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 led 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

Demographics of analysis population

	Serostatus				
	AQP4+ (N = 80)	**MOG+ (N = 10)**	**Double Seronegative (N = 14)**	**Unknown (N = 7)**	**P-value**
Age at time of first event: Mean (SD)	10.9 (3.9)	8.0 (4.3)	9.3 (4.6)	11.0 (4.0)	0.165[1]
Gender					0.464[2]
Male	10 (13%)	3 (30%)	3 (21%)	1 (14%)	
Female	70 (88%)	7 (70%)	11 (79%)	6 (86%)	
Race					0.478[2]
White	33 (42%)	7 (70%)	6 (46%)	2 (29%)	
Black	37 (47%)	2 (20%)	5 (38%)	3 (43%)	
Other	8 (10%)	1 (10%)	2 (15%)	2 (29%)	
Ethnicity					0.653[2]
Hispanic or Latino	15 (20%)	1 (11%)	3 (21%)	0 (0%)	
Not Hispanic or Latino	61 (80%)	8 (89%)	11 (79%)	5 (100%)	
First MS agent					0.362[2]
azathioprine	12 (16%)	1 (13%)	1 (7%)	1 (17%)	
mycophenolate mofetil	12 (16%)	1 (13%)	3 (21%)	0 (0%)	
rituximab	32 (42%)	1 (13%)	3 (21%)	2 (33%)	
IVIG	6 (8%)	3 (38%)	3 (21%)	2 (33%)	

[1] Kruskal-Wallis test.
[2] Chi-squared test.

Annual Relapse Rate

	First-line treatments		First-line treatments AQP4+	
Therapy	**Unadjusted ARR**	**N**	**Unadjusted ARR**	**N**
Azathioprine	0.73 (0.27, 2.00)	15	0.76 (0.24, 2.39)	12
Mycophenolate mofetil	0.40 (0.18, 0.89)	16	0.43 (0.17, 1.07)	12
Rituximab	0.25 (0.13, 0.46)	38	0.25 (0.13, 0.48)	32
IVIG	0.56 (0.26, 1.20)	14	0.63 (0.26, 1.55)	6

*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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