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Alternative Therapies to Immunoglobulin for Multifocal Motor Neuropathy

Rapid Review

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Abbreviations

Ig	immunoglobulin
IVIg	intravenous immunoglobulin
MMN	multifocal motor neuropathy

Key Messages

- We did not find any evidence regarding the clinical effectiveness and safety of alternative treatments to IV Immunoglobulin (IVIg) compared to IVIg or placebo for multifocal motor neuropathy that met our inclusion criteria for this review.
- We did not find any evidence-based guidelines regarding the use of alternative treatments to IVIg for multifocal motor neuropathy that met the criteria for this review.

Context and Policy Issues

Multifocal motor neuropathy (MMN) is a rare disorder in which focal areas of multiple motor nerves are attacked by the immune system.[1] It is slowly progressive and characterized by asymmetric weakness of the limbs without affecting sensory nerves.[1] The prevalence of the disease is estimated to be 0.6 to 2 per 100,000 population in North America and Europe.[1] It involves upper limbs more than lower limbs, and occurs more frequently in males than females, with a ratio of 2.7 to 1.[1] Disease onset can occur between the ages of 20 to 70 years, with a mean age onset 40 years.[1,2] MMN is diagnosed by nerve conduction studies showing multifocal conduction block on electrophysiological testing.[1] However, some patients with MMN have no detectable conduction block.[1] Other findings that support the diagnosis of MMN are the abnormal A waves on electrodiagnostic studies, axonal sprouting on motor nerve biopsies, and increased signal intensities on T2-weighted magnetic resonance images of the brachial plexus, a network of nerves that sends signals from the from the spinal cord to the shoulder, arm, and hand.[1] Thirty percent to 80% of patients with MMN have elevated serum anti-GM1 (ganglioside-monosialic acid) antibodies.[1] These antibodies are, however, not specific to MMN and can be found in other immune-mediated neuropathies.[2]

Immunoglobulins (Ig) are therapeutic products purified from pooled blood plasma from healthy donors.[3] Ig can be administered through intramuscular, IV or subcutaneous injection.[3] IV Ig (IVIg) is a treatment option for MMN.[4] A recent systematic review has found that initial therapy with IVIg may improve muscle strength and functional disability compared with placebo in many patients with MMN.[5] Dosing of IVIg is usually initiated at a total of 2 g/kg given over 2 to 5 days (e.g., 0.4 g/kg daily for 5 consecutive days).[4] Maintenance IVIg dose ranges from 0.4 g/kg once weekly to 2 g/kg every 8 weeks depending on response and tolerance.[4]

The demand for Ig has been steadily increasing every year for the treatment of various autoimmune and inflammatory diseases including MMN.[6,7] Due to the COVID-19 pandemic that has had a strong impact on global blood and plasma collection, countries around the world are experiencing a decline in Ig products.[6] The shortage of the Ig products together with their increasing demand has made it necessary to re-evaluate alternative treatment options. Alternative treatments to IVIg for MMN include immunomodulating drugs such as cyclophosphamide, rituximab, mycophenolate mofetil, beta-interferon, cyclosporin, azathioprine, infliximab, corticosteroids, and plasma exchange.[2,8] The clinical effectiveness of some of these alternative treatments remains unclear or controversial.[2,8,9]

The objective of this report is to summarize the evidence regarding the clinical effectiveness and safety of alternative treatments to IVIg, specifically corticosteroids and plasma exchange, compared to IVIg or placebo for MMN. This report also aims to summarize the recommendations from evidence-based guidelines regarding alternative treatments to IVIg given to this population.

Research Questions

1. What is the clinical effectiveness of alternative treatments to IVIg compared to IVIg or placebo for MMN?
2. What is the safety of alternative treatments to IVIg compared to IVIg or placebo for MMN?
3. What are the evidence-based guidelines regarding the use of alternative treatments to IVIg for MMN?

Methods

Literature Search Methods

An information specialist conducted a literature search on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevancy. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. Search concepts were developed based on the elements of the research questions and selection criteria. The main search concept was multifocal motor neuropathy, with relevant MeSH focused to the "drug therapy" subheading. A supplemental search was conducted for multifocal motor neuropathy with CADTH-developed search filters applied to limit retrieval to guidelines. The search was completed on March 24, 2023 and limited to English-language documents published since January 1, 2018.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, or were published before 2018.

Table 1: Selection Criteria

Criteria	Description
Population	Patients with multifocal motor neuropathy
Intervention	Corticosteroids (e.g., prednisolone), plasma exchange
Comparator	Q1 to Q2: IV immunoglobulin, placebo Q3: Not applicable
Outcomes	Q1: Clinical benefits (e.g., improvement in disability, change in muscle strength, resolution of conduction block, health-related quality of life) Q2: Harms (e.g., adverse events, severe adverse events) Q3: Recommendations regarding best practices (e.g., which alternative to use, dose and timing of treatment, indications)
Study designs	Health technology assessments, systematic reviews, evidence-based guidelines

Summary of Evidence

Quantity of Research Available

A total of 329 citations were identified in the literature search. Following screening of titles and abstracts, 323 citations were excluded and 6 potentially relevant reports from the electronic search were retrieved for full-text review. No potentially relevant publications were retrieved from the grey literature search for a full-text review. None of these 6 potentially relevant articles met the inclusion criteria and they were excluded from this report for various reasons. Appendix 1 presents the PRISMA[10] flow chart of the study selection.

Summary of Findings

No relevant health technology assessments, systematic reviews, or evidence-based guidelines were identified regarding the clinical effectiveness, or recommendations for alternative treatments to IVIg (i.e., corticosteroids, plasma exchange) compared to IVIg or placebo for MMN; therefore, no summary can be provided.

Limitations

No relevant health technology assessments, systematic reviews, or evidence-based guidelines were identified that met the criteria for this review. This report may be limited by the literature search time frame (i.e., 2018 onward). It is unknown whether there is relevant literature published more than 5 years ago.

Conclusions and Implications for Decision- or Policy-Making

No relevant literature was identified to answer the research questions; therefore, conclusions could not be provided regarding the clinical effectiveness and safety, or recommendations on the use of alternative treatments to IVIg for MMN.

Recent nonsystematic reviews[2,8,9] have reported that older studies conducted in the 1990s have shown that steroids and plasma exchange were ineffective in MMN, and might result in clinical worsening in some cases. Thus, it is unlikely that these therapies can be considered as alternative treatments to IVIg for MMN during drug shortages. The lack of published evidence may have precluded the formation of appropriate guidelines on the treatment options in MMN. Until new available clinical evidence and guidelines for alternative treatments to IVIg for MMN are available, especially steroids and plasma exchange, their place in clinical practice remains unclear.

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Appendix 1: Selection of Included Studies

Figure 1: Selection of Included Studies