Sildenafil Exposure in the Neonatal Intensive Care Unit

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Disclosures

Krystle Perez has documented that her presentation involves comments or discussion of unapproved or off-label, experimental, or investigational use of sildenafil. The authors have no financial relationships to disclose or conflicts of interest to resolve.

Introduction

• Pulmonary hypertension is associated with high morbidity and mortality in term and preterm infants.
• Sildenafil is FDA approved for adults with pulmonary arterial hypertension as it promotes pulmonary vasodilation.
• Despite anecdotal use, there is no conclusive evidence to support sildenafil use in the neonatal intensive care unit (NICU).

Objective

• To determine the epidemiology and clinical outcomes of term and preterm infants exposed to sildenafil.

Methods

• A retrospective cohort of infants born between 2001 and 2011 at ≥23 weeks gestational age was assembled using the Pediatrix Data Warehouse.
• Data were obtained from admission, discharge, and daily progress notes.
• Contingency table analysis was performed to examine the association between characteristics of the infants and categorized gestational age.

Results

Table. Demographic Data and Outcomes of Infants Exposed to Sildenafil

<table>
<thead>
<tr>
<th>GA</th>
<th>&lt;32 weeks Mage</th>
<th>≥32 weeks Mage</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>463</td>
<td>321</td>
</tr>
<tr>
<td>Male</td>
<td>281 (61%)</td>
<td>205 (64%)</td>
</tr>
<tr>
<td>Antenatal steroids, yes (%)</td>
<td>354 (76%)</td>
<td>32 (10%)</td>
</tr>
<tr>
<td>Delivery, cesarean section (%)</td>
<td>334 (72%)</td>
<td>220 (62%)</td>
</tr>
<tr>
<td>Median gestational age, wk (5th, 95th%-ile)</td>
<td>25 (23, 30)</td>
<td>38 (32, 48)</td>
</tr>
<tr>
<td>Median birth weight, g (5th, 95th%-ile)</td>
<td>680 (430, 1408)</td>
<td>3020 (1494, 4210)</td>
</tr>
</tbody>
</table>

Diagnoses (%)

Pulmonary hypertension: 363 (79%) 341 (92%)
Meconium aspiration syndrome: 0 48 (13%)
Diaphragmatic hernia: 2 (7%) 70 (19%)
Congenital heart disease: 55 (12%) 103 (28%)
Chronic lung disease: 382 (80%) 176 (48%)
Interventions (%)
Mechanical ventilation: 305 (71%) 179 (51%)
Inhaled nitric oxide: 268 (59%) 255 (68%)
Surfactant: 361 (79%) 140 (38%)
Outcome (%)
| Death | 101 (23%) | 68 (18%) |

*11 infants missing data. GA = gestational age.

Figure 1. Sildenafil Exposure by Admit Year

*Data for 6 months of 2011

Figure 2. Sildenafil Exposure by Gestational Age

Figure 3. Age at First Sildenafil Exposure

Figure 4. Survival Curves for Infants Exposed to Sildenafil

Conclusions

• Sildenafil use has increased in NICUs nationwide.
• Pulmonary hypertension and chronic lung disease were the most common diagnoses in exposed infants <32 weeks and ≥32 weeks gestational age.
• Despite sildenafil use, exposed infants often die.
• More research is needed to determine the efficacy and safety profile of sildenafil in infants.