled prostacyclin on airway caliber and function. Given that airway hyper-reactivity has been reported to be common among pediatric patients with idiopathic pulmonary hypertension, therapies that may exacerbate airway function should be carefully evaluated.

**METHODS:** Spirometry was obtained on 12 patients (age range 6.9 to 16.5 years) previously diagnosed with PAH before and after iloprost inhalation utilizing standard ATS criteria. All subjects were also on oral pulmonary vasodilator therapy at the time of testing.

**RESULTS:** Five of 12 patients developed a decrease in the FEF 25-75 of more than 15% (range 17-53%) following inhaled iloprost therapy and four had a concomitant drop of 7% or more in FEV1 (range 7 - 18%). In two of these patients, the drop in lung function was considered significant enough to preclude further use of iloprost. In two patients given albuterol after iloprost, there was an improvement in expiratory flows to baseline. Frank wheezing was not seen in these patients.

**CONCLUSION:** Inhaled iloprost, a recently introduced drug for PAH, can lead to acute lower airway obstruction. Chest pain is a reported adverse effect of inhaled iloprost therapy. Airway reactivity following inhaled iloprost may be one mechanism for chest pain in such patients.

**CLINICAL IMPLICATIONS:** Pulmonary function testing before and after inhaled prostacyclin therapy should be performed in pediatric patients with PAH before initiating chronic therapy with iloprost due to

possible airway obstruction. Further studies are needed to determine if this effect is preventable with inhaled corticosteroids and/or with beta2 agonists.

**DISCLOSURE:** Kelly Smith, Consultant fee, speaker bureau, advisory committee, etc, Co-therix.

### SERUM KL-6 LEVELS IN CHILDREN WITH INBORN ERRORS OF SURFACTANT METABOLISM AND NEUROENDOCRINE CELL HYPERPLASIA OF INFANCY

Minh L. Doan MD<sup>\*</sup> Haibin Zhang MD Okan Elidemir MD Philip G. Black MD Dion M. Roberts MD Robin R. Deterding MD Leland L. Fan MD Baylor College of Medicine, Texas Children's Hospital, Houston, TX

**PURPOSE:** Children's interstitial lung disease (chILD) encompasses a heterogeneous group of rare diffuse lung disorders with varying prognoses. More severe forms include the inborn errors of surfactant metabolism (IESM), such as surfactant protein C (SP-C) and ABCA3 deficiency. In contrast, neuroendocrine cell hyperplasia of infancy (NEHI) is considered a benign form. KL-6, a glycoprotein expressed mainly by activated type 2 pneumocytes, has been shown to be elevated in serum in a variety of interstitial lung diseases in both adults and children. Since alveolar epithelial cell hyperplasia is a common histologic feature of IESM, but not of NEHI, we hypothesized that KL-6 would be elevated in IESM, but not in NEHI.

**METHODS:** We measured KL-6 levels in the serum of a cohort of 10 healthy control children, 10 children with IESM, (including 4 with SP-C deficiency and 6 with ABCA3 deficiency), and 2 children with NEHI.

**RESULTS:** The mean ( $\pm$  SEM) serum KL-6 levels were 206 ( $\pm$  47), 3039 ( $\pm$  817), and 181 ( $\pm$  135) U/ml, for the control, IESM, and NEHI groups, respectively. Serum KL-6 levels were significantly elevated in the IESM group when compared to the control group (p<0.01) and the NEHI group (p<0.01). There was no difference in serum KL-6 levels between the control and NEHI groups (p=0.89).

**CONCLUSION:** Children with IESM have elevated serum KL-6 levels, in contrast to those with NEHI who have normal KL-6 levels.

**CLINICAL IMPLICATIONS:** Serum KL-6 may be a useful biomarker for distinguishing between severe and benign forms of chILD.

**DISCLOSURE:** Minh Doan, None.

### A THREE-YEAR LONGITUDINAL FOLLOW-UP STUDY OF A COHORT OF CHILDREN WITH BRONCHOPULMONARY DYSPLASIA (BPD)

Khoulood F. Fakhoury MBBS<sup>\*</sup> Charles Seller BBA Susan Pilney MBA Julie Katkin MD Baylor College of Medicine, Houston, TX

**PURPOSE:** This is a three-year prospective study to describe the characteristics, clinical course and Infant pulmonary function (PFTs) of children with BPD.

**METHODS:** Children diagnosed with BPD were identified from a teaching hospital neonatal ICU and followed at 3,6,9,12,18,24 and 36 months following discharge. Medical history and physical exam, were obtained each visit. PFTs were performed at 6, 12 and 24 months. Descriptive and correlation data analysis were performed.

**RESULTS:** 65 children (47% females, 39% Caucasian, 25% Hispanic, 36% African American) were recruited and 31 completed 36 months follow-up. 89% of children were < 28 weeks gestational age and 82% weighed <1000 grams. Cough and wheezing were reported by a significant number of children throughout the study. At 36 months cough was reported by 75% of children, wheezing in 30% and shortness of breath in 28% of children. At 24 months PFT's showed expiratory flow obstruction in 50% of children at 6 and 12 months and 45% at 24 months. Significant bronchodilator response was present in 30%, 23% and 21% of children at 6, 12, 24 months, respectively. This response diminished with time in all children but this was more pronounced in children with severe airway obstruction at baseline (<5th percentile flow). The majority of children with severe obstruction didn't show improvement in their flows over time. Inhaled steroid use correlated inversely with expiratory flow values (P value.037), however, the use of bronchodilators and diuretics did not. Functional residual capacity (FRC) showed a linear increase over time. The use of inhaled steroids positively correlated with FRC values (P=.03), but not the use of oxygen, bronchodilator or diuretics.

**CONCLUSION:** The majority of current BPD children are very premature with very low birth weight. Pulmonary symptoms continue to