RITUXIMAB IS EFFECTIVE REGARDLESS OF INITIAL AND MAINTENANCE DOSES IN NEUROMYELITIS OPTICA SPECTRUM DISORDERS (NMOSDs). EXPERIENCE FROM THIRD LEVEL HOSPITAL IN MEXICO

Casallas-Vanegas Adriana[1] MD, Gomez-Figueroa Enrique[1] MD, Zabala Angeles Indhira[1] MD, García-Estrada Christian[1] MD, López Martínez Ramón[1] MD, Neri Daniel[1] MD, Simón Miguel[1] MD, Corona Teresita[1] MD, Flores-Rivera José de Jesús[1]MD, Rivas-Alonso Verónica[1] MD.

[1]Neurology Department, Instituto Nacional de Neurología y Neurocirugía, México City, México.

Introduction

Neuromyelitis Optica (Spectrum Disorders. NMOSDs) is an inflammatory condition of the central nervous system, preferentially affects the optic nerves and spinal cord. Aggressive immunosuppression is essential to prevent it and improve quality of life. Rituximab (RTX) is a chimeric monoclonal antibody directed against CD20 epitope expressed on pre-B and mature B cells and is used to treat antibody-mediated autoimmune diseases. However, randomized controlled trials in NMO are relatively few, and no established guidelines have been established for RTX treatment

Objective

Demonstrate RTX clinical efficacy regardless doses administered in NMOSDs patients.

Methods

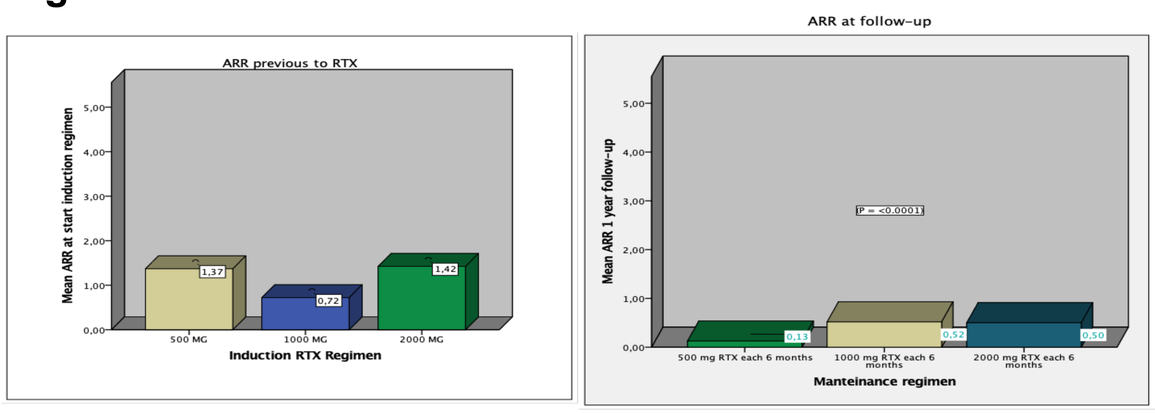
This is a retrospective, longitudinal observational study in a tertiary hospital in Mexico City. Of 342 patients with myelitis, neuritis, area postrema syndrome or diencephalic syndrome, 66 satisfied NMOSD 2015 diagnostic criteria (Wingerchuk et al., 2015) and that started treatment with RTX.

Demographic and clinical data were obtained at baseline (date of RTX start); treatment infusions and clinical course data were collected and updated every 6 months. We used Cell-based indirect immunofluorescence assay (CIIFA) for aquaporin 4 (AQP4) antibody detection, and flow cytometry CD 19 Y CD 20 serum counts.

Results

12 patients (18,2%) were male, 54 (81,1%) female. The most frequent RTX induction regimen was 2000 mg 15 day apart (55%), followed by 1000 mg (36,4%). Single 500 mg of RTX in 5 patients (7,5%). 65,2% were AQP4 antibody positive, 27,3% negative. ARR reduced from 1,15 ±1,18 to 0,46 with RTX (P = <0.0001). Figure 1. In patients with relapses, ARR dropped from 1,66 to 1,22 relapses per year, 73.49% relative risk relapse decrease. Previous to RTX ARR in 500 mg subgroup was 1,36, with RTX 0,4. For 1000 mg initial and maintenance doses ARR was 0,7 and follow-up 0,4. Table 1.

Figure 1.



ARR before and after RTX treatment. Here we show all cumulative ARR trough time.

Discusion

In this observational study run in Mexico city, we confirm RTX efficacy in preventing attacks in patients with NMOSD. We enrolled patients that have been treated with RTX and that completed at least the induction regimen. Demographic and clinical characteristics of enrolled patients are in line with previous literature reports, showing a high prevalence of woman among NMOSD patients, often with autoimmune co-morbidities.

The current study in Mexican patients demonstrates a marked beneficial effect of rituximab treatment on patients with NMOSD, showing stability on EDSS and marked decrease in ARR; even in active patients with relapses RTX at lower doses had excellent results decreasing ARR from 1,36 to 0,4.

Our results supported recent reports about the shortterm efficacy of RTX in NMO and the recent advice to use RTX as a first-line treatment.

Table 1.

500 mg RTX Patient ID	Previous relapses	Post treatment relapses	Previous ARR	1 year follow up ARR	Previous EDSS	1 year follow up EDSS	CD 19/CD20 cell count
4	1	1	0,13	1.0	4.0	3,5	CD19 0,01% CD20 0,01%
9	5	1	5,0	1.0	2	2,0	
3	2	0	1,0	0.0	1	1,0	CD19 1,3% CD20 1,5%
1	4	0	0,5	0,0	1	1,0	
2	2	0	0,22	0,0	2,5	2,5	

ARR 1.36, and after RTX treatment 0,4. (P= 0,0001)

In this study, we decided to repeat RTX infusion every 6 months. This fixed scheme allowed a control of the disease 39 (59,9%).

Here, patients with an initial dose of 500 mg RTX were identified (N=5); the results regarding disability scale and annual relapse rate did not differ compared to higher doses of RTX. Comparing subgroups, we demonstrated the effectiveness of rituximab even at doses of 500 mg biannual, observed that CD 19 and CD 20 cell counts in them were higher, opening the door to the debate of whether CD 19 and CD 20 counts are a real face biomarker of RTX clinical efficacy evidenced in this study.

Conclusion

The treatment of NMOSDs with rituximab in Mexican patients demonstrate marked and sustained ARR reduction regardless initial and maintenance regimen and, is well tolerated RTX is a promising treatment option for patients with NMOSD, even if there are still some open questions as the best scheme to adopt and the duration of treatment. Finally, larger cohorts of patients are warranted to define the utility of different biomarkers as surrogate factors of RTX clinical/biological activity and efficacy.

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