

**Clinical Question:**

Pt is a 41 YOF with PMHx of myasthenia gravis who presented to the ED with blurry and double vision, as well as bilateral weakness of the arms and legs. She states her symptoms feel similar to previous myasthenia gravis exacerbations. She was admitted to the medicine floor for further treatment with IVIG therapy.

In patients experiencing myasthenic gravis crises, does treatment with intravenous immunoglobulin (IVIG) compared to plasmapheresis lead to faster clinical improvement and better functional outcomes?

**PICO Question:**

<b>P</b>	<b>I</b>	<b>C</b>	<b>O</b>
Myasthenia gravis crises	IVIG therapy	Plasmapheresis	Clinical improvement
Myasthenia gravis exacerbation	Intravenous immunoglobulin		Time to clinical improvement
			Better functional outcome
			Quality of life

**Search Strategy:**

PubMed:

Myasthenic gravis crisis AND IVIG AND Plasmapheresis: 60 results

Filters: free full text, meta analysis, RCT, systematic review: 3 results

Myasthenic gravis exacerbation AND IVIG AND Plasmapheresis: 51 results

Filters: free full text, meta analysis, RCT, systematic review: 3 results

Myasthenia gravis crisis AND Intravenous immunoglobulin AND Plasmapheresis AND Clinical improvement: 23 results

Filters: free full text, meta analysis, RCT, systematic review: 2 results

Google Scholar:

IVIG vs plasmapheresis for myasthenia gravis crisis: 6,210 results

Filters: since 2022, review articles, sort by relevance: 493 results

Time to clinical improvement in myasthenia gravis crisis with IVIG vs plasmapheresis:  
4,930 results

Filters: since 2026, review articles, sort by relevance: 426 results

Cochrane:

Myasthenic crisis AND plasmapheresis: 6 results

How I chose the articles:

In order to choose valuable articles, I prioritized selecting articles that represent the highest levels of evidence, including systematic reviews, meta-analyses, and RCTs. To achieve this, I applied database filters. Although the process was time consuming, I was able to identify two systematic reviews/meta-analyses. For the remaining two articles, I selected retrospective cohort studies, which still provide valuable evidence, as they analyze previously collected data by grouping patients based on treatments (exposures) and comparing outcomes between the groups. Two of my articles came from Google Scholar, while my other two came from PubMed. There was limited research on IVIG compared to plasmapheresis for myasthenic crisis on Cochrane. Specifically, Google Scholar provided a large number of articles to choose from, even after filters were applied. My first step in choosing the articles included reading the titles and abstracts, ensuring that they included a comparison between IVIG and plasmapheresis. Some of the articles I came across only focused on one or the other, therefore they were not picked. I wanted my articles to specifically address my PICO question comparing the two treatments. Further, I assessed the outcomes studied; I chose articles that measured time to clinical improvement and quality of life (including mortality rates).

I also chose studies that were conducted recently, and all of the studies I chose are within a time frame of 2021-2025. I thought this was important because medical evidence is constantly evolving, and newer research is more likely to reflect current practice, guidelines, and patient populations, which increases reliability. Filters were very helpful in narrowing down articles based on a recent time frame.

A minor limitation I encountered included the limited availability of full text articles. To ensure my articles addressed my PICO question to the highest extent, I wanted full access

to the study to read through the introduction, how the study was conducted, and the results. Even with filters applied, many articles that seemed great to use were not fully accessible. This took more time to find articles that I was able to access freely.

### **Articles Chosen:**

1. Pavlekovics, M., Engh, M. A., Lugosi, K., Szabo, L., Hegyi, P., Terebessy, T., Csukly, G., Molnar, Z., Illes, Z., & Lovas, G. (2023). Plasma exchange versus intravenous immunoglobulin in worsening myasthenia gravis: A systematic review and meta-analysis with special attention to faster relapse control. *Biomedicines*, 11(12), 3180. <https://doi.org/10.3390/biomedicines11123180> ; Link: <https://www.mdpi.com/2227-9059/11/12/3180>

### Abstract:

Currently used rescue interventions to prevent rapid myasthenic deterioration are plasma exchange (PLEX) and intravenous immunoglobulin (IVIG). We investigated the evidence to determine whether the two methods were interchangeable or whether one was superior to the other. This review was registered on PROSPERO (CRD42021285985). Only randomized controlled trials (RCTs) comparing the efficacy and safety of PLEX and IVIG in patients with moderate-to-severe myasthenia gravis (MG) were included. Five major databases were systematically searched (PubMed, CENTRAL, Embase, Scopus, and Web of Science). Odds ratios (OR) with 95% confidence intervals (CI) were calculated for adverse events and mean differences (MD) for changes in quantitative myasthenia gravis scores (QMG). Three RCTs met the inclusion criteria. Two investigating 114 patients in total were eligible for meta-analysis to analyze efficacy and safety. For the change in QMG score, the MD was -2.8 (95% CI: -5.614-0.113), with PLEX performing better. For adverse events, an OR of 1.04 was found (95% CI: 0.25-4.27). This study demonstrated a low risk of bias in evaluating treatment efficacy but indicated a high risk of bias in assessing procedural safety outcomes. Although the results did not show any significant difference, there was a tendency indicating faster efficacy of PLEX in the first two weeks of treatment. In such a critical clinical condition, this tendency may be clinically meaningful, but further studies should clarify this benefit.

### Key points:

- No statistical difference in overall efficacy or safety between IVIG and plasmapheresis (PLEX)
- PLEX may lead to faster clinical improvement, especially in the first 2 weeks, compared to IVIG

I chose this article because it is a systematic review and meta-analysis of RCTs, which provides high level of clinical evidence. Although only a small number of RCTs were available, they minimize confounding variables and increase reliability of the results. The study evaluates IVIG vs plasmaphoresis in patients with moderate-severe MG (including crises), which directly aligns with my PICO question. Additionally, it evaluates outcomes such as clinical improvement and time to improvement. Ultimately, the study identified a trend toward faster improvement with plasmaphoresis within the first 2 weeks compared to IVIG.

2. Maroney, M., Diehl, T., Blaney, E., Zurob, S., Tauseef, A., Mirza, M., & Abdul Jabbar, A. B. (2025). Clinical and economic outcomes of myasthenia gravis and myasthenic crisis when treated with PLEX and IVIG. *Frontiers in Neurology*, 16, 1713388.

<https://doi.org/10.3389/fneur.2025.1713388> Link:

<https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2025.1713388/full>

#### Abstract:

**Introduction:** Myasthenia gravis is an autoimmune disorder characterized by muscle weakness, with myasthenic crisis representing a life-threatening exacerbation requiring respiratory support. Acute treatment options include plasmapheresis (PLEX) and intravenous immunoglobulin (IVIG). Prior studies have reported mixed results regarding the relative effectiveness of these therapies, although recent evidence suggests that PLEX may provide faster and more noticeable clinical improvement. The objective of this study was to evaluate differences in clinical and economic outcomes among U.S. patients hospitalized for myasthenia gravis or crisis who received PLEX, IVIG, both, or neither treatment.

**Methods:** Myasthenia gravis and crisis admissions from 2017 to 2022 were collected using the National Inpatient Sample. Admissions were categorized by treatment: IVIG, PLEX, both, or neither. To minimize selection bias, admissions were propensity-matched for IVIG and PLEX. Differences in mortality were evaluated using logistic regression models. Length of stay and inflation-adjusted total charge were assessed using linear regression models.

**Results:** Most admissions received neither PLEX nor IVIG. Compared to treatment with neither, treatment with IVIG, PLEX, or both were not associated with significant differences in mortality; however, they were linked to longer hospital stays and higher total charge. A

direct comparison of PLEX vs. IVIG revealed similar mortality and total charges, although length of stay was longer for PLEX. Older age was associated with increased mortality.

Discussion: Although PLEX has been advocated as first-line therapy due to rapid clinical improvement, national data do not clearly indicate a superior treatment option, with similar mortality and total charges observed across therapies.

I chose this article because it directly compares IVIG and plasmaphoresis (PLEX) in patients with myasthenia gravis and myasthenic crises using a large US database. Retrospective cohort studies provide valuable evidence by analyzing data based on different treatments and comparing groups exposed to it vs not exposed. The study evaluates important outcomes such as mortality, length of stay, and cost, showing that IVIG and plasmaphoresis have similar mortality, though PLEX is associated with longer hospital stays.

3. Ipe, T. S., Rengarajan, A., Muralidharan, R., & Abraham, O. C. (2021). Therapeutic plasma exchange in myasthenia gravis. *Frontiers in Neurology*, 12, 662856.

<https://doi.org/10.3389/fneur.2021.662856> Link:

<https://pmc.ncbi.nlm.nih.gov/articles/PMC8439193/>

#### Abstract:

Background: Patients with Myasthenia Gravis (MG) can be treated acutely with therapeutic plasma exchange (TPE) or intravenous immune globulin (IVIG). To date, there is no definitive understanding of which of the two treatments is more effective and safer. The purpose of this study was to systematically review the literature on the comparative efficacy and safety of TPE to other available treatments for MG.

Methods: A systematic literature search for studies published between 1997 and 2017 was performed per Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines using two database sources, MEDLINE (through the PubMed database) and Cochrane Library.

Results: The search strategy resulted in 535 articles whose abstracts were reviewed. Among these, 165 full texts articles were reviewed for eligibility and 101 articles were excluded. Of the 165 articles, 64 articles were included for a systematic literature and 11 articles for a meta-analysis.

Conclusions: This systematic literature review and meta-analysis of treatment options showed that there was a higher response rate with TPE than IVIG in acute MG patients and patients undergoing thymectomy. There was no difference in mortality between the two treatment options. Our findings highlight the need for additional randomized clinical trials in these patients with MG.

I chose this article because it is a systematic review and meta-analysis which provides high level of evidence, and compares plasmapheresis and IVIG in patients with myasthenia gravis. This article includes a large number of studies, increasing the strength and reliability of its conclusions. The outcomes evaluated include response rate and mortality rates, which relates to my PICO question addressing functional outcomes.

4. Zain, A., Khan, M. A., Fatima, A., Ahmed, S., & Iqbal, M. (2024). Comparative analysis of intravenous immunoglobulins (IVIG) versus plasmapheresis (PLEX) in the management of myasthenic crisis. *Cureus*, 16(9), e68895. <https://doi.org/10.7759/cureus.68895> ; Link: <https://pmc.ncbi.nlm.nih.gov/articles/PMC11458158/pdf/cureus-0016-00000068895.pdf>

#### Abstract:

Myasthenia gravis (MG) is an autoimmune disorder affecting postsynaptic membranes in neuromuscular junctions, presenting as fatigable muscle weakness. Myasthenic crisis is a life-threatening complication characterized by severe respiratory insufficiency necessitating invasive or noninvasive ventilation. Two rapid therapies used to manage myasthenic crises are intravenous immunoglobulins (IVIg) and plasmapheresis (PLEX). Their comparative effectiveness remains equivocal. Our article examines evidence from several clinical trials and observational studies, in order to determine the superiority of one treatment over the other. Multiple factors can complicate the choices between two treatments. We concluded that the choice between PLEX and IVIg is multifaceted, guided by individual patient characteristics, institutional resources, and clinician preference. While PLEX can be considered as first-line for rapid clinical outcomes, it is hard to pick one treatment over the other, and careful consideration of comorbidities and resource

availability is crucial. Our article highlights the need for further research to establish definitive guidelines and enhance patient outcomes in myasthenic crisis patients.

Key points:

- Plasmaphoresis (PLEX) demonstrated better short-term outcomes, including higher extubation rates at 2 weeks and improved functional recovery at 1 month
- Faster clinical improvement was seen with PLEX
- Both PLEX and IVIG were effective overall, with no clear long-term superiority established

I chose this article because it directly compares IVIG and plasmaphoresis in patients with myasthenic crisis, which directly relates to my PICO question. The study incorporates evidence from multiple clinical and observational studies to evaluate clinical effectiveness, and the findings emphasize that while plasmaphoresis may lead to faster clinical improvement, overall outcomes remain similar and treatment choice depends on patient factors. This supports the idea that management should be individualized, which is important when applying any evidence to clinical practice.

Author (Date)	Level of Evidence	Sample/Setting (# of subjects/studies, cohort, definition, etc)	Outcome(s) studied	Key findings	Limitations and Biases
Pavlekovics, M., Engh, M. A., Lugosi, K., Szabo, L., Hegyi, P., Terebessy, T., Csukly, G., Molnar, Z., Illes, Z., & Lovas, G. (2023)	Systematic review & meta-analyses of RCTs	<p><b>Population:</b> adult pts (&gt;18) with moderate-severe Myasthenia Gravis, including crises/acute exacerbations</p> <p><b>Studies:</b> 3 studied included in systematic review (114 patients) &amp; 2 studies included in meta-analyses comparing IVIG vs plasmapheresis (PLEX); 5 major databases used</p> <p><b>Setting:</b> no single location; data pooled from multiple international studies &amp; databases</p>	<p>Primary outcomes: clinical improvement/ efficacy</p> <p>Secondary outcomes: speed of symptom improvement, safety and adverse events, hospital-related outcomes</p> <p>Tool used: quantitative myasthenia gravis scores (QMG); assesses 13 major symptoms on a scale of 0-3 (a higher score indicates a more severe condition)</p>	<p>-There was no clear superiority overall between IVIG &amp; PLEX in long-term efficacy</p> <p>-PLEX may lead to faster clinical improvement (pts who received PLEX had on average 2.8 lower scores on QMG after 2 weeks of tx compared to IVIG); benefit of PLEX especially in respiratory crisis over IVIG</p> <p>-IVIG may have advantages in tolerability and ease of use (less invasive)</p> <p>-No significant difference between PLEX &amp; IVIG in terms of side effect profile</p>	<p>-Limited # of RCTs available</p> <p>-Heterogeneity between studies (differences in patient severity and treatment protocols)</p> <p>-Potential publication bias (studies demonstrating faster improvement with PLEX or positive tx effects may have been more likely to be published, while studies showing minimal differences between therapies may have been underreported)</p>
Maroney, M., Diehl, T., Blaney, E., Zurob, S., Tauseef, A., Mirza, M., & Abdul Jabbar, A. B. (2025)	Retrospective cohort study	<p><b>Data source:</b> US National Inpatient Sample</p> <p><b>Time frame:</b> 2017-2022</p> <p><b>Population:</b> hospitalized pts <math>\geq 18</math> with Myasthenia Gravis or myasthenic crisis</p> <p><b>Sample size:</b> ~14,360 MG pts ~43,840 MG crisis pts</p> <p><b>Groups compared:</b> IVIG, plasmapheresis (PLEX), both tx's, neither tx; 9,530 pts received IVIG, 9,835 received PLEX, 825 received both</p>	<p>Primary outcome: in-hospital mortality</p> <p>Secondary outcomes: length of stay &amp; total hospital charge</p>	<p>-Tx of MG and MG crisis with both IVIG and PLEX was associated with highest mortality rate, longest hospital stay, and greatest total charges</p> <p>-There was no significant difference in mortality or cost between IVIG and PLEX</p> <p>-Longer hospital stays associated with PLEX compared to IVIG</p>	<p>-Because this was a retrospective cohort, causation cannot be established (only association)</p> <p>-Selection bias (sicker pts may have been more likely to be treated with PLEX)</p> <p>-Confounding (more severe disease at baseline, comorbidities, variability in tx protocols, access to resources)</p> <p>-Database limitations (relies on ICD coding accuracy)</p>

					-No functional outcomes (does not directly measure symptom improvement or time of improvement)
Ipe, T. S., Rengarajan, A., Muralidharan, R., & Abraham, O. C. (2021)	Systematic review and meta-analysis	<p><b>Population:</b> pts with myasthenia gravis</p> <p><b>Studies:</b> 535 abstract articles were reviewed; among these, 156 full text articles were reviewed for eligibility &amp; 101 were excluded; 64 articles were included for systematic literature and 11 articles for meta-analysis</p> <p><b>Setting:</b> studies were conducted in various clinical/hospital settings internationally</p> <p><b>Definition of intervention:</b> comparison of therapeutic plasma exchange (TEP) vs IVIG for acute MG management</p>	<p>Primary outcomes: clinical response rate/improvement in MG symptoms</p> <p>Secondary outcomes: time for clinical improvement, need for mechanical ventilation, length of hospital stay, adverse events</p>	<p>-TPE showed greater overall clinical improvement compared to IVIG in acute MG pts</p> <p>-TPE provides more rapid symptom relief in myasthenic crisis pts</p> <p>-No difference in mortality rates between TPE and IVIG</p> <p>-IVIG and TPE are both valid first line options, especially when one is contraindicated</p> <p>-Clinical decision to chose IVIG vs TPE depends on pt context; choice is often influenced by availability, patient stability, and contraindications (i.e hemodynamic stability for TPE)</p>	<p>-Heterogeneity of studies; variability in study designs, patient severity &amp; treatment protocols</p> <p>-Selection bias; sicker pts may have been preferentially treated with one therapy over the other</p> <p>-Possibly that the search may not have captured all relevant studies; potential gaps include non-English articles, articles published prior to 1997, or articles for which full text copies could not be obtained</p>
Zain, A., Khan, M. A., Fatima, A., Ahmed, S., & Iqbal, M. (2024)	Retrospective cohort study	<p><b>Population:</b> pts diagnosed with myasthenic crisis</p> <p><b>Sample size:</b></p> <ul style="list-style-type: none"> <li>-Gajdos et al. (87 pts with MG exacerbations)</li> <li>-Qureshi et al. (54 episodes of myasthenic crises)</li> <li>-Wang et al. (40 pts with myasthenic crises)</li> <li>-Barth et al. (84 pts with mod-severe MG)</li> </ul>	<p>Primary outcomes: clinical improvement/functional outcomes</p> <p>Secondary outcomes: length of hospital stay, time to clinical improvement, need for mechanical ventilation, adverse events</p>	<p>-PLEX is associated with a more rapid improvement of clinical outcomes compared to IVIG</p> <p>-PLEX showed superior short-term outcomes (higher rates of extubation at 2 weeks)</p> <p>-Both PLEX and IVIG have comparable long</p>	<p>-Retrospective design (cannot establish causation, only association)</p> <p>-Lack of randomization (treatment groups were not evenly matched) —&gt; confounding variables</p>

		<p>-Murthy et al. (23 episodes of myasthenic crises)</p> <p>-Pavlekovics et al. (114 pts with mod-severe MG)</p> <p><b>Setting:</b> hospital based clinical setting</p> <p><b>Cohort design:</b> pts were grouped based on tx received (IVIG vs PLEX)</p>		<p>term efficacy (no sufficient data to establish superiority of one over the other)</p> <p>-The decision to choose IVIG or PLEX should be based on individual cases</p>	<p>-Small sample sizes</p> <p>-Variability in management; differences in availability of resources</p>
--	--	---	--	--	--

### Conclusion(s):

- Pavlekovics et al. (2023)

- Based on this article, both plasmapheresis (PLEX) and IVIG are equally effective overall for treating worsening myasthenia gravis, particularly when assessing the long term. It was found that PLEX does tend to produce a faster clinical improvement, which can be especially important in more severe cases, such as patients at risk of respiratory compromise. Using the quantitative myasthenia gravis score (QMG), patients who were treated with PLEX had lower scores after two weeks of treatment when compared with IVIG. There were no major differences in safety profiles between the two treatment options in the analyzed study. The evidence of this study is limited by small sample sizes and few available RCTs, meaning further research is required in order to obtain stronger conclusions.

- Maroney et al. (2025)

- This article showed no clear superiority between IVIG and plasmapheresis (PLEX) as treatment in patients with myasthenic crises; they had similar mortality rates and overall effectiveness. Further, the study suggested that PLEX may lead to faster clinical improvement when compared with IVIG, but it did not show a meaningful advantage in major outcomes such as mortality. PLEX was also found to be associated with a longer length of hospital stay than IVIG. Treatment with both IVIG and PLEX was associated with longer hospital stays and higher costs compared to no treatment. The article highlighted that treatment choice should be dependent on patient factors, hospital resources, and clinical context rather than assumed superiority.

- Ipe et al. (2021)

- This article concludes that therapeutic plasma exchange (TPE) for patients with myasthenia gravis (and crises) demonstrates a higher clinical response rate than IVIG, as well as faster clinical improvement, making it particularly useful in severe or rapidly progressing cases. There was no significant difference in mortality between IVIG and TPE. The article goes on to

highlight that both TPE and IVIG are valid first-line therapies, and treatment choice should be individualized based on patient condition and clinical context.

- Zain et al. (2024)

- This article concludes that plasmaphoresis (PLEX) may provide superior short-term outcomes compared to IVIG in patients with myasthenic crisis, but both therapies remain effective and clinically appropriate. PLEX was associated with higher rates of extubation at 2 weeks and improved functional recovery at 1 month when compared with IVIG. PLEX was also associated with faster clinical improvement, likely due to its MOA of direct removal of circulating autoantibodies, leading to faster symptom relief.

Overall:

Across multiple studies, including systematic reviews, meta-analyses, and retrospective cohorts, both plasmaphoresis and intravenous immunoglobulin are consistently shown to be effective first-line therapies for the management of myasthenia gravis exacerbations/crises. There is no clear evidence across the articles I have chosen that demonstrate superiority in one treatment over the other in regards to long term outcomes or mortality. However, a consistent finding across the studies show that plasmaphoresis tends to provide faster clinical improvement, likely due to its direct removal of circulating autoantibodies. This advantage is especially relevant in severe or rapidly progressing cases of myasthenia gravis, such as patients at risk for respiratory compromise, where quicker symptom relief may be critical. One of the studies also suggests improved short-term outcomes with plasmaphoresis. Despite these benefits, plasmaphoresis does not demonstrate a significant advantage over IVIG. Some limitations across the studies include small sample sizes, heterogeneity in study design, and lack of high quality RCTs, highlighting the need for further research.

Ultimately, the choice between plasmaphoresis and IVIG should be individualized, taking patient factors into account such as disease severity, patient stability, comorbidities and access to resources, rather than choosing one based on superiority.

**Clinical bottom line:**

I would say that the overall weight of evidence between all 4 of my articles is moderate, with a mix of higher-level and lower-level studies. Two of the included articles (Pavlekovics et al., 2023 and Ipe et al., 2021) are systematic reviews and meta-analyses, which strengthen the evidence by synthesizing multiple studies and minimizing individual bias. However, there were limitations in the number of available RCTs to choose from, as well as relatively small pooled sample sizes, which makes a study less accurate and harder to apply clinically. The other two studies (Maroney et al., 2025 and Zain et al., 2024) are retrospective cohort studies, which provide valuable real-world data, but are limited by selection bias, confounding variables and lack of randomization. Across all 4 of my included studies, there were limitations such as heterogeneity in patient populations and treatment protocols which limits direct comparison, in this case, between IVIG and plasmaphoresis (PLEX) in the management of myasthenic crises.

Despite these weaknesses, a consistent trend across all studies increases confidence in overall conclusion, particularly regarding faster clinical improvement with PLEX. One article (Zain et al., 2024) also showed improvement in short-term outcomes with PLEX. Even still, the magnitude of effect between PLEX and IVIG is generally small. There was no significant difference in mortality or long-term outcomes across all 4 studies, and the differences between PLEX and IVIG are not large enough to demonstrate clear superiority of one therapy over the other in all patients.

The faster onset of action with PLEX, however, is clinically meaningful. This is highly relevant in myasthenic crisis patients, where rapid improvement can reduce risk of respiratory failure and shorten time on mechanical ventilation. Given that PLEX directly removes circulating autoantibodies and often produces quicker symptom relief, it may be particularly beneficial in the acute phase of severe or rapidly progressing crisis. IVIG, while sometimes slower in onset, still provides effective immunomodulatory benefits and comparable long-term outcomes. Therefore, one potential clinical consideration is the use of PLEX initially for immediate stabilization and rapid symptom control, followed later by IVIG for continued immunomodulatory support and maintenance of clinical improvement. Although the current evidence does not definitively establish superiority of sequential therapy over either treatment alone, this approach may be reasonable in select critically ill patients and highlights an area where further research is needed.

Important gaps remain in the current evidence, such as lack of large, high quality RCTs and variability in patient populations and treatment protocols. Further studies should aim to include larger sample sizes, standardize outcome measures, and identify specific patient populations that benefit more from PLEX vs IVIG. Overall, in the 41 YOF who presented with myasthenic crisis, it is safe to conclude that plasmapheresis therapy would lead to faster clinical improvement, but not necessarily improved functional outcomes.