Title: Sildenafil Use in an Infant Population: A Retrospective Review
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Background: The FDA recommends that sildenafil not be prescribed to children with pulmonary arterial hypertension (STARTS-1). STARTS-1 did not include children less than 1 year of age and the mortality risk in infants is unknown.

Methods: We conducted a retrospective review of hospitalized infants in the intensive care units of Children’s Hospital Los Angeles (CHLA) who received sildenafil between 2008-2012 documented in pharmacy records. We excluded patients with complex congenital heart disease. We analyzed patient characteristics, comorbidities and dose of sildenafil used with the primary outcome being survival at discharge. Sildenafil dose ranges were based on the STARTS-1 trial; low=<1.5mg/kg/day; medium=1.5-3.75mg/kg/day; high=3.76-7.5mg/kg/day; very high=>7.5mg/kg/day.

Results: 526 patients (2008-2012) received sildenafil: 392 were infants. 147 infants without complex congenital heart disease were studied.

Median age at start of sildenafil was 12.5 days (range 0-320). 34% of patients were admitted to CHLA with a prior diagnosis of pulmonary hypertension from a referral hospital. 76% patients had severe pulmonary hypertension based on echocardiogram. 46% of patients were born preterm of which 82% had bronchopulmonary dysplasia. 80% of patients had persistent pulmonary hypertension of the newborn. 98% of patients required invasive ventilatory support, vasopressors (89%), ECMO (35%) and additional pulmonary vasodilators (17%) during hospitalization. 26% of patients who survived required home mechanical ventilation.

Our data revealed 29% mortality at discharge. The patients who died were more likely to be full-term (59%), males (58%), with simple congenital heart disease (79%) of which 97% were unrepaired. Patients who died were younger compared to those alive at discharge (median age 36 days vs 96 days, respectively). Four (10%) patients who died had alveolar capillary dysplasia on autopsy. Among those with congenital diaphragmatic hernia who died, 50% were unrepaired.

There was a statistically significant difference in mortality with increased dose of sildenafil (p<0.00). Mortality was increasing with increased sildenafil dose, low (14%), medium (19%), high (49%), and very high (90%). When compared to mortality statistics of CHLA’s ICUs for the same period, the mortality in our population was 4.6 compared to 1.3 per 1000 patient-days.

Conclusion: Sildenafil was given to critically ill infants with multiple risk factors for mortality. Though higher doses cannot be causally related to mortality, there appears to be no added benefit to therapy by escalating the sildenafil dose.

Type: Clinical Science