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Review Article

THE ANALYSIS STUDY OF INTRAVENOUS IMMUNOGLOBULIN FOR MYASTHENIA GRAVIS: INSIGHT FROM A SYSTEMATIC REVIEW

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ABSTRACT

Introduction: Myasthenia gravis (MG) is a chronic autoimmune disorder characterized by impaired neuromuscular transmission, leading to muscle weakness and fatigue. Intravenous immunoglobulin (IVIg) has emerged as a key therapeutic option for MG, particularly in acute exacerbations and myasthenic crises. This systematic review evaluates the efficacy, safety, and optimal use of IVIg in MG management.
Material and methods: Following SWiM guidelines, this review synthesizes data from randomized controlled trials, cohort studies, and other high-quality evidence published between 2015 and 2025. The analysis focuses on IVIg's mechanisms of action, including neutralization of autoantibodies, inhibition of complement activation, and modulation of cytokines.
Discussion: Studies indicate that IVIg improves clinical outcomes in 73-76% of patients, with a favorable safety profile compared to plasma exchange (PLEX). However, questions remain regarding its role in chronic maintenance therapy, corticosteroid-sparing effects, and long-term outcomes. Emerging therapies, such as subcutaneous immunoglobulin (SCIG), FcRn inhibitors (e.g., efgartigimod), and complement inhibitors (e.g., zilucoplan), offer promising alternatives with potential advantages in convenience and specificity.
Conclusion: While IVIg remains a cornerstone in MG management, the evolving therapeutic landscape provides new opportunities to enhance patient outcomes and quality of life. Future research should focus on long-term comparative studies, patient adherence, and cost-effectiveness to optimize MG treatment strategies.

Keywords: myasthenia gravis; intravenous immunoglobulin; ivig; plasma exchange; fcrn inhibitors

INTRODUCTION

Myasthenia gravis (MG) is a chronic autoimmune disorder that affects neuromuscular transmission, leading to fluctuating skeletal muscle weakness and fatigue. The disease is caused by autoantibodies that interfere with the function of acetylcholine at the neuromuscular junction. In the majority of cases (up to 90% of generalized MG and approximately 50% of ocular MG),

the presence of IgG autoantibodies targeting the nicotinic acetylcholine receptor (AChR) can be detected.[1,2] These autoantibodies contribute to the pathogenesis of MG by blocking receptor activation, cross-linking receptors to promote internalization, and activating the complement cascade, which leads to the destruction of the neuromuscular junction.[3] Additionally, around 35% of patients who do not have detectable anti-AChR antibodies are found to have autoantibodies directed against muscle-specific tyrosine kinase (MuSK), which plays a crucial role in neuromuscular junction development and function.[4,6] In a subset of MG patients who test seronegative for both AChR and MuSK antibodies, emerging evidence suggests the presence of low-avidity autoantibodies or antibodies targeting other neuromuscular proteins, further complicating disease classification and treatment strategies.[7] Clinically, MG manifests as progressive muscle weakness that worsens with activity and improves with rest. While some patients experience mild symptoms limited to ocular muscles, others develop generalized MG, which affects limb, bulbar, and respiratory muscles. Severe exacerbations, known as myasthenic crises, can be life-threatening due to respiratory failure or significant bulbar dysfunction leading to aspiration pneumonia. Managing MG requires a multidisciplinary approach, incorporating symptomatic and immunomodulatory therapies to prevent disease progression and reduce the risk of crises.[8,9]

The current treatment strategies for MG include acetylcholinesterase inhibitors (such as pyridostigmine) to enhance neuromuscular transmission, as well as long-term immunosuppressive therapies, including corticosteroids and steroid-sparing agents (e.g., azathioprine, mycophenolate mofetil, or rituximab). Thymectomy is also recommended for certain subsets of patients, particularly those with thymoma or early-onset MG. In cases of acute deterioration, therapeutic plasma exchange (PLEX) and intravenous immunoglobulin (IVIg) are often used as rapid-acting interventions to stabilize patients.[2-4] Plasma exchange was introduced in the 1970s as a short-term intervention

to rapidly remove pathogenic autoantibodies from circulation. Early studies demonstrated its efficacy in providing transient symptom relief, particularly during myasthenic crises or as a preoperative treatment before thymectomy. However, its invasive nature, requirement for specialized equipment, and potential complications (such as hypotension, infections, and coagulopathy) have limited its widespread use in long-term MG management.[7,9]

IVIg emerged as an alternative to plasma exchange after its initial success in treating immune thrombocytopenic purpura in the 1980s. IVIg contains pooled immunoglobulin G (IgG) antibodies derived from healthy donors, which modulate the immune response through several mechanisms, including neutralization of autoantibodies, inhibition of complement activation, and suppression of pro-inflammatory cytokines. Early studies suggested that IVIg could provide clinical benefits in MG, particularly during acute exacerbations. Several observational studies and small randomized controlled trials (RCTs) reported improvement rates ranging from 73% to 76% among MG patients treated with IVIg. Given its favorable safety profile and ease of administration compared to plasma exchange, IVIg has been widely adopted in clinical practice as a first-line therapy for myasthenic crises and as an adjunct to long-term immunosuppressive therapy.[2] Despite its widespread use, the optimal role of IVIg in MG remains uncertain. Key questions persist regarding its efficacy in different clinical scenarios, such as acute exacerbations versus chronic MG maintenance therapy. Additionally, the ideal dosing regimen, the duration of effect, and the long-term impact on corticosteroid-sparing strategies remain areas of active investigation. While IVIg is generally well tolerated, concerns about cost-effectiveness, accessibility, and potential adverse effects (e.g., renal impairment, thromboembolic events, and aseptic meningitis) further emphasize the need for a comprehensive evaluation of its benefits and risks.

This systematic review aims to synthesize the available clinical

evidence regarding the efficacy, safety, and optimal use of IVIg in the treatment of MG. By analyzing data from randomized controlled trials, cohort studies, and other high-quality evidence, this review seeks to provide clinicians with evidence-based recommendations on the role of IVIg in MG management. The review will also explore potential confounding factors, including concomitant use of corticosteroids and immunosuppressants, to better understand the therapeutic landscape of IVIg in MG.

MATERIAL AND METHODS

Protocol

This systematic review follows the synthesis without meta-analysis (SWiM) guidelines to ensure methodological rigor, transparency, and reproducibility. The objective is to systematically evaluate the efficacy, safety, and clinical outcomes of intravenous immunoglobulin (IVIg) in the treatment of myasthenia gravis (MG). Specifically, this review will assess the role of IVIg in different clinical settings, including myasthenic crises, maintenance therapy, and perioperative management. Additionally, we will explore the impact of IVIg on functional improvement, the need for ventilatory support, corticosteroid-sparing effects, and its comparative efficacy versus plasma exchange (PLEX) or other immunomodulatory treatments.

Criteria for Eligibility

This review will include peer-reviewed studies published between 2015 and 2025 that investigate the efficacy and safety of IVIg in MG treatment. Eligible studies must provide quantitative assessments of clinical outcomes related to IVIg therapy in MG patients.

The inclusion criteria for this research involve patients diagnosed with myasthenia gravis (MG), including both generalized and ocular types. The main intervention studied is intravenous immunoglobulin (IVIg) therapy, which is compared to placebo, standard care, plasma exchange (PLEX), or other immunomodulatory treatments like corticosteroids, rituximab, and eculizumab. Primary outcomes focus on improvements in MG-specific clinical measures, such as the Quantitative Myasthenia Gravis

(QMG) score, Myasthenia Gravis Foundation of America (MGFA) classification, and MG-Activities of Daily Living (MG-ADL) scale. Secondary outcomes include the need for mechanical ventilation, reduction in corticosteroid use, length of hospital stay, and adverse effects such as thromboembolic events, kidney issues, and infusion-related reactions. The study design is restricted to randomized controlled trials (RCTs), cohort studies, or case-control studies that evaluate IVIg in MG treatment, and only English-language publications are considered.

Exclusion criteria remove review articles, meta-analyses, conference abstracts, and expert opinions. Studies that do not directly examine the effectiveness and safety of IVIg in MG are excluded, along with animal studies and in vitro experiments. This ensures the analysis is based on relevant, high-quality clinical evidence.

Search Strategy

A comprehensive literature search will be conducted using electronic databases, including **PubMed, Embase, Cochrane Library, Web of Science, and Scopus**. Search terms will be designed to capture studies evaluating IVIg in MG treatment. Boolean search strings will include:

("Myasthenia gravis" OR "MG") AND ("Intravenous immunoglobulin" OR "IVIg") AND ("Efficacy" OR "Clinical outcomes")

("Myasthenia crisis" OR "Generalized MG") AND ("IVIg" OR "Immunotherapy") AND ("Plasma exchange" OR "PLEX")

("Myasthenia gravis" AND "IVIg") AND ("Safety" OR "Adverse effects")

Data Retrieval

Titles and abstracts will be screened for relevance. Full-text articles meeting inclusion criteria will be reviewed, and the following data will be extracted: the study characteristics include details such as the year of publication, location, sample size, and study duration to provide context for the research. Intervention specifics focus on the IVIg regimen, including the dose, frequency, and duration of treatment. Participant demographics encompass age, gender, Myasthenia Gravis

Foundation of America (MGFA) classification, and comorbidities to better understand the population studied. Clinical outcomes are evaluated through changes in key MG-specific measures such as the Quantitative Myasthenia Gravis (QMG) score, MG-Activities of Daily Living (MG-ADL) scale, and MGFA Post-Intervention Status (MGFA-PIS) score. Additionally, outcomes include the need for mechanical ventilation or ICU admission, hospital length of stay, corticosteroid-sparing effects, and adverse events such as infusion-related reactions, thrombosis, and renal dysfunction.

Quality assessment and data synthesis involve a systematic evaluation of the methodological rigor of the included studies, ensuring the reliability and validity of the findings. This process includes analyzing potential biases, consistency of results, and the overall strength of the evidence to draw meaningful conclusions.Independent reviewers will assess study quality using the **JBI Critical Appraisal Tools**. Any discrepancies will be resolved through discussion or consultation with a third reviewer. A qualitative synthesis will summarize findings based on treatment settings (myasthenic crisis, chronic MG, perioperative use). If data homogeneity allows, a meta-analysis will estimate pooled effect sizes for IVIg efficacy, safety, and comparative outcomes with other therapies. Subgroup analyses will be performed based on disease severity, IVIg dosing regimens, and patient characteristics.

RESULTS

Our research team will gather publications from reputable sources such as Embase, PubMed, and Web of Science. After a screening process, studies meeting the inclusion criteria will be selected for detailed analysis (Figure 1). The extracted data will be systematically compiled into Table 2 for structured presentation.

A compilation of studies explores various treatments for myasthenia gravis (MG), including intravenous immunoglobulin (IVIg), subcutaneous immunoglobulin (SCIg), efgartigimod, and zilucoplan. Research indicates that both IVIg and SCIg are effective

and well-tolerated, with SCIg offering a more convenient administration route. A Canadian retrospective study (Bourque et al., 2016) highlighted successful disease control in patients switching from IVIg to SCIg. While a trial by Bril et al. (2023) found no significant difference between IGIV-C and placebo in reducing corticosteroid dose, other studies, such as Karelis et al. (2019) and Pasnoor et al. (2023), demonstrated positive outcomes with IGIV-C and SCIg administration. Furthermore, a phase 3 trial (Howard et al., 2024) showed noninferiority of efgartigimod PH20 SC compared to IV in reducing IgG levels, and a phase 2 trial (Howard et al., 2020) demonstrated improvements with zilucoplan. Overall, these studies suggest that IVIg and SCIg are effective and well-tolerated treatments for MG, with SCIg offering a convenient alternative to IVIg. Newer therapies like efgartigimod and zilucoplan also show promise in treating MG.

Table 1. The literature included in this study

Author	Origin	Method	Sample Size	Result
Bourque et al. (2016).[10]	Canada	a retrospective cohort study.	9 myasthenia gravis patients.	During the study, four patients declined to switch from IVIg to SCIg—two due to self-injection phobia and two due to satisfaction with IVIg. Nine MG patients initiated SCIg between January and December 2015. Six switched for home convenience, two had discontinued IVIg due to allergies, and one, lost to follow-up for 10 years, restarted treatment due to worsening MG. All nine had prior prednisone and pyridostigmine use, with at least one additional immunosuppressant (azathioprine in eight, mycophenolate in two). Three were intolerant to azathioprine, and six discontinued prednisone—four achieving control with azathioprine and immunoglobulin, while two avoided immunosuppressants due to intolerance or fear of side effects. The mean age was 50.6 years (range 21–84). Five were AChR antibody-positive, one was AChR and MUSK-negative, and two lacked MUSK testing due to early diagnosis. Three had thymoma, and four underwent thymectomy, while five opted against it. Disease duration ranged from 1–31 years (mean 11.8). Seven remained on symptomatic or immunomodulating therapy during SCIg, with MG severity graded as mild to moderate (MGFA II-III).
Bril et al. (2023).[11]	Multicenter study	randomized double-blind placebo-controlled trial	The trial had a total sample size of 60 patients, all of whom were randomized into two groups: 30 received immunoglobulin (IGIV-C) and 30 received placebo	The primary endpoint (≥50% reduction in CS dose) showed no significant difference between the IGIV-C treatment (60.0% of patients) and placebo (63.3%). There were no significant differences for secondary endpoints. Safety data indicated that IGIV-C was well tolerated.
Karelis et al. (2019).[12]	India	prospective, open-label, non-controlled 28-day clinical trial	Forty-nine subjects enrolled.	Forty-nine subjects enrolled. The change in QMG score at Day 14 was significant ($p < 0.001$) in the Evaluable (-6.4, n = 43) and Safety (-6.7, n = 49) populations. Among evaluable subjects, Day 14 response rates were 77, 86, and 88% for QMG, MG Composite, and MG-ADL, respectively. IGIV-C showed good tolerability with no serious adverse events.
Pasnoor et al. (2023).[13]	Multicenter.	prospective, open-label, non-controlled 28-day clinical trial.	23 patients in the ISP, and 22 entered the ETP.	A total of 12 subjects (54.5%) were female, and 18 (81.8%) were White, with mean age 51.4 ± 17 years. We obtained Week 12 ETP QMG data on 19 of 22; one subject withdrew from ETP owing to clinical deterioration, and two subjects withdrew due to dislike of needles. On primary analysis, 19 of 22 participants (86.4%, 95% confidence interval = 0.72-1.00) were treatment successes using last observation carried forward

				(p = 0.018). Secondary efficacy measures supported MG stability. SCIg was safe and well tolerated, and IgG levels were stable. Treatment satisfaction was comparable between ISP and ETP.
Howard et al. (2024).[14]	US	phase 3, randomized, open-label, parallel-group, multicenter clinical trial	153 participants screened for ADAPT-SC, 111 were enrolled (Fig. 2); 55 were randomly assigned to efgartigimod PH20 SC and 55 to efgartigimod IV.	Primary endpoint was percentage change from baseline in total immunoglobulin G (IgG) level at week 4 (1 week after the fourth administration). Secondary efficacy endpoints assessed number and percentage of Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) responders and mean change from baseline in total score for each measure. The primary endpoint was met, demonstrating noninferiority in total IgG reduction between efgartigimod PH20 SC 1000 mg and efgartigimod IV 10 mg/kg. Clinically meaningful improvements were seen as early as 1 week following the first administration in both treatment arms, with maximal improvements at week 4. Continued treatment cycles of efgartigimod PH20 SC in ADAPT-SC+ have demonstrated long-term safety and consistent improvements in MG-ADL total score. Findings from ADAPT-SC and ADAPT-SC+ demonstrate similar safety and efficacy as observed in the placebo-controlled ADAPT study.
Díez-Porras et al. (2020).[15]	Spain	single centre, prospective, monitoring, post-authorization study.	45 patients included in the analysis.	Monitoring was performed with validated scales, questionnaires, and blood tests over a 6-week period. Only 4.4% had severe adverse effects related to IVIG and 86.7% improved clinically. Notably, only 2.2% had a paradoxical symptom exacerbation in the first weeks of starting prednisone, which was statistically lower than the 42% reported in a historical series.
Howard et al. (2020).[16]	North America	Randomized, double-blind, placebo-controlled phase 2 clinical trial at 25 study sites.	The study of 44 patients was well balanced across the 3 treatment arms with respect to key demographic and disease-specific variables.	The mean age of patients across all 3 treatment groups ranged from 45.5 to 54.6 years and most patients were white (average proportions across 3 treatment groups: 78.6%-86.7%). Clinically meaningful and statistically significant improvements in primary and key secondary efficacy endpoints were observed. Zilucoplan at a dose of 0.3 mg/kg SC daily resulted in a mean reduction from baseline of 6.0 points in the QMG score (placebo-corrected change, -2.8; P = .05) and 3.4 points in the MG Activities of Daily Living score (placebo-corrected change, -2.3; P = .04). Clinically meaningful and statistically significant improvements were also observed in other secondary endpoints, the MG Composite and MG Quality-of-Life scores. Outcomes for the 0.1-mg/kg SC daily dose were also statistically significant but slower in onset and less pronounced than with the 0.3-mg/kg dose. Rescue therapy (intravenous immunoglobulin or plasma exchange) was required in 3 of 15, 1 of 15, and 0 of 14 participants in the placebo, 0.1-mg/kg zilucoplan, and 0.3-mg/kg zilucoplan arms,

				respectively. Zilucoplan was observed to have a favorable safety and tolerability profile.
Alcantara et al. (2020).[17]	Canada	Retrospective, repeated-measures design study.	Thirty-four patients were treated with chronic Ig therapy (30 IVIG/SCIG, three SCIG, one IVIG).	The mean durations of IVIG and SCIG periods were 21.8 ± 19.4 (range 3–64) months and 19.5 ± 11.3 (range 5–45) months respectively. There was a significant reduction in MGII scores (27.7 ± 15.7 baseline; 22.0 ± 17.4 IVIG period; 19.5 ± 18.1 SCIG period; F = 17.9; d.f. = 1.7; P < 0.01), pyridostigmine and immunosuppressant use (P = 0.00). The outcome 'percentage of normal' had a significant positive association with both treatments (P = 0.00).

Table 2. Critical appraisal of Study

Parameters	Bourque et al. (2016)	Bril et al. (2023)	Karelis et al. (2019)	Pasnoor et al. (2023)	Howard et al. (2024)	Díez-Porras et al. (2020)	Howard et al. (2020)	Alcantara et al. (2020)
1. Bias related to temporal precedence								
Is it clear in the study what is the "cause" and what is the "effect" (ie, there is no confusion about which variable comes first)?	Clear temporal order, but retrospective design limits causality	Clear cause-effect relationship due to RCT design	Clear temporal order, but lacks control group	Clear temporal order, but lacks control group	Clear temporal order due to RCT design	Clear temporal order, but observational study	Clear cause-effect relationship due to RCT design	Clear temporal order, but retrospective design limits causality
2. Bias related to selection and allocation								
Was there a control group?	No control group, selection bias possible	Control group included (placebo-controlled)	No control group, potential selection bias	No control group, potential selection bias	Control group included (randomized comparison)	No control group, potential selection bias	Control group included (placebo-controlled)	No control group, potential selection bias
3. Bias related to confounding factors								
Were participants included in any comparisons similar?	Participants may differ in baseline characteristics	Randomization reduces confounding	Participants may differ in baseline characteristics	Participants may differ in baseline characteristics	Randomization reduces confounding	Participants may differ in baseline characteristics	Randomization reduces confounding	Participants may differ in baseline characteristics
4. Bias related to administration of intervention/exposure								
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Differences in prior treatments (e.g., azathioprine use)	Standardized administration of IGIV-C	Differences in prior treatments	Differences in prior treatments	Standardized administration of efgartigimod	Differences in prior treatments	Standardized administration of zilucoplan	Differences in prior treatments
5. Bias related to assessment, detection, and measurement of the outcome								
Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Were the outcomes of participants included in any comparisons measured in the same way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were outcomes measured in a reliable way?	Outcome measured but potential recall bias	Multiple measurements pre/post intervention, standardized outcome measures	Pre/post outcome measurement performed, but no control group	Pre/post outcome measurement performed, but no control group	Standardized outcome measurements and follow-up	Standardized outcome measures but observational design	Multiple measurements pre/post intervention, standardized outcome measures	Outcome measured but potential recall bias
6. Bias related to participant retention								
Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Some patients lost to follow-up	Follow-up was complete	Follow-up was complete	Some withdrawals, reasons described	Follow-up was complete	Follow-up was complete	Follow-up was complete	Some patients lost to follow-up
7. Statistical conclusion validity								
Was appropriate statistical analysis used?	Small sample, limited statistical power	Appropriate statistical analysis used	Statistical methods used but lacks a control group	Statistical methods used but lacks a control group	Appropriate statistical analysis used	Statistical methods used appropriately	Appropriate statistical analysis used	Small sample, limited statistical power

DISCUSSION

IVIg exerts its immunomodulatory effects through multiple mechanisms that help restore immune balance. Several key factors involved in the pathogenesis of myasthenia gravis (MG) are relevant to the therapeutic actions of IVIg, including antibodies, complement, cytokines, FcγRIIb, T cells, antigen-presenting cells (APCs), and immunoregulatory genes.[2,18-20]

Effects of IVIg on Antibodies

IVIg influences antibodies through several mechanisms. First, it provides idiotypic antibodies that can neutralize pathogenic autoantibodies. Immunoglobulins contain idiotypes that form monomers or dimers. Since IVIg is derived from thousands of donors, up to 40% of the immunoglobulins in IVIg exist as dimeric pairs. These idiotypes bind to circulating pathogenic autoantibodies, leading to their neutralization and degradation. [2,18-20]

Second, IVIg modulates B-cell trophic factors such as B-cell activating factor (BAFF) and A Proliferation-Inducing Ligand (APRIL), both of which influence B-cell survival and differentiation. BAFF levels are elevated in MG patients but can be suppressed by IVIg. [2,18-20]

Third, IVIg saturates neonatal Fc receptors (FcRn), which accelerates the degradation of pathogenic immunoglobulin G (IgG) and lowers circulating antibody levels. FcRn, found on many cell surfaces, normally recycles IgG through endosomes, returning it to the circulation. However, when IVIg saturates FcRn, excess immunoglobulins—including anti-acetylcholine receptor (AChR) autoantibodies—are diverted to lysosomes for degradation. In experimental autoimmune MG (EAMG), IVIg administration resulted in reduced IgG levels and a significant clinical improvement in a dose-dependent manner. [2,18-20]

Effects of IVIg on Complement

In MG, pathogenic antibodies bind to complement proteins at the neuromuscular junction, contributing to disease pathology. Studies have shown that complement component C3b is markedly elevated in MG patients, with one study reporting a

geometric mean uptake value for C3 of 10,570 counts/min in MG patients compared to 3,459 in healthy controls. Complement activation leads to the formation of C3a and C3b, which subsequently contribute to the membrane attack complex (MAC), causing target cell lysis. [2,18-20]

IVIg suppresses complement activation by inhibiting C3a and C3b, thereby interfering with MAC formation. In patients with dermatomyositis, IVIg significantly reduced complement consumption within two days of infusion, with C3b and MAC deposits disappearing from muscle biopsies post-treatment. IVIg-mediated complement inhibition also reversed microvasculopathy and perifascicular atrophy, leading to neovascularization and restoration of muscle architecture, correlating with clinical improvement. The degree of C3 inhibition by IVIg is dose-dependent. [2,18-20]

Effects of IVIg on Cytokines

IVIg influences cytokine profiles in MG. In the EAMG model, IVIg downregulated pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNFα) while upregulating anti-inflammatory cytokines like IL-4 and IL-10. Additionally, IVIg has been shown to counteract IL-1-induced damage; in vitro studies demonstrated that IL-1 caused the destruction of cultured human myotubes, which was prevented by IVIg administration. [2,18-20]

Effects of IVIg on FcγRIIb

FcγRIIb is an inhibitory receptor found on B cells and macrophages. On B cells, it transduces inhibitory signals, preventing their differentiation into IgG-producing plasma cells. The absence of FcγRIIb is associated with autoimmune disease development. IVIg upregulates FcγRIIb, thereby blocking antibody-dependent cell-mediated cytotoxicity and enhancing therapeutic efficacy. This mechanism has been demonstrated in chronic inflammatory demyelinating polyneuropathy (CIDP), where patients with active disease exhibited reduced FcγRIIb levels in memory B cells and monocytes. IVIg administration led to FcγRIIb upregulation in these cells, correlating with clinical

improvement. Similar effects are presumed in MG and other autoimmune conditions. [2,18-20]

Effects of IVIg on T Cells and APCs

IVIg modulates T-cell activity and co-stimulatory molecules. In the EAMG model, IVIg treatment reduced the expression of CD40 ligand, a key co-stimulatory molecule, which correlated with clinical benefit. Additionally, major histocompatibility complex (MHC) class I expression, which is upregulated in muscle biopsies from patients with inflammatory myopathies, was significantly downregulated following IVIg treatment. [2,18-20]

Preliminary data suggest that a subset of regulatory T cells (Tregs) expressing cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) is functionally impaired in MG patients. IVIg therapy expanded this Treg subset, indicating a potential role in immune regulation. [2,18-20]

MG Treatment Approaches

Standard symptomatic treatment includes pyridostigmine, often combined with corticosteroids or steroid-sparing immunosuppressants for moderate MG. In severe cases, IVIg, plasmapheresis, or immunoadsorption may be required, with intensive care necessary during exacerbations. Screening for thymoma is essential for all MG patients, as thymectomy may be indicated in AChR antibody-positive individuals aged 18–60 years with a disease duration of less than five years. [2,18-20]

The studies analyzed in this review provide a comprehensive overview of immunoglobulin-based therapies and emerging targeted treatments for myasthenia gravis (MG). They highlight the effectiveness, safety, and practical considerations of intravenous immunoglobulin (IVIG) and subcutaneous immunoglobulin (SCIG), as well as newer treatments like efgartigimod and zilucoplan. [2,18-20]

IVIG vs. SCIG: Efficacy, Safety, and Patient Preferences

The comparison between IVIG and SCIG is a critical aspect of MG management. IVIG has long been a standard treatment for MG, particularly for acute exacerbations,

while SCIG has gained attention as a maintenance therapy.

Bourque et al. (2016) explored the use of SCIG as an alternative to IVIG and found it to be an effective option for MG patients. One of the primary advantages of SCIG is its convenience, allowing patients to self-administer the treatment at home. This can be particularly beneficial for individuals who experience adverse effects related to IVIG infusions, such as headaches, flu-like symptoms, or infusion-related reactions. However, the study also highlighted that some patients preferred IVIG due to a reluctance to self-administer SCIG, particularly those with needle phobia.[10]

Similarly, Alcantara et al. (2020) demonstrated the benefits of long-term maintenance therapy with both IVIG and SCIG, noting significant improvements in MG severity scores. Patients on these therapies required lower doses of corticosteroids and other immunosuppressants, suggesting that immunoglobulin therapy plays a role in reducing overall medication burden.[17]

Pasnoor et al. (2023) further investigated the transition from IVIG to SCIG and found that most patients maintained stable disease control with SCIG. While a minority of patients withdrew due to discomfort with self-injections, those who continued the therapy reported comparable treatment satisfaction and stable IgG levels. This supports SCIG as a viable alternative for MG patients seeking a more flexible treatment option without frequent hospital visits.[13]

Corticosteroid-Sparing Effects of IVIG

One of the debated aspects of IVIG therapy is its role in reducing corticosteroid dependence. Bril et al. (2023) conducted a randomized double-blind placebo-controlled trial to evaluate whether IVIG could serve as a corticosteroid-sparing agent in MG. Interestingly, their findings did not demonstrate a significant difference between the IVIG and placebo groups regarding corticosteroid reduction, suggesting that IVIG's primary role may be in symptom management rather than modifying long-term corticosteroid requirements.[11]

In contrast, Díez-Porras et al. (2020) focused on the potential of IVIG in preventing MG exacerbations triggered by prednisone initiation. Their findings showed a remarkably low exacerbation rate (2.2%) in patients receiving IVIG, compared to historical data indicating a 42% exacerbation rate in patients who started prednisone without IVIG. This suggests that IVIG may have a protective effect when corticosteroid therapy is introduced, reducing the risk of early worsening often seen in MG patients.[15]

Emerging Therapies: Efgartigimod and Zilucoplan

Beyond conventional immunoglobulin therapy, newer targeted treatments are being explored to provide additional therapeutic options for MG.

Howard et al. (2024) conducted the ADAPT-SC study, which assessed the efficacy of subcutaneous efgartigimod PH20, a neonatal Fc receptor (FcRn) inhibitor. The study demonstrated that SC efgartigimod was non-inferior to IV administration in terms of reducing total IgG levels and improving MG symptoms. This is significant because FcRn inhibitors directly target the pathogenic IgG autoantibodies responsible for MG, providing a more specific and mechanistic approach compared to traditional IVIG or SCIG. The ability to administer efgartigimod subcutaneously further expands treatment flexibility for patients who prefer home-based therapies.[14]

Another promising treatment is zilucoplan, a complement inhibitor evaluated by Howard et al. (2020) in a randomized controlled trial. Zilucoplan at a dose of 0.3 mg/kg demonstrated statistically significant improvements in Quantitative Myasthenia Gravis (QMG) and MG Activities of Daily Living (MG-ADL) scores, suggesting effective symptom control. Importantly, zilucoplan was well tolerated, with a favorable safety profile and a reduced need for rescue therapy, positioning it as a potential treatment option for moderate-to-severe MG.[16]

Clinical Implications and Future Directions

The findings from these studies emphasize the evolving landscape of MG treatment, where patients now

have multiple therapeutic options beyond corticosteroids and acetylcholinesterase inhibitors. SCIG has emerged as a practical alternative to IVIG, particularly for maintenance therapy, while FcRn inhibitors and complement inhibitors represent promising targeted approaches with potentially improved efficacy and safety profiles.

Future research should focus on further research is essential to fully understand the long-term implications of various myasthenia gravis (MG) treatments. Long-term comparative studies are needed to assess the durability of response and safety profiles of subcutaneous immunoglobulin (SCIG), efgartigimod, and zilucoplan in comparison to intravenous immunoglobulin (IVIG) and conventional immunosuppressants. Understanding patient adherence, preferences, and the impact of self-administered therapies on daily life is also crucial for optimizing treatment strategies and improving quality of life. As newer therapies emerge, cost-effectiveness analyses are necessary to guide healthcare policy and insurance coverage decisions, ensuring that effective treatments are accessible. In conclusion, while IVIG remains a vital part of MG management, SCIG offers a convenient alternative, and novel therapies like efgartigimod and zilucoplan hold the potential to revolutionize MG treatment by providing targeted approaches.

CONCLUSION

The systematic review of intravenous immunoglobulin (IVIg) for myasthenia gravis (MG) highlights its significant role in managing this chronic autoimmune disorder. IVIg has demonstrated efficacy in acute exacerbations, myasthenic crises, and as an adjunct to long-term immunosuppressive therapy. Future research should focus on long-term comparative studies, patient adherence, quality of life, and cost-effectiveness to optimize MG management.

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