Efficacy of rituximab at different doses in Neuromyelitis Optica Spectrum Disease (NMOSD). Experience in patients of a tertiary level hospital in Mexico

Introduction.
Neuromyelitis Optica (NMO) is an inflammatory demyelinating central nervous system disease, with recurrent attacks of severe bilateral optic neuritis and longitudinally extensive transverse myelitis. Aggressive immunosuppression is essential to prevent clinical relapses and permanent disability. Rituximab, a monoclonal antibody to CD20, has been found effective in several reports and small uncontrolled studies. There is a paucity of data regarding its use in Mexican patients and furthermore dosage scheme recommendations.

Objectives.
The aim of this study was to report the results of rituximab at different scheme doses in NMO spectrum disorders (NMOSDs) in the Mexican population.

Methods.
This study is a retrospective, observational study in a tertiary hospital in Mexico City. Of 271 patients with myelitis, neuritis, area postrema syndrome or diencephalic syndrome, 66 had a diagnosis of NMOSD as per the 2017 international consensus on NMOSD.
All patients of NMOSD were seen from January 1, 2010, to August 1, 2019, had taken at least 2 doses of rituximab, first cycle two doses 2 weeks apart, and subsequent cycles at 500 mg, 1000 mg or 2000 mg intravenous administration each six months.

Results.
A total of 66 patients of NMOSD were evaluated during the study, of which 12 (18,2%) were male and 54 (81,1%) were female. Median age of diagnosis of NMOSD was 36.2 ± 12.01 years and a mean of 5,85 ± 4,03 years of disease. At the moment of diagnosis, 38 patients (57,6%) had attack of optic neuritis, whereas 21 patients (31,8%) had spinal cord symptoms and, seven patients (10,6%) presented with area postrema syndrome. 43 patients (65,2%) were AQP4 antibody positive, 18 (27,3%) negative and 5 patients did not have this biomarker. 21 patients (31,81%) had CD 19 and CD 20 levels after rituximab infusion. Lower CD 19 count was 0,0 and higher 1,30 (Mean 0,45); lower CD 20 count was 0,00 and higher 1,5 (mean 0,41). The median interval from onset of NMO to treatment with rituximab was 27,9 ± 42,9 months. The most frequent first dose of rituximab was 1000 mg divided in two applications (51,5%), followed by 2000 mg (43,9%) at the same scheme of administration. Before starting rituximab, the patients had a median of three attacks. In the study, 39 (59,1%) of 66 patients were completely relapse free after starting treatment with rituximab. 24 patients (36,4%) suffered just 1 relapse. Mean ARR reduced from 1,15 ±1,18 to 0.5 after therapy (P = <0.0001). Even in each patient who had relapses, the ARR dropped after starting rituximab and the mean ARR in these patients dropped from 1,66 to 1,22 relapses per year, a decrease of 73.49 % relative risk of relapse

Conclusion.
The treatment of NMOSDs with different doses of RTX in Mexican patients reduces the frequency of relapses and is well tolerated. There is not a significant impact in EDSS score. The higher counts of CD 19 and CD 20 cells were reported in 500 mg induction and maintenance rituximab doses.