DECREASE OF RELAPSE RATE IN NEUROMIELITIS OPTICA PATIENTS (AQP4 POSITIVE) AT THE NATIONAL INSTITUTE OF NEUROLOGY AND NEUROSURGERY (MEXICO).

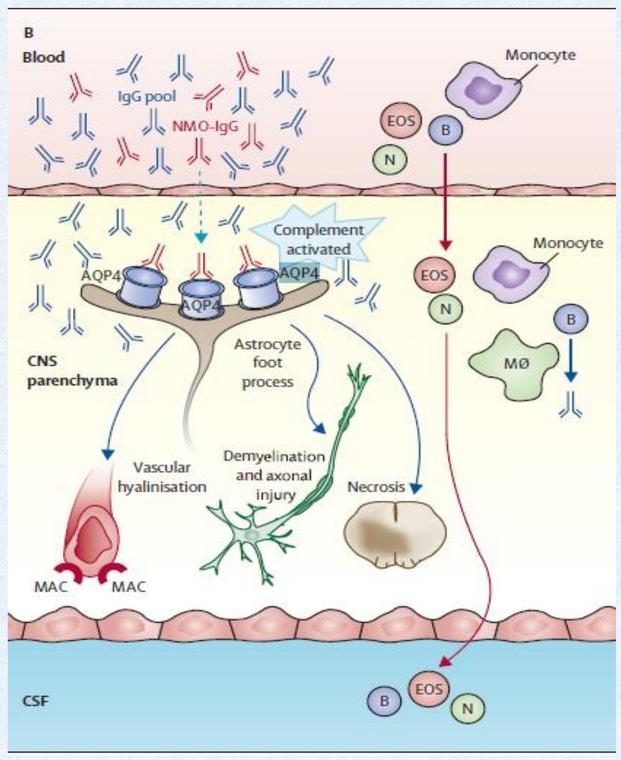
Castillo G., Omar I.[1], Rivas A. Verónica[2] Rodríguez Ch., Emmanuel[1], Vargas S., Sarah B,[1], Santos D., Marco[1],, Rito G., Yamel C[2], Corona V., Teresa[3], Flores R., Jose J.[4]

1 High Specialty in Multiple Sclerosis Course, 2 Demyelinating Diseases Clinica, 3 Neurodegenerative Diseases Laboratory. 4 Department of Neurology.
National Institute of Neurology and Neurosurgery, Mexico City, Mexico.

INTRODUCTION. Neuromyelitis Optica (NMO) is a spectrum of autoimmune, inflammatory and demyelinating disorders of the Central Nervous System (CNS), which affect optic nerve and spinal cord, but also the area postrema, other brainstem regions, diencephalon and some typical brain areas. In 2004, was published the relationship between NMO and an antibody against the aquaporin 4 (AQP4 IgG +). water channel. These antibodies are synthesized mainly outside of the CNS, and binds with high affinity to the third extracellular domain of the AQP4, when this ocurr, it is produced AQP dysfunction, its internalization, activation of effector cells and exert their astrocytotoxic effect primarily through the activation of complement.

It is recommended to begin an immunosuppressive therapy after the first attack as a preventive relapse treatment. There is no published data about the clinical response to different treatments in order to reduce the risk of relapse of NMO patients in Mexican population. Therefore, this study has been carried out to know the clinical response, measured by rate relapse with the different medications in the population of the National Institute of Neurology and Neurosurgery (Mexico).

Objectives. Analyze the clinical response to treatment measured by the annualized relapse rate (ARR) and progression of disability (EDSS) as well as clinical and demographic variables in subjects with NMO IgG (+) in the population of the National Institute of Neurology and Neurosurgery.(Mexico)



Wingerchuk DM, The spectrum of neuromyelitis optica. Lancet Neurol. 2007 Sep;6(9):805-15.

METHOD. It is an observational, retrospective study. Clinical and demographic variables were obtained from the clinical record; as well as the annualized relapse rate (ARR) and disability score measured by EDSS of patients who have received at least one year of immunosuppressant treatment for preventive treatment of relapses, from January 2010 to June 2017.

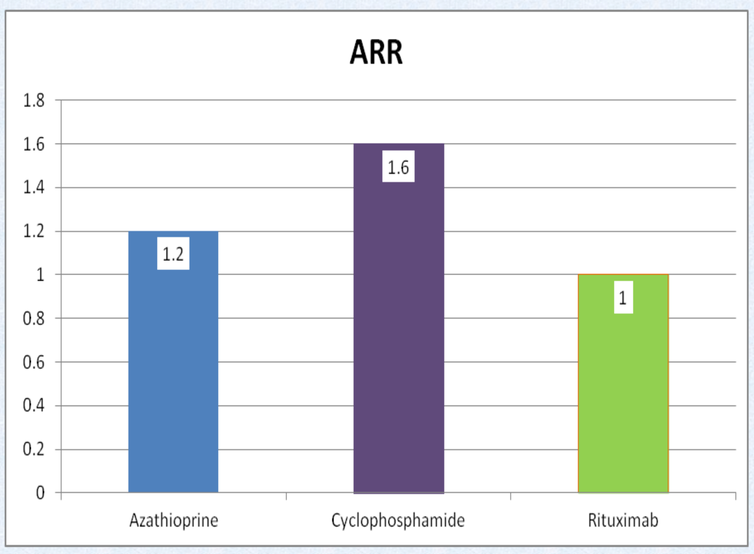
RESULTS. 60 patients were included in the study. At the moment of the diagnosis the mean age was 38.2 years, 88.3% were female.

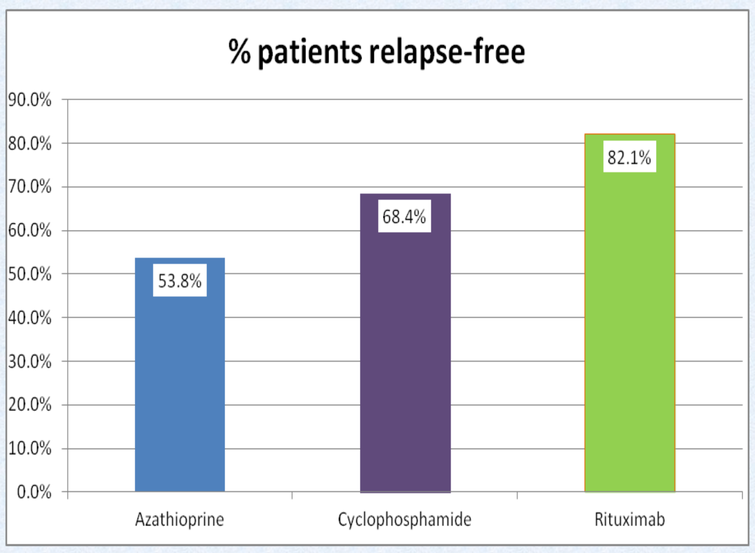
.

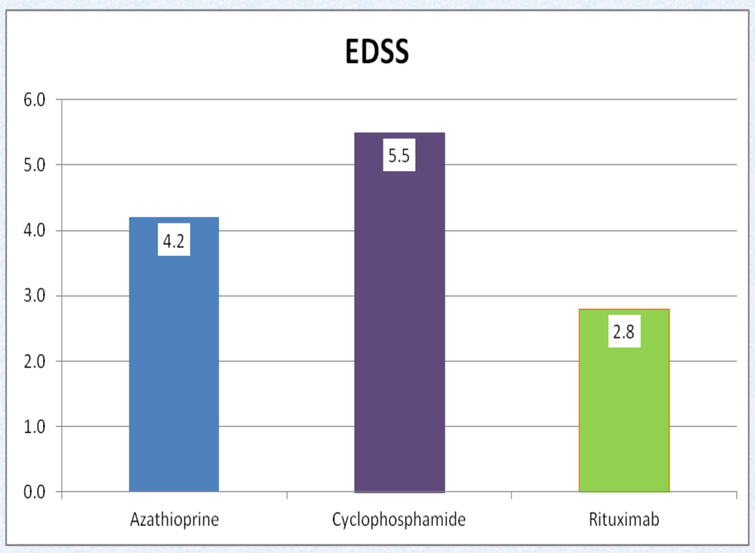
They were divided into three groups based on their treatment. 13 patients were on treatment with Azathioprine with a medium follow-up of 42 months (12-93m), 19 with Cyclophosphamide with a medium follow-up of 15 months (12-18m) and 28 with Rituximab. with a medium follow-up of 28 months (12-57m)

Characteristics	Azathioprine N= 13	Cyclophosphamide N= 19	Rituximab N= 28	Total N= 60
Average age at diagnosis	35.9 (20-55)	41.4 (17-55)	37.1 (18-53)	38.2
Female (%)	11 (84.6)	17 (89.5)	25 (89.3)	53 (88.3)
Male (%)	2 (15.4)	2 (10.5)	3 (10.7)	7(11.7)

In the group of patients treated with Azathioprine the ARR was 1.2, in the cyclophosphamide group 1.6, and in the group of Rituximab was 1.0. In the group treated with Azathioprine, 58% of the patients were free of relapses during treatment, 68.4% with cyclophosphamide and 82.1% with Rituximab. Regarding the disability measured by EDSS, an average score of 4 was found in the Azathioprine group, 5.5 in the Cyclophosphamide group and 2.8 in the group treated with Rituximab.







CONCLUSIONS. The results of the study have a predominance of female patients in a ratio of 9: 1 compared to male, and a mean age of diagnosis of 38.2 years this coincide with the reported in the literature. mean age of diagnosis of 38.2 years

.

Patients with a diagnosis of NMO IgG + in immunosuppressive treatment for preventive relapse, with Rituximab present significantly higher response to treatment, demonstrated by a lower rate of relapse, higher remission rate and lower EDSS. It is observed that in our population with a diagnosis of NMO IgG +,the response to treatment with the three drugs used is similar to that reported in the literature, and we can then take as a reference what has been reported in other populations for the treatment of this disease.

With these results, the use of Rituximab is supported as the treatment of choice in NMO, however, because some patients do not have access to this medication because of the cost, we observed that it is a good option to treat them with Cyclophosphamide since in our population it is observed a superior response to Azathioprine.

References:

1. Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, Chitnis T, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology 2015; 85: 177-89.
2. Lennon VA, Wingerchuk DM, Kryzer TJ, Pittock SJ, Lucchinetti CF, Fujihara K, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. Lancet 2004; 364: 2106-12.
3. A.S. Verkman,J. Ratelade,A. Rossi,H. Zhang,L. Tradtrantip Aquaporin-4: orthogonal array aseembly CNS functions, and role in neuromyelitis óptica. Acta Pharmacologica Sinica, 32 (2011), pp. 702-710
4. Etemadifar M, Nasr Z, Khalili B, Taherioun M, Vosoughi R. Epidemiology of neuromyelitis optica in the world: a systematic review and meta-analysis. Mult Scler Int. 2015;2015:174720.
5. Weinshenker, Brian G., Wingerchuk, Dean M., Neuromyelitis Spectrum Disorders, Mayo Clin Proc., April 2017;92(4):663-679.
6. Papadopoulos, Marios C, Bennet, Jeffrey L., Verkman, Alan S. Treatment of neuromyelitis optica: state-of-the-art and emerging therapies, Nature Reviews Neurology 10, 493–506 (2014).
7. Kessler, Remi A., Mealy, Maureen A., Levy, Michael. Treatment of Neuromyelitis Optica Spectrum Disorder: Acute, Preventive, and Symptomatic. Curr Treat Options Neurol. 2016 January ; 18(1): 2.
8. Etemadifar M, Salari M, Mirmosayyeb O, et al. Efficacy and safety of rituximab in neuromyelitis optica: Review of evidence. Journal of Research in Medical Sciences : The Official Journal of Isfahan University of Medical Sciences. 2017;22:18