Exclusive enteral nutrition therapy in pediatric Crohn’s disease results in long-term avoidance of corticosteroids: results of a propensity score-matched cohort analysis

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Presented by: Jessica Connors, PhD
Disclosures

Dr. Johan Van Limbergen
- Nestlé, Janssen

Dr. Anthony Otley
- Nestlé, AbbVie, Janssen, Optimer, Astra Zeneca, Astellas, Shire
Exclusive enteral nutrition (EEN) induction therapy

- Recommended as a first-line treatment in pediatric Crohn’s disease (CD)
- Complete liquid formula diet (PO or NG) for 4-12 weeks
- Equal efficacy with corticosteroids (CS)
  - Low risk, mucosal healing, improved nutritional status
  - Early steroid avoidance
Study Aim

To compare short- and long-term outcomes in pediatric CD patients initially managed with EEN or corticosteroid (CS) therapy
Located in Halifax, Nova Scotia

Tertiary pediatric GI care for Maritime provinces

EEN is regularly offered as first-line treatment for CD patients

Nova Scotia has highest incidence of pediatric-onset CD in Canada

Adapted from: Benchimol et al. (2017) Am. J. Gastroenterol.
Methods

Retrospective chart review (January 2001 to March 2015) of pediatric patients newly diagnosed with CD who received either EEN or CS for induction

Propensity score matching:
- Controls for treatment selection bias
- Propensity score = probability of treatment given a set of observed baseline covariates
- Patients with most similar scores are matched
127 patients identified:
  46 CS
  81 EEN

5 excluded
(switched therapy):
  3 CS → EEN
  2 EEN → CS

122 included:
  43 CS
  79 EEN

Propensity score matching

111 patients:
  35 CS
  76 EEN

Baseline covariates:
• age
• gender
• weight
• height
• PCDAI
• disease location
• disease behavior
• perianal disease
Baseline clinical and phenotypic characteristics of matched cohort

<table>
<thead>
<tr>
<th></th>
<th>CS (n=35)</th>
<th>EEN (n=76)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male/female)</td>
<td>9/26</td>
<td>28/48</td>
<td>0.28</td>
</tr>
<tr>
<td>Median age, y [range]</td>
<td>12.2 [6.8-16.0]</td>
<td>11.9 [3.3-16.3]</td>
<td>0.17</td>
</tr>
<tr>
<td>PCDAl score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild &lt;30</td>
<td>12 (34.3)</td>
<td>37 (48.7)</td>
<td>0.27</td>
</tr>
<tr>
<td>Moderate ≥30 to &lt;40</td>
<td>14 (40.0)</td>
<td>20 (26.3)</td>
<td></td>
</tr>
<tr>
<td>Severe ≥40</td>
<td>9 (25.7)</td>
<td>19 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Anthropometrics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height z-score (Htz) (mean ± SD)</td>
<td>-0.01 ± 1.1</td>
<td>-0.44 ± 1.2</td>
<td>0.07</td>
</tr>
<tr>
<td>Growth failure (Htz ≤1.65), n (%)</td>
<td>1 (2.9)</td>
<td>13 (17.1)</td>
<td>0.06</td>
</tr>
<tr>
<td>BMI z-score (mean ± SD)</td>
<td>-0.58 ± 1.3</td>
<td>-1.2 ± 1.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Disease location, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L1</td>
<td>3 (8.6)</td>
<td>7 (9.2)</td>
<td>0.58</td>
</tr>
<tr>
<td>L2</td>
<td>4 (11.4)</td>
<td>4 (5.3)</td>
<td></td>
</tr>
<tr>
<td>L3</td>
<td>12 (34.3)</td>
<td>20 (26.3)</td>
<td></td>
</tr>
<tr>
<td>L1 + L4</td>
<td>1 (2.9)</td>
<td>4 (5.3)</td>
<td></td>
</tr>
<tr>
<td>L2 + L4</td>
<td>5 (14.3)</td>
<td>8 (10.5)</td>
<td></td>
</tr>
<tr>
<td>L3 + L4</td>
<td>10 (28.6)</td>
<td>33 (43.4)</td>
<td></td>
</tr>
<tr>
<td>Disease behaviour, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B1</td>
<td>35 (100)</td>
<td>75 (98.7)</td>
<td>1.00</td>
</tr>
<tr>
<td>B2</td>
<td>0</td>
<td>1 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Perianal disease, n (%)</td>
<td>4 (11.4)</td>
<td>3 (3.9)</td>
<td>0.20</td>
</tr>
</tbody>
</table>
## Outcomes

### Short-term outcomes:
- **Response**: $\Delta\text{PCDAI} \geq 12.5$, w/o height item
- **Remission**: PCDAI $\leq 7.5$, w/o height item

### Long-term outcomes:
- **Steroid exposure**
- **Escalation to biologics**
- **Disease progression**: extension, onset of B2/B3 behavior, onset of perianal disease
- **Linear growth**
- **Complications**: hospitalizations, surgery

<table>
<thead>
<tr>
<th>12 weeks</th>
<th>1 yr</th>
<th>2 yrs</th>
<th>4 yrs</th>
<th>6 yrs</th>
</tr>
</thead>
</table>

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**Notes:**
- PCDAI: Pediatric Crohn's Disease Activity Index
- $\Delta$: change in a value

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**Symbols:**
- $\geq$: greater than or equal to
- $\leq$: less than or equal to
- #: pound symbol

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**Institutions:**
- IWK Health Centre
- Dalhousie University
- MiraPeds.ca
EEN induced higher rates of remission compared to CS

![Graph showing treatment response and percent remission](image_url)
EEN was associated with long-term steroid avoidance

% Steroid naive

<table>
<thead>
<tr>
<th>Time from diagnosis (years)</th>
<th>% of EEN-treated patients</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>47%</td>
<td>76</td>
</tr>
<tr>
<td>4</td>
<td>40%</td>
<td>48</td>
</tr>
<tr>
<td>6</td>
<td>19%</td>
<td>21</td>
</tr>
</tbody>
</table>
Long-term steroid avoidance was not associated with increased biologic use

% Steroid naïve, +/- biologics

\[
\begin{array}{c}
\text{Time from diagnosis (years)} \\
2 \quad 4 \quad 6
\end{array}
\]

\[
\begin{array}{c}
\% \text{ of EEN-treated patients} \\
0 \quad 20 \quad 40 \quad 60
\end{array}
\]

- n=76
- n=48
- n=21

- no biologic use
- biologic use
EEN- and CS-treated groups had comparable biologic use by maximum follow-up
EEN-treated group exhibited early linear growth improvement
Disease progression and complications were comparable between CS- and EEN-treated groups

<table>
<thead>
<tr>
<th></th>
<th>CS</th>
<th>EEN</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of perianal disease, n (%)</td>
<td>1 (3.2)</td>
<td>5 (7.0)</td>
<td>0.66</td>
</tr>
<tr>
<td>Onset of stricturing behavior, n (%)</td>
<td>2 (5.7)</td>
<td>6 (8.2)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Anatomic extension, n (%)</strong> c</td>
<td>0 (0.0)</td>
<td>8 (26.7)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hospitalization, n (%)</td>
<td>8 (22.9)</td>
<td>11 (14.8)</td>
<td>0.42</td>
</tr>
<tr>
<td>Surgery, n (%)</td>
<td>2 (5.7)</td>
<td>3 (4.1)</td>
<td>0.66</td>
</tr>
</tbody>
</table>

*Patients with perianal disease at diagnosis were not included*

*One patient presenting with stricturing behavior at diagnosis was not included*

*Patients with maximal disease extension at diagnosis and/or did not undergo follow-up endoscopic/radiological assessments were not included*
Limitations

- Retrospective data collection
  - 14+ year period (2001 to 2015)
  - Changing practices (e.g. biologic protocols) and parameters for assessment (e.g. fecal calprotectin, MR enterography)

- Potential covariates (‘hidden bias’) not included in propensity score
Conclusion

• EEN induced higher rates of remission compared to CS

• EEN had an early positive impact on linear growth

• Long-term steroid avoidance via EEN is feasible without increased need for escalation to biologics, or increased complications or need for surgery

• A subgroup of pediatric CD patients may benefit most from early nutrition-focused intervention
Acknowledgments

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Dr. Amy Grant
Dr. Nick Giffin
Brad MacIntyre
Dr. Mohsin Rashid
Dr. Gamal Mahdi
Dr. Angela Noble
Biological markers for EEN- and CS-treated groups

- **Albumin**
  - **CS** vs **EEN**:
    - BSL 4-12 wks: No significant difference.
    - 4-12 wks: CS shows a decrease compared to EEN.

- **ESR**
  - **CS** vs **EEN**:
    - BSL 4-12 wks: No significant difference.
    - 4-12 wks: CS shows a decrease compared to EEN.

- **Platelets**
  - **CS** vs **EEN**:
    - BSL 4-12 wks: No significant difference.
    - 4-12 wks: CS shows an increase compared to EEN.
Propensity score matching: before and after

Unmatched cohort

Matched cohort

% of patients

propensity score

% of patients

propensity score