The Power of Outpatient Botulinum Injections in Preventing Hirschsprung Associated Enterocolitis

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The Power of Outpatient Botulinum Injections in Preventing Hirschsprung Associated Enterocolitis

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- No disclosures

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Hirschsprung Disease (HSCR) = lack of migration of the ganglion cells in the rectum and distal colon\textsuperscript{1}

- Aganglionic limb lacks peristalsis, leading to obstruction
- The proximal ganglionic limb becomes dilated

Surgical Treatment for HSCR

- Determine where ganglion cells are present
- Remove aganglionic (diseased) colon
- “pull-through” ganglionic intestine to anus
- Preserve anal sphincter function
Hirschsprung Associated Enterocolitis

- Hirschsprung associated enterocolitis (HAEC) is a potentially life-threatening complication of HSCR

  • Responsible for ½ of all HSCR-associated deaths\(^1\)

  • Incidence of HAEC = 2-35\(^\%\)\(^2\)-\(^4\)

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Hirschsprung Associated Enterocolitis

- **Risk factors**: long-segment disease, Trisomy 21, and prior episodes of HAEC

- **Symptoms**:)
  - Abdominal distention
  - Loose stools
  - Fever
  - Explosive diarrhea
  - Rectal bleeding
  - Toxic Megacolon
  - Shock
Mainstay of Treatment: 1,2
- Rectal irrigations
- Antibiotics

Standardization of Care: 3
- Decreased length of stay
- Earlier oral intake
- Less use of TPN

Botulinum Toxin Injections

Stasis from obstruction at the level of the internal anal sphincter (IAS) may contribute to HAEC\(^1,2\) and obstructive symptoms and potentially decrease the number of hospitalizations for enterocolitis\(^2,3\).

Other studies: Botulinum injections improve obstructive symptoms in up to 82% of patients and cause a reversible relaxation of the IAS and obstructive symptoms.\(^2\)
Aim

To determine if outpatient botulinum injections:

- Delayed the development of HAEC

- Increased the interval between HAEC admissions
HAEC Protocol

- Initiated in 2018
- Utilized for inpatient HAEC management
- Development of Comprehensive Colorectal Center
Comprehensive Colorectal Center

- Includes pediatric surgery, gastroenterology, urology, gynecology
- Dedicated outpatient nurses to help triage patient phone calls
- Education for parents on symptoms of HAEC and performing rectal irrigations
- Routine clinic visits (1 month, 3 months, 6 months, and 1 year post-surgery
Methods

▪ Retrospective Review

▪ Inclusion Criteria:
  – Time period: July 2010 – July 2020
  – Patients diagnosed with Hirschsprung disease
  – Status-post pull-through procedure

▪ Exclusion Criteria:
  – No episode of HAEC or no outpatient BT injections received
Methods

Three Groups:
- Patients who never received BT injections
- Patient who developed HAEC prior to first BT injection
- Patients who received BT injection prior to first HAEC episode

Primary Outcome Measures:
- Number of HAEC episodes
- Timing to Recurrent HAEC episode
Continuous variables compared used one-way ANOVA test

Proportions compared using Chi-Square test

STATA® used for analysis

p< 0.05 = statistic significance
Results

- Demographics: 80 patients
  - 60 (75%) male
  - 55 (69%) Caucasian
  - 15 (19%) had Trisomy 21
  - 58 (73%) had short-segment disease

- Pull-through Technique:
  - 36 (45%) had Soave
  - 31 (39%) had Swenson
  - 8 (10%) had Duhamel

Median time to pull-through: 150 days (IQR 16, 132)
Results

- 46 patients (64%) had at least one episode of HAEC
  - Median time from pull-through to HAEC episode: 71 days (IQR 16, 443)

- 64 patients (89%) had at least one outpatient BT injection
  - Median time from pull-through to BT injection: 486 days (IQR 91, 1325)
  - Median number of BT injections: 2 (IQR 1, 2)
## Results

<table>
<thead>
<tr>
<th></th>
<th>Never Received BT Injections (n=9)</th>
<th>HAEC Prior to BT Injection (n=35)</th>
<th>BT Injection prior to HAEC (n=28)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Gender</td>
<td>8 (89%)</td>
<td>26 (74%)</td>
<td>20 (71%)</td>
<td>0.57</td>
</tr>
<tr>
<td>Caucasian</td>
<td>6 (67%)</td>
<td>27 (77%)</td>
<td>19 (68%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Trisomy 21</td>
<td>2 (22%)</td>
<td>5 (14%)</td>
<td>7 (25%)</td>
<td>0.55</td>
</tr>
<tr>
<td><strong>Length of Disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Short Segment</td>
<td>6 (67%)</td>
<td>25 (71%)</td>
<td>21 (75%)</td>
<td>0.88</td>
</tr>
<tr>
<td>-Long Segment</td>
<td>0 (0%)</td>
<td>6 (17%)</td>
<td>5 (18%)</td>
<td>0.84</td>
</tr>
<tr>
<td>-Unknown</td>
<td>3 (33%)</td>
<td>4 (11%)</td>
<td>2 (7%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Ostomy Prior to Pull-through</td>
<td>7 (78%)</td>
<td>21 (60%)</td>
<td>16 (57%)</td>
<td>0.53</td>
</tr>
<tr>
<td><strong>Type of Pull-through</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Soave</td>
<td>5 (56%)</td>
<td>16 (46%)</td>
<td>12 (43%)</td>
<td>0.80</td>
</tr>
<tr>
<td>-Swenson</td>
<td>1 (11%)</td>
<td>14 (40%)</td>
<td>13 (46%)</td>
<td>0.16</td>
</tr>
<tr>
<td>-Duhamel</td>
<td>0 (0%)</td>
<td>3 (8%)</td>
<td>3 (11%)</td>
<td>0.96</td>
</tr>
<tr>
<td>-Unknown (OSH)</td>
<td>3 (33%)</td>
<td>2 (6%)</td>
<td>0 (0%)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Median Time to Pull-through (IQR)</strong></td>
<td>274 days (12, 718)</td>
<td>143 days (16, 341)</td>
<td>143 days (14, 230)</td>
<td>0.48</td>
</tr>
</tbody>
</table>
# Results

<table>
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<th>BT Injection Prior to HAEC (n=28)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterocolitis Episode</td>
<td>4 (44%)</td>
<td>23 (66%)</td>
<td>2 (7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to Enterocolitis Episode (Range)</td>
<td>5 – 28 days</td>
<td>9 – 746 days</td>
<td>24 and 406 days</td>
<td>0.29</td>
</tr>
<tr>
<td>Number of Total HAEC Episodes (Range)</td>
<td>1 – 11</td>
<td>1 - 12</td>
<td>0 - 1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinic Visits Prior to Enterocolitis Episode</td>
<td>1 (0, 2)</td>
<td>1 (1, 3)</td>
<td>3 (2, 4)</td>
<td>0.01</td>
</tr>
<tr>
<td>Phone Calls Prior to Enterocolitis Episode</td>
<td>0 (0, 1)</td>
<td>1 (0, 2)</td>
<td>6 (5, 7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Contacts with Surgery Team Prior to Enterocolitis Episode</td>
<td>3 (2, 4)</td>
<td>2 (1, 6)</td>
<td>9 (7.5, 12.5)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Comparison of Patients Treated after the Formation of the Comprehensive Colorectal Center

<table>
<thead>
<tr>
<th></th>
<th>HAEC Prior to BT Injection (n=10)</th>
<th>BT Injection Prior to HAEC (n=15)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to First Enterocolitis Episode</td>
<td>27 days (15, 80)</td>
<td>248 days (52, 443)</td>
<td>0.02</td>
</tr>
<tr>
<td>Time to First Botox Injection</td>
<td>98 days (28, 194)</td>
<td>38 days (35, 58)</td>
<td>0.18</td>
</tr>
<tr>
<td>Number of Clinic Visits</td>
<td>1.5 (0, 2)</td>
<td>3 (2, 4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Number of Phone Calls to CCC</td>
<td>2 (1, 3)</td>
<td>6 (5, 7)</td>
<td>0.004</td>
</tr>
<tr>
<td>Number of Contacts with CCC Team</td>
<td>2.5 (2, 4)</td>
<td>9 (8, 9)</td>
<td>0.004</td>
</tr>
</tbody>
</table>
Limitations:

- Retrospective review
- Pre-surgical factors (HAEC episodes prior to pull-through) were not included in analysis

Future Research:

- Prospective trials are needed to develop best practice guidelines for both inpatient and outpatient HSCR management
Conclusions

- Use of outpatient Botulinum toxin injections:
  - Decrease episodes of Hirschsprung associated enterocolitis
  - Increase the interval between HAEC episodes

- Use of a multidisciplinary colorectal center can help triage symptoms as an outpatient
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