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Immunossuppression in Neuromyelitis Optica Spectrum Disorder: A Trial Sequential Analysis and Updated Meta-Analysis

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We use this protocol and it's working

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Disclaimer

This research has no financial support.

Abstract

Neuromyelitis Optica Spectrum Disorder (NMOSD) is a devastating, disabling, autoimmune disease with a prevalence of up to 10 cases per 100,000 people. Although NMOSD pathophysiology is not yet fully understood, disruption of the blood-brain barrier (BBB) possibly initiates the disease course through AQP4-IgG passive transit into the CNS compartment, with subsequent absorption by perivascular astrocytes endfeet expressing. NMOSD treatment is based on treating and preventing attacks by administering both high-dose glucocorticoids and long-term immunosuppressive therapy. The most recommended first-line therapy for NMOSD is Rituximab, Azathioprine, and Mycophenolate mofetil. Once NMOSD treatment with RTX, AZA, and MMF effects still have to be explored, the purpose of our study is to fill the gap of previous studies by assessing RTX isolated effectiveness and its comparative safety and efficacy when compared to AZA and MMF for NMOSD patients in a more critical statistical analysis.

Guidelines

This study will be conducted following PRISMA guidelines.

Troubleshooting

Abstract

1 Review title:
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2 PICO:
Population - patients diagnosed with Neuromyelitis Optica Spectrum Disorder;
I - Rituximab;
C - No control or Azathioprine and/or Mycophenolato mofetil;
O - Annualized Relapse Rate; Expanded Disability Status Scale; Time to fisrt relapse; Adverse events (Leukopenia, infection, elevated transaminase levels, and gastrointestinal disturbance)

3 Exclusion criteria:
1 - studies with no Rituximab group;
2 - unclear division between Multiple Sclerosis or Mog-Antibody Associated Disease patients;
3 - conference abstracts;

4 Searches:
We searched MEDLINE, SCOPUS, Web of Science, and Cochrane Central Register of Controlled Trials from inception to April 28, 2024
Search strategy: ("Neuromyelitis Optica" OR "Neuromyelitis Optica Spectrum Disorder" OR NMOSD OR "Devic's Syndrome" OR Anti-aquaporin OR Anti-NMO OR Anti-AQ4) AND (Anti-CD20 OR Rituximab OR Rituxan OR MabThera)

5 Data extraction:
Five authors (A.M.A., F.W.F., P.M., C.R.D., and M.R.R.) will independently conducted data extraction, collecting the following
information from each study: type of study, race, therapy characteristics, age (years), AQP4-Ab positive patients, duration of diagnosis and mean follow-up.

6 Endpoints:
The primary outcomes will be the (1) annualized relapse rate (ARR) and the (2) expanded disability status scale (EDSS). We will conduct a (3) subgroup analysis with studies providing ARR and EDSS information for a direct comparison with RTX, AZA, and/or MMF. In these analyses, we will include all studies reporting both the baseline and follow-up mean values for ARR and EDSS. Also, we will assess the (4) time to relapse after treatment by comprising studies reporting the comparative risk between RXT, AZA, and/or MMF. Secondary outcomes included (5) tolerability analysis through the following adverse events (AEs): (a) Infection; (b) Liver transaminases elevation; (c) Leukopenia; and (d) Gastrointestinal disturbances. Also, we will measured the overall risk by combining all AEs in a unified analysis. Additionally, A sensitivity analysis will be

undertaken to explore ARR and EDSS outcomes through trial sequential analysis (TSA). Finally, for outcomes informed by more than 10 studies, we will visually inspect funnel plots and performe Egger's test to assess publication bias.

7 Statistical Analysis:
We will conduct the statistical analysis with RStudio version 4.3.2, Review Manager 5.4.1, and the TSA program. For continuous outcomes, we will measure the Mean Difference between groups. For dichotomous outcomes, we wil use Risk Ratios. To assess the time to first relapse, we will comprise Hazard Ratios. We will assess heterogeneity with I^2 statistics. All analysis wil be conducted with a confidence interval of 95%.

8 Quality Assessment:
Trials quality will be assessed using the Cochrane Risk of Bias in Observational Studies of Exposures (ROBINS-E) tool for observational studies and the Cochrane Risk of Bias for Randomized trials (RoB 2) for randomized controlled trials (RCT).

9 Keywords: Neuromyelitis Optica Spectrum Disorder; Rituximab; Azathioprine; Mycophenolate mofetil; Meta-Analysis; Trial Sequential Analysis