Therapeutic Response in Pediatric Neuromyelitis Optics Spectrum Disorder

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Background: Pediatric NMOSD

• Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune condition which can lead to significant disability.
• AQP4-IgG is a serum biomarker found in approximately 80% of patients, and a proportion of the remaining 20% may be accounted for by MOG-IgG and double seronegative (DS).
• Approximately 4% of the NMOSD cases are pediatric onset.
• At present, there are limited studies that aim at guiding physicians in their treatment choices for NMOSD in children.
Objectives

• To evaluate the effect of different disease modifying therapies (DMT) with respect to attack prevention in children with NMOSD.
Design/Methods

• Multi-center observation cohort study that included 12 clinical centers participating in the US Network of Pediatric MS Centers.

• Children aged 18-year-old or younger diagnosed with NMOSD diagnostic criteria and classified via serostatus as AQP4+, MOG+, or DS.

• Clinical data, including demographics, attack details, type of initial DMT (rituximab, mycophenolate mofetil, azathioprine, IVIg) and neurological visit data were extracted from charts, centrally collected in a database, and analyzed.

• Treatment response in the three serostatus subgroups was evaluated.

• Effect of DMTs on annualized relapse rate (ARR) was assessed by negative binomial regression.
Results: Baseline characteristics

- 111 pediatric patients with NMOSD

<table>
<thead>
<tr>
<th>Demographics of analysis population</th>
<th>AQP4+ (N = 80)</th>
<th>MOG+ (N = 10)</th>
<th>Double Seronegative (N = 14)</th>
<th>Unknown (N = 7)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at time of first event:</strong> Mean (SD)</td>
<td>10.9 (3.9)</td>
<td>8.0 (4.3)</td>
<td>9.3 (4.6)</td>
<td>11.0 (4.0)</td>
<td>0.165¹</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.464²</td>
</tr>
<tr>
<td>Male</td>
<td>10 (13%)</td>
<td>3 (30%)</td>
<td>3 (21%)</td>
<td>1 (14%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>70 (88%)</td>
<td>7 (70%)</td>
<td>11 (79%)</td>
<td>6 (86%)</td>
<td></td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.478²</td>
</tr>
<tr>
<td>White</td>
<td>33 (42%)</td>
<td>7 (70%)</td>
<td>6 (46%)</td>
<td>2 (29%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>37 (47%)</td>
<td>2 (20%)</td>
<td>5 (38%)</td>
<td>3 (43%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>8 (10%)</td>
<td>1 (10%)</td>
<td>2 (15%)</td>
<td>2 (29%)</td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.653²</td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>15 (20%)</td>
<td>1 (11%)</td>
<td>3 (21%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>61 (80%)</td>
<td>8 (89%)</td>
<td>11 (79%)</td>
<td>5 (100%)</td>
<td></td>
</tr>
<tr>
<td><strong>First MS agent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.362²</td>
</tr>
<tr>
<td>azathioprine</td>
<td>12 (16%)</td>
<td>1 (13%)</td>
<td>1 (7%)</td>
<td>1 (17%)</td>
<td></td>
</tr>
<tr>
<td>mycophenolate mofetil</td>
<td>12 (16%)</td>
<td>1 (13%)</td>
<td>3 (21%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>rituximab</td>
<td>32 (42%)</td>
<td>1 (13%)</td>
<td>3 (21%)</td>
<td>2 (33%)</td>
<td></td>
</tr>
<tr>
<td>IVIG</td>
<td>6 (8%)</td>
<td>3 (38%)</td>
<td>3 (21%)</td>
<td>2 (33%)</td>
<td></td>
</tr>
</tbody>
</table>

¹ Kruskal-Wallis test.
² Chi-squared test.
# Annual Relapse Rate

<table>
<thead>
<tr>
<th>Therapy</th>
<th>First-line treatments</th>
<th></th>
<th>First-line treatments</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted ARR</td>
<td>N</td>
<td>Unadjusted ARR</td>
<td>N</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>0.73 (0.27, 2.00)</td>
<td>15</td>
<td>0.76 (0.24, 2.39)</td>
<td>12</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>0.40 (0.18, 0.89)</td>
<td>16</td>
<td>0.43 (0.17, 1.07)</td>
<td>12</td>
</tr>
<tr>
<td>Rituximab</td>
<td>0.25 (0.13, 0.46)</td>
<td>38</td>
<td>0.25 (0.13, 0.48)</td>
<td>32</td>
</tr>
<tr>
<td>IVIG</td>
<td>0.56 (0.26, 1.20)</td>
<td>14</td>
<td>0.63 (0.26, 1.55)</td>
<td>6</td>
</tr>
</tbody>
</table>

*Note: there were 7/111 who were untreated for first-line treatments
*Note: there were 4/80 who were untreated for first-line treatments for the AQP4 subset
Strengths and limitations

- **Strengths:**
  - Multicenter data from large cohort of pediatric NMOSD patients
  - Data collected over the last 10 years
  - Comparative effectiveness of initial treatment

- **Limitations:**
  - Lack of information about short term safety, tolerability and side effects
  - Cannot exclude residual confounding
Conclusions

• This retrospective study showed that rituximab is associated with a lowered annual relapse rate in pediatric NMOSD and in particular in the AQP4+ subgroup.
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