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\(^1\)

- 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

  - Incidence of HAEC = 2-35%

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
HAEC Treatment

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 potentially decrease the number of hospitalizations for obstructive symptoms and enterocolitis\(^2,3\).

Other studies: Botulinum injections improve obstructive symptoms and cause a reversible relaxation of the IAS and may contribute to HAEC\(^1,2\).
To determine if outpatient botulinum injections:

- Delayed the development of HAEC
- Increased the interval between HAEC admissions
- 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
Statistical Analysis

- 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)
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></td>
<td></td>
<td></td>
<td>0.53</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><strong>0.01</strong></td>
</tr>
<tr>
<td>Median Time to Pull-through (IQR)</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

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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</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</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>
## Subgroup Analysis

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
Acknowledgements

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