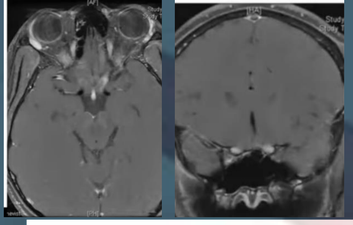

RITUXIMAB AS A PROPHYLACTIC AGENT IN RECURRENT PEDIATRIC AUTOIMUNE OPTIC NEURITIS –A RETROSPECTIVE PROSPECTIVE ANALYSIS FROM A TERTIARY CARE CENTRE

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INTRODUCTION

- Rituximab is a chimeric monoclonal anti CD20 antibody that induces B cell depletion resulting in decrease in antibody mediated immunity
- In Pediatric Neurology, the use of Rituximab has increased significantly in various autoimmune neuroinflammatory disorders.
- Optic neuritis is a sentinel event in autoimmune demyelinating disorders which include MOGAD, NMOSD and pediatric onset Multiple sclerosis.
- We performed this study to assess the role of Rituximab in children with pediatric autoimmune optic neuritis.

OBJECTIVES

- To assess the role of Rituximab as a prophylactic agent in children presenting with autoimmune optic neuritis.
- To look at a clinical profile of children who present with optic neuritis.

MATERIALS AND METHODS

Study design: Descriptive, retrospective prospective analysis

Study population: A total of 23 children diagnosed with optic neuritis secondary to autoimmune demyelination were enrolled.

Study duration/ place : Pediatric Neurology department, Apollo Children's hospital, Chennai for a duration of 3 years (July 2020 – July 2023).

Inclusion criteria: All children aged 5-18 years presenting with optic neuritis with a suspected autoimmune demyelinating disease

Exclusion criteria: Children with autoimmune diseases presenting solely with neurological manifestations, infectious and post-traumatic optic neuropathies.

We collected data pertaining to the demographics, clinical presentation, serological diagnosis and neuroimaging findings in children presenting with optic neuritis after ruling out infectious causes. These children were then followed up for at least 4 years to look at recurrences and relapses. Acute episode was managed with pulse steroids and steroid taper over 4-6 weeks. Rituximab treatment protocol: Rituximab was given as the first line prophylactic agent in children with poly-phasic disease or with a high risk of relapse in a monophasic illness. The dose used was 375 mg/m^2 as slow intravenous infusion under monitoring after premedication with paracetamol and chlorpheniramine. CD19/20 levels were monitored at baseline, 4 weeks, 12 weeks and 6 monthly for suppression . A value <0.1% was considered well suppressed.

Outcome was assessed based on clinical status and number of relapses before and after initiation of Rituximab. Infusion related adverse effects were included.

RESULTS

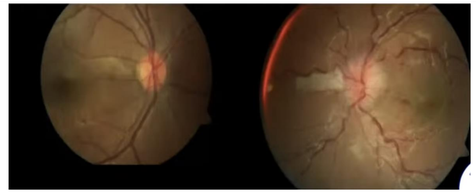
- Age at diagnosis ranged from 6.5 to 16 years, male female ratio was 0.9:1.
- Optic nerve involvement was bilateral in 38%(8).
- 11 children had isolated optic neuritis and 12 children had optic neuritis plus disease.
- Eye pain was a presenting feature in 14.2%., 4/23 had additional neurological deficits at the first presentation along with optic neuritis. Nineteen out of 23 children were given rituximab and followed up for a duration of 3-4 years. The improvement in outcome was based on number of relapses and recovery.
- Among the subgroups, children with polyphasic MOGAD and seronegative demyelinating illness showed lower rates of relapse (0-1) and better chances of complete recovery.
- Two children with pediatric onset multiple sclerosis showed refractory clinical course needing further treatment.
- All 19 children had a documented well suppressed CD19/CD20 levels after the first infusion of Rituximab. Three children had a clinical relapse and incidentally CD19/20 levels showed a rising trend (mean 5%). Four children had a rising trend in B cell subset population who received repeat dose of Rituximab and did not show any clinical relapses.
- Infusion related complications were reported in three out of 19 children. Fever with chills and redness was the only side effect among our cohort which was managed with antipyretics and antihistaminic and transiently stopping the infusion. No side effects led to withdrawal of the infusion. No long term side effects were reported.

Table 1: Basic demographics of children enrolled in the study

Characteristics	MOGAD (n=11)	NMOSD (n=1)	Pediatric onset MS (n=4)	Sero-negative (n=7)
Male/Female (n)	6/5	0/1	0/4	5/2
Age at onset	6.9 -13.2 years	13.5 years	14-16 years	8-14 years
Optic neuritis plus disease	5	1	4	2
Monophasic/Polyphasic	Monophasic 4 Polyphasic 7	Polyphasic 1	Polyphasic 4	Monophasic 4/ Polyphasic 3
Total number of children who received rituximab	9	1	4	5
Other second line therapies	1 MMF		2 MMF	

Table 2: : Rituximab related characteristics

Characteristics	MOGAD		NMOSD	Pediatric onset MS	Sero-negative	
	Monophasic	Poly phasic			Monophasic	Poly phasic
Total number of children who received Rituximab	4	5	1	4	2	3
Number of doses	1-3 doses	1-2 doses	3 doses	1-3 doses	1 dose	2-3 doses
Number of relapses before treatment with Rituximab	1	1-3 (n=3)	2	4(n=4)	nil	1-3
Number of relapses after treatment with Rituximab	Nil	1 (n=1)	0	2 (n=2)	nil	nil
Recovery	3 – complete recovery 1 - partial recovery	3 – Complete recovery 1- Partial recovery	1 – Partial Recovery	2 Partial recovery 2 complete recovery	2 partial recovery	2 partial recovery 1 full recovery



DISCUSSION

- ON is one of the most common symptom of acquired demyelinating disorders. (1)
- Children with CNS demyelination(2), MOG positivity(3) showed an aggressive course.
- Rituximab treatment is associated with a reduced relapse rate in MOGAD and NMOSD.
- B cell reconstitution is a strong predictor for clinical relapse,
- Several studies demonstrate that Rituximab is more effective in preventing relapses in children with NMOSD compared to MOGAD. Our study demonstrate efficacy of Rituxmab in preventing relapses in children with MOGAD.
- Regarding adverse events associated with Rituximab, our study showed minor side effects and none relating to discontinuation of treatment. Rates of infection were nil in our study

The small sample size was the major limitation in our study.

CONCLUSION

- The presence of bilateral eye involvement can be a pointer towards an underlying autoimmune process.
- Once infectious causes are ruled out, neuroimaging is important in looking for silent CNS demyelination
- MOG sero-positivity and presence of CNS demyelination is a pointer towards need for prophylactic therapy.
- Rituximab is a good prophylactic agent and monitoring the CD19/CD20 suppression plays a role in deciding the rituximab doses.

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