



Failure to treatment with Rituximab in patients with AQP4+ Neuromyelitis optica and NMO spectrum from the demyelinating diseases clinic of the "National Institute of Neurology and Neurosurgery Manuel Velasco Suárez"

Dra. Fernanda Flores Alfaro¹, Dra. Verónica Rivas Alonso¹, Dr. José de Jesús Flores Rivera¹

¹. Instituto Nacional de Neurología y Neurocirugía. Manuel Velasco Suárez. CDMX. Clínica de Enfermedades Desmielinizantes.

Introduction: In daily practice we are faced with cases in which patients diagnosed with neuromyelitis optica who are being treated with drugs such as Rituximab, suffer relapses of the disease despite the adequate dose and frequency of the drug. Clinically a single relapse can be devastating, leaving the patient disabled. Therefore, it is important for the patient to detect these in order to make a change in treatment.

We studied patients under follow-up by the clinic for demyelinating diseases with a diagnosis of neuromyelitis optica AQP4 (+) and patients with a diagnosis of neuromyelitis optica spectrum disorder (NMO SD). We analyzed the frequency of relapses prior to the start of any disease-modifying therapy, the frequency of relapses after the start of disease-modifying treatment, the frequency, the dose of the drugs and triggering factors. Patients were studied from the date of diagnosis of the disease until December 2022.

Methods: Observational and retrospective study of patients from the National Institute of Neurology "Dr. Manuel Velasco Suárez" with a diagnosis of neuromyelitis optica AQP4 (+) or NMOSD over 18 years of age, with complete records, with laboratories such as: complete blood count and cytology of cerebrospinal fluid; and who have Magnetic Resonance of the brain and cervical or thoracic spinal cord.

Results: The number of relapses before treatment and after treatment with rituximab was analyzed, as well as the annualized rate of relapses before and after treatment, finding a significant decrease with the use of rituximab.

The use of other immunosuppressants such as azathioprine, mycophenolic acid, methotrexate and cyclophosphamide, finding that 41.3% of the patients had previously used any of these immunosuppressants and that changes to treatment were made due to adverse effects from their use, due to treatment failure or for having reached the maximum recommended dose, as in the case of cyclophosphamide. Treatment failure was considered in patients who had treatment with rituximab with full induction dose and subsequent dose in the following 6 months.

Number of relapses, Annualized Relapse Rate (ARR) in AQP4 + and - patients

	Total	AQP4+	AQP4-	P
Number of relapses before treatment (SD)	2.61 (1.65)	2.65 (1.67)	2.51 (1.61)	0.54
Number of relapses after treatment (SD)	0.14 (0.488)	0.18 (0.56)	0.02 (0.16)	0.01
TAR before treatment (SD)	0.73 (0.74)	0.69 (0.74)	0.82 (0.74)	0.49
TAR post treatment (SD)	0.02 (0.10)	0.03 (0.12)	0.00 (0.03)	0.013
Outbreaks during the course of the disease (SD)	2.93 (DE 1.93)	3.02 (2.02)	2.71 (1.72)	0.25

Data are presented as mean $\pm$ SD and n/N (%).

P values indicate differences between patients with AQP4 + and -

P<0.05 was considered statistically significant.

*Fisher's exact test.

Patients with NMO AQP4 + and AQP4 -

	Total	AQP4+	AQP4-	P
Patients	121	86 (71.1%)	35 (28.9%)	.
Gender (%)				0.20
Men	20 (16.5%)	13 (15.1)	7 (20%)	
Women	101 (83.5%)	73 (84.9%)	28 (80%)	
Age, mean (SD)	42.89 (12.86)	44.98 (13.08)	37.74 (10.85%)	0.18
Age of onset of symptoms (SD)	36.59 (12.87)	38.18 (13.02)	32.65 (11.79)	0.36
Systemic Autoimmune Disease	11 (9.1%)	9 (10.8 %)	2 (5.7%)	0.09
Disease duration in months (SD)	73.4 (60.75)	80.06 (67.02)	57 (37.52)	0.008
EDSS (SD)	5.023 (2.35)	5.23 (2.42)	3.66 (1.52)	0.30

Data are presented as mean $\pm$ SD and n/N (%).

P values indicate differences between patients with AQP4 + and -

P<0.05 was considered statistically significant.

*Fisher's exact test.

Conclusion: The use of rituximab is a good therapeutic option in patients with neuromyelitis optica, however up to 9.09% of patients had treatment failure and it is important to consider other treatment strategies in them.

The use of rituximab is safe in patients, since adverse effects were only reported in 1.7% (anaphylaxis, fever, rash, thrombocytopenia).