Chronic Sildenafil Use following PGE Exposure in Infants with Congenital Diaphragmatic Hernia

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BACKGROUND

- Congenital diaphragmatic hernia (CDH) is a congenital anomaly that is often complicated by pulmonary hypertension (PH).
- Prostaglandin E1 (PGE) infusion to maintain ductus arteriosus patency and relieve the pressure-loaded right ventricle has been reported in this population[1].
- PGE has also been shown to reduce pulmonary vascular resistance, thereby improving PH in this population[2].
- The impact of PGE on subsequent need for chronic PH therapy (i.e., sildenafil) has not been examined.

OBJECTIVE

To describe patterns of sildenafil usage following PGE exposure in infants with CDH-PH

HYPOTHESIS

PGE exposure will mitigate or delay the need for subsequent chronic PH therapy in CDH.

METHODS

- Retrospective chart review performed from January 2011 through September 2021
- **Inclusion Criteria:** Initial hospitalization, with diagnosis of CDH + exposure to PGE for treatment of PH
- **Exclusion Criteria:** Cyanotic congenital heart disease or major structural birth defects
- Demographics, clinical characteristics, outcomes of interest, and medication data were collected
- Patterns of sildenafil use and outcomes of interest following PGE exposure were identified and described using descriptive statistics
- Post-hoc analysis was performed using bivariate statistics to determine demographic/clinical differences between survivors and non-survivors

Demographics	
Number of CDH Patients, N	18
Male n, (%)	12 (67)
Median Gestational Age wks [IQR]	38 [36 2/7, 38 6/7]
Median Birthweight grams [IQR]	2885 [2388, 3088]
Average % O/E TFLV %, std	27 +/-13.3
Average % Liver Herniation %, std	25 +/-12.2
FETO n, (%)	7 (39)
Median Repair, days	2.5 [2, 4]
Patch Repair n, (%)	15 (83)
Left CDH n, (%)	13 (76)
Right CDH n, (%)	4 (22)
Bilateral CDH n, (%)	1 (6)
ASD or PFO n, (%)	15 (83)
VSD n, (%)	3 (17)

Table 1: Patient Demographics. The table illustrates clinical characteristics and patient demographics within the cohort.

	Surviving Infants	Non-Survivors	p-value
Total Number of CDH Infants n, %	12 (67)	6 (33)	-
Male n, (%)	8 (67)	4 (67)	p=1.0
Median Gestational Age wks, std	38 ± 1.2	36 ± 3.0	p=0.078
Median Birthweight grams, std	2469 ± 628	3090 ± 665	p=0.076
Average % O/E TFLV %, std	32 ± 12	15 ± 6	p=0.007*
Average % Liver Herniation %, std	22 ± 12.6	32 ± 8.52	p=0.101
FETO n, (%)	4 (33)	3 (50)	p=0.627
iNO Exposure n, (%)	12 (100)	6 (100)	p=1.0
ECMO n, (%)	9 (75)	6 (100)	p=0.515
Sildenafil Use n, (%)	11 (92)	5 (83)	p=1.0
Median Age at PGE Initiation days, [IQR]	1.0 [1,2]	5.0 [4,5]	p=0.003*

Table 2: Post-hoc Analysis of Survivors vs. Non-Survivors. Survivors had less severe prenatal markers of disease (32% ± 12 vs. 15% ± 6, p=0.007) than non-survivors. Survivors also demonstrated earlier median age of initiation of PGE (1.0 days IQR [1,2] vs. 5.0 IQR [4,5], p-0.003).

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RESULTS

- 18 infants with CDH were identified. Patient demographic information can be seen in **Table 1.**
- Average Observed: Expected Total Fetal Lung Volume (O/E TFLV) for included infants was in the severe range (27% ± 13.3) with the majority requiring patch repair (83%).
- 16/18 (89%) of infants were started on sildenafil at a median age of 6.5 days (IQR [4.75, 9.25]).
- Sildenafil was not started in two PGE-exposed infants due to early mortality (n=1) and mild disease severity not requiring escalation of care (n=1).
- 3/11 surviving infants started on sildenafil were weaned off prior to discharge
- 3/5 non-survivors died of ECMO complications. The remaining 2/5 died from sepsis.
- **Table 2** demonstrates Post-hoc analysis of survivors vs. non-survivors **.**

CONCLUSION/NEXT STEPS

- Most infants treated with PGE still required sildenafil therapy for the treatment of PH in the first 10 days of life.
- However, the cohort represented a severe group of CDH patients, demonstrated by the low O/E TFLV. The only surviving infant not requiring sildenafil therapy had mild prenatal disease severity.
- Interestingly, non-surviving infants were started on PGE later in life despite more severe prenatal markers of disease than survivors.
- Next steps: 1. Compare timing of sildenafil therapy to disease matched infants NOT exposed to PGE and 2. compare outcomes of early vs. late PGE exposure.

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