## IVIG Demonstrates Effectiveness in Several Neuroimmune Conditions, Indicating Potential for Long COVID Treatment

Key Takeaways

- IVIG is effective in treating neuroimmune conditions like CIDP and GBS, comparable to plasma exchange therapy.
- Its potential in treating COVID-19 and PASC is being explored, with mixed results and inconclusive efficacy.
- IVIG may mitigate cytokine storms in severe COVID-19 cases, but further investigation is needed.
- The therapy's role in ME/CFS is uncertain due to inconsistent trial outcomes, warranting further research.

Intravenous immunoglobulin (IVIG) has proven efficacy in autoimmune neuropathies, with mixed but promising outcomes in severe COVID-19 cases and post-acute sequelae of SARS-CoV-2 infection trials.

Intravenous immunoglobulin (IVIG) has been studied in hundreds of disorders across multiple disease states, with its efficacy being demonstrated in inflammatory, infectious, and autoimmune diseases, among others. In particular, the field of neuroimmunology has benefited from the proliferation of IVIG, with the therapy proven as highly effective in conditions such as <u>myasthenia gravis</u> and chronic inflammatory demyelinating polyneuropathy (CIDP).<sup>1-3</sup>

New research has focused on the therapeutic effects of IVIG in treating SARS-CoV-2 infection, the virus that causes COVID-19. Some clinical trials have <u>indicated</u> the therapy's effectiveness in small population subsets, but overall, research regarding outcomes in treating acute COVID-19 has been inconclusive.<sup>1,4</sup>

As COVID-19 spread and the pandemic continued, a significant proportion of patients began to experience persistent symptoms or develop additional complications, even after their disease recovery. This has become known as post-acute sequelae of SARS-CoV-2 infection (PASC), often referred to as long COVID. Due to its mechanisms being hypothesized to stem from inflammation, IVIG has become a potential candidate for treating patients with this condition.<sup>1</sup>

The investigators conducted a review of IVIG use in treating neuroimmune conditions, in addition to providing an update on the benefits and limitations of the therapy in acute COVID-19 and PASC. By examining the outcomes of IVIG treatment across multiple diseases, the investigators sought to gain an understanding of the potential associations that could inform the optimization of future IVIG utilization.<sup>1</sup>

IVIG could improve the condition of patients with autoimmune neuropathies, including CIDP, Guillain-Barré syndrome (GBS), and multifocal motor neuropathy. Studies have found that IVIG is at least as effective as plasma exchange therapy in treating GBS. When IVIG is administered

to patients with GBS, innate and adaptive immunity are activated, which enable the neutralization of neuromuscular blocking antibodies associated with GBS complications.<sup>1</sup>

Long-term efficacy of IVIG in patients with CIDP has been previously demonstrated, with studies indicating reduction in relapse rates and patient disability for up to 6 months of treatment. CIDP and GBS are thought to be similar in etiology, leading investigators to determine that the therapeutic mechanisms of IVIG would also be similar between the conditions.<sup>1</sup>

Of particular interest is the potential use of IVIG in treating myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). The mechanism behind the condition is unclear, but there has been a well-established link between ME/CFS and other autoimmune conditions. In some patients, an autoimmune etiology has been observed, which could prove a valuable association for the treatment of other autoimmune conditions such as PASC.<sup>1</sup>

However, IVIG use in controlled trials of patients with ME/CFS have garnered mixed results, with numerous trials generating contradictory outcomes, making the therapy's role as a first-line treatment uncertain.<sup>1</sup>

In patients with COVID-19, IVIG use has been found to be most effective in serious cases and in immunocompromised patients. This is potentially due to the therapy's ability to mitigate the excessive inflammatory response that is associated with critical illness, called a cytokine storm. Overall, results regarding the therapy's efficacy in acute COVID-19 remain inconclusive, with additional investigation recommended by the study authors.<sup>1</sup>

Studies analyzing IVIG as a treatment for PASC have been lacking in strong efficacy data. One trial, conducted by Thompson et al, examined 9 patients with PASC who were treated with long-term, high-dose immunoglobulin therapy. All patients in the trial reported significant clinical improvements, but the study investigators have acknowledged that these benefits are primarily subjective. Now, other clinical trials are underway to further investigate IVIG's effectiveness in PASC.<sup>1,5</sup>

As previously mentioned, IVIG has elicited favorable results in treating ME/CFS, especially in patients where the onset of disease was caused by an acute viral infection. Furthermore, a growing body of work is demonstrating similarities between PASC and ME/CFS; although not well characterized, the conditions share a potential "autoimmune nature" that is worth further investigation.<sup>1</sup>

"IVIG therapy is an important therapeutic modality for the management of inflammatory conditions and further research should continue to delineate specifications (dosage, timing, Ig type) for its use in known and emerging neuroimmune conditions, acute COVID-19, and PASC," the study authors concluded.<sup>1</sup>

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