Anesthetic Considerations for Spinal Muscular Atrophy Patients Undergoing Spinraza (Nusinersen) Therapy


1. Children’s Hospital of Philadelphia (CHOP), Philadelphia, PA, Department of Anesthesiology and Critical Care Medicine
2. University of Pennsylvania Perelman School of Medicine

Background

- Spinal muscular atrophy (SMA) is a motor neuron disorder caused by a defect in the SMN1 gene that is necessary for muscle survival
- Nusinersen (Spinraza) is the first pharmacological treatment for SMA
- Spinraza is given intrathecally and increases SMN protein levels by altering the splicing of SMN2 messenger RNA

Case Series

- 52 patients were selected to receive Spinraza (Table 1)
- Ages 3 months – 36 years
- SMA types 1 – 3
- 44 patients underwent intrathecal injection of Spinraza
- Four loading doses on days 1, 15, 29, and 58 followed by doses every 120 days

<table>
<thead>
<tr>
<th>Patient Demographic</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at Initial Presentation</strong></td>
<td></td>
</tr>
<tr>
<td>3-12 months</td>
<td>1</td>
</tr>
<tr>
<td>1-4 years</td>
<td>14</td>
</tr>
<tr>
<td>5-9 years</td>
<td>12</td>
</tr>
<tr>
<td>10-17 years</td>
<td>16</td>
</tr>
<tr>
<td>&gt;18 years</td>
<td>9</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>25</td>
</tr>
<tr>
<td>Female</td>
<td>27</td>
</tr>
<tr>
<td><strong>SMA Type</strong></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td>3</td>
<td>22</td>
</tr>
</tbody>
</table>

Pre-operative Process

- Multi-disciplinary evaluation by anesthesia, neurology, pulmonary
- Staggered the patients’ dose schedules
- Continuity of care was provided by anesthesia nurse practitioners
- Procedure location was based on anticipated difficulty of lumbar puncture (LP) and anticipated anesthetic challenge
- Patients instructed to bring their non-invasive respiratory support devices
- Clear liquids encouraged until 2 hours prior to arrival
- Before the procedure, IV placed, labs drawn to check coagulation studies and platelet count, hydration started, topical lidocaine applied

Results

- Anesthetic management varied from anesthesia standby to general anesthesia with a supraglottic airway in 3 patients
- Most patients received IV anesthetic with midazolam, propofol, or dexmedetomidine and a natural airway
- 11 patients received inhalational anesthetic for at least 1 LP
- 9 patients ages 10 years and older tolerated all LPs with only local anesthesia and midazolam
- 9 patients who initially needed anesthesia required only midazolam and a Child Life Specialist on subsequent injections
- 2 patients had a tracheostomy and 2 used home BiPAP
- No patients required escalation of care due to respiratory support
- Complications
  - Pain at injection site (6)
  - Vomiting (3)
  - Mild headache requiring only supportive care (9)
- 3 patients had unsuccessful LPs
  - 2 required Interventional Radiology
  - 1 had a previous posterior spinal fusion requiring a laminectomy to initiate therapy that was complicated by dural tear and CSF leak requiring ICU admission

Conclusions

- A comprehensive perioperative program can successfully screen and prepare SMA patients for Spinraza therapy and allocate resources efficiently
- Although SMA patients are particularly vulnerable to post-anesthesia respiratory issues, nearly all patients tolerated their brief anesthetic well and were discharged home after observation
- Many patients did well with anesthesia for their first LP, and then after they became familiar with the procedure only required anesthesia standby for subsequent LPs