Assessing outcomes in pediatric patients with pulmonary hypertension following treatment with sildenafil or tadalafil

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Introduction

According to the 2015 American Heart Association and American Thoracic Society (AHA/ATS) guidelines for the treatment of pediatric pulmonary hypertension, pulmonary hypertension (PH) in children can lead to significant morbidity and mortality resulting in poor long term outcomes in patients with severe PH. PDE-5 inhibitors are one of the primary classes of pharmacologic agents used to treat and manage pediatric PH. Sildenafil has historically been the primary PDE-5 inhibitor of choice, however it requires frequent dosing due to its short half-life. Tadalafil is an alternative PDE-5 inhibitor with a much longer half-life that allows once daily dosing. It has shown to be well tolerated, safe, and effective in adults with PH but there is little study data available for use in children with PH.

Objective

To assess outcomes in pediatric patients with pulmonary hypertension following treatment with tadalafil or sildenafil

Methods

- Retrospective Chart Review of a single site
- SSM Health IRB approved
- Inclusion Criteria:
  Inpatient and outpatient SSM Cardinal Glennon patients aged 2 months to less than 18 years who were treated with tadalafil or sildenafil for pulmonary hypertension.

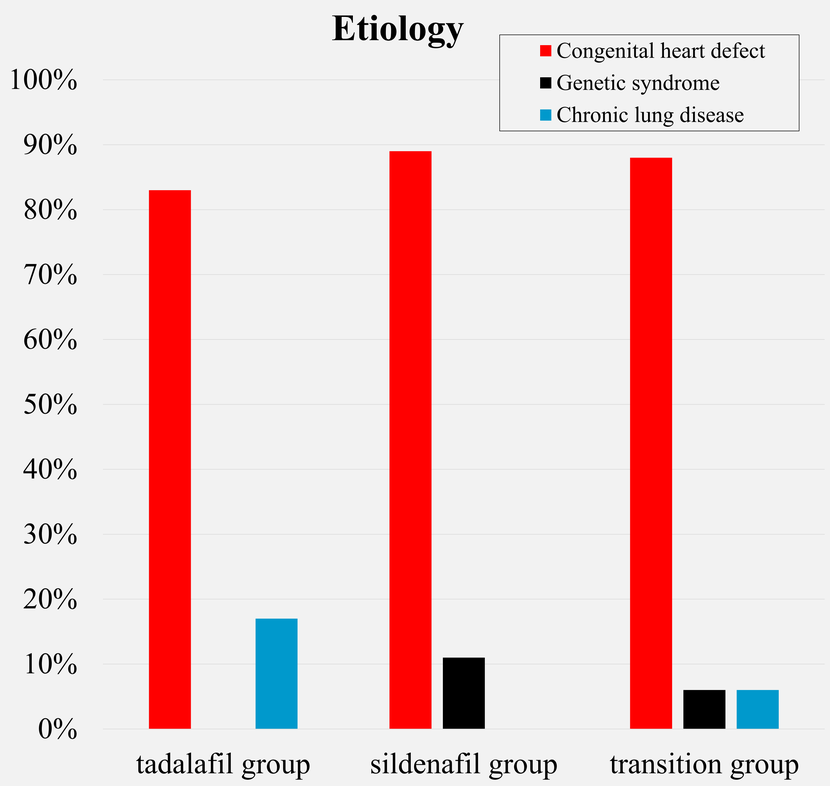
- Exclusion Criteria:
  Inpatient and outpatient SSM Cardinal Glennon patients less than 2 months of age, patients who lacked ECHO or CATH data, or were diagnosed with congenital diaphragmatic hernia, Trisomy 13 or 18, or pulmonary vein anomalies.

- Data Collected:
  - patient demographics (age upon therapy initiation; sex; ethnicity, weight upon first dose, etiology of PH)
  - age upon therapy initiation
  - weight upon therapy initiation
  - duration of therapy
  - pulmonary vascular resistance (PVR)
  - tricuspid valve regurgitation (TVR)
  - right ventricle systolic pressure (RVSP)
  - adverse effects
  - mortality within one year of therapy initiation
- Data Analysis: descriptive statistics

Results

	sildenafil Group n = 9	tadalafil group n = 12	transition group sildenafil n = 16	transition group tadalafil n = 16
Gender (male/female)	6/3	4/8	4/12	
Ethnicity (n/% Caucasian)	9 (100)	12 (100)	16 (100)	
Age upon therapy initiation (months)	6.6 (2.7-166)	6.6 (2.3-165.8)	6.3 (2.7-183.8)	
Weight upon therapy initiation (kg)	6.3 (2.15-42.5)	5.3 (4.3-38.3)	6.5 (3.4-33.1)	
Dose upon therapy initiation (mg)	1.4 (0.3-20)	5 (1.25-10)	9.7 (2.4-20)	4 (0.85-10)
Duration of therapy (days)	860 (10-2383)	367 (22-791)	321 (4-816)	604 (3-1831)
PVR (Wood units)	2.72 (1.47-7.21), n = 4	1.57 (0.7-6.03), n = 4	N/A	
TVR (m/s)	3.01 (2.8-4.9), n = 5	3.3 (1.35-4.1), n = 7	3.2 (2.07-4.0), n = 5	3.85 (3.49-4.43), n = 6
RVSP (mmHg)	36.2 (31-96.2), n = 5	43.53 (7.45-68.7), n = 7	44.95 (29.8-80), n = 6	58.35 (48.6-78.7), n = 6
Adverse effects experienced, n (%)	4 (33)	0	3 (19)	0
Mortality within 1 year of therapy initiation, n (%)	1 (8)	2 (22)	0	3 (19)

*values are presented as median (range), or n (%)



Discussion

- Most common etiology for PH was secondary to congenital heart defect
- 1 year mortality appeared lowest in sildenafil group, with the tadalafil and transition group having similar mortality
- Tadalafil appeared to be well tolerated with no documented adverse effects
- Difference of RVSP and TVR between sildenafil and tadalafil in transition group may be due to progression of disease
- Limitations: single center retrospective design, small ethnically homogenous sample size, treatment duration assessed using inpatient or clinic progress notes, ECHO and CATH data not consistently recorded with each procedure, unable to assess severity of disease in each group, and no outpatient adverse event data available

Conclusion

- Tadalafil appeared to be well tolerated but due to the limitations of the study, no conclusions could be drawn regarding the effects of tadalafil in pediatric patients with pulmonary hypertension. Larger studies are required to further assess the effects of tadalafil in this patient population.