Clinical Outcomes in Patients With Parkinson's Disease Treated With a Monoamine Oxidase Type-B Inhibitor: A Cross-Sectional Study

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Disclosures

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• K. Dashtipour is a scientific advisor for Teva Neuroscience.

CE Learning Objective

• Identify the clinical outcome that is modified by long-term MAO-B inhibitor treatment in Parkinson’s disease (PD)

Parkinson’s Disease Treatment

Clinical outcomes focus on motor metrics.1
1. Bradykinesia, rigidity, tremor

Must also include:1
2. Levodopa non-responsive symptoms
3. Non-motor symptoms
4. Dyskinesias

Background

• MAO-B inhibitors (rasagiline, selegiline)
  – Long-term motor outcomes documented1
  • Data gap on long-term, clinically meaningful outcomes in:
    – levodopa non-responsive symptoms2
    – non-motor symptoms2
    – motor complications (dyskinesias)3

Self-Assessment Question 1

Traditionally, clinical outcomes for PD treatment focuses on:
A. Dyskinesia
B. Motor metrics
C. Non-motor symptoms
D. Levodopa non-responsive symptoms

Research Question

Objective

- To evaluate the risk of developing levodopa non-responsive symptoms* in MAO-B inhibitor users vs. non-users.

*taxonomic term: includes non-motor & dyskinesia

Methods

- Retrospective, cross-sectional
  - MAOB-I current users vs non-users (Nov. 2011)
- Inclusion:
  - PD diagnosis, ICD-9 332
  - Current use of PD medications
- Exclusion:
  - MAOB-I users <1 year treatment
  - Non-users: history of MAOB-I use
- Primary Outcomes:
  - dementia, dyskinesias, falls, freezing of gait, hallucinations

Statistical Analysis

- Baseline characteristics: Descriptive statistics.
- Clinical outcomes: Multivariate logistic regression analysis to estimate effect of MAOB-I (use vs. no use)
  – adjusted for sex, age, months since diagnosis, and levodopa equiv. dose.
  – Alpha was set at 0.05.

Results: Baseline

- N = 301 met inclusion/exclusion criteria

<table>
<thead>
<tr>
<th></th>
<th>MAOB-I Users</th>
<th>MAOB-I Non-users</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>180</td>
<td>121</td>
</tr>
<tr>
<td>Sex Female</td>
<td>78</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>43.3</td>
<td>45.5</td>
</tr>
<tr>
<td>Male</td>
<td>102</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>56.7</td>
<td>54.5</td>
</tr>
<tr>
<td>Levodopa Yes</td>
<td>134</td>
<td>115</td>
</tr>
<tr>
<td></td>
<td>74</td>
<td>95</td>
</tr>
<tr>
<td>Pramipexole Yes</td>
<td>29</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td>13.2</td>
</tr>
<tr>
<td>Ropinirole Yes</td>
<td>37</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>20.4</td>
<td>16.4</td>
</tr>
<tr>
<td>Amantadine Yes</td>
<td>36</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>19.9</td>
<td>20.5</td>
</tr>
</tbody>
</table>

* N = 180 (rasagiline / selegiline = 172 / 8)

Results: Baseline

<table>
<thead>
<tr>
<th></th>
<th>MAOB-I Users</th>
<th>MAOB-I Non-users</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>180</td>
<td>121</td>
</tr>
<tr>
<td>Mean</td>
<td>70.1</td>
<td>72.5</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>10.4</td>
<td>10.6</td>
</tr>
<tr>
<td>Age (years)</td>
<td>73.5</td>
<td>108.7</td>
</tr>
<tr>
<td>Months since diagnosis</td>
<td>86.5</td>
<td>134.0</td>
</tr>
<tr>
<td>Levodopa equiv. dose (mg)</td>
<td>645</td>
<td>791</td>
</tr>
<tr>
<td>MAOB-I duration (years)</td>
<td>2.6</td>
<td>-</td>
</tr>
</tbody>
</table>

Results: MAOB-I Users vs. Non Users

- Multivariate logistic regression analysis*

<table>
<thead>
<tr>
<th></th>
<th>p-value</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia</td>
<td>0.213</td>
<td>0.708</td>
</tr>
<tr>
<td>Dyskinesia</td>
<td>0.038</td>
<td>0.558</td>
</tr>
<tr>
<td>Falls</td>
<td>0.543</td>
<td>0.861</td>
</tr>
<tr>
<td>FoG</td>
<td>0.548</td>
<td>0.852</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>0.596</td>
<td>0.866</td>
</tr>
</tbody>
</table>

*Adjusted for sex, age, months since diagnosis, and levodopa equiv. dose.

Self-Assessment Question 2

Long term treatment with rasagiline reduces the risk of:
A. dementia
B. dyskinesia
C. falls
D. freezing of gait
E. hallucinations

MAOB-I Users vs. Non-User: Dyskinesia Outcome Separation

<table>
<thead>
<tr>
<th>Dyskinesia &amp; Duration of Use</th>
<th>p-value</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1 Year to &lt; 2 years vs. None</td>
<td>0.325</td>
<td>0.673</td>
</tr>
<tr>
<td>&gt;2 Years to &lt; 3 years vs. None</td>
<td><strong>0.002</strong></td>
<td><strong>0.143</strong> (0.04 – 0.48)</td>
</tr>
<tr>
<td>&gt;3 Years to &lt;4 years vs. None</td>
<td>0.173</td>
<td>0.521</td>
</tr>
<tr>
<td>&gt;4 years vs. None</td>
<td>0.927</td>
<td>0.966</td>
</tr>
</tbody>
</table>

Adjusted for sex, age, months of diagnosis, and levodopa equiv. dose.

Conclusions

- MAOB-I users associated with (44%) less risk of dyskinesia up to 3 years.
- Levodopa-sparing? Possibly
- Disease modifying? Possibly
- Beyond 3 yrs loss of benefit?
- Due to disease burden?
- Next step: quasi-experimental (e.g., cohort) or prospective, controlled studies.
- Limitations:
  - Retrospective imprecision
  - Unidentified confounders

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