



Reassessing IVIg therapy in chronic inflammatory demyelinating polyradiculoneuropathy during COVID-19: a chance to verify the need for chronic maintenance therapy

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Abstract

The outbreak of a severe acute respiratory syndrome caused by a novel coronavirus (COVID-19), has raised health concerns for patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), who are frequently on long-term immunotherapies. Treatment with IVIg does not increase the risk of contracting COVID-19, and the IVIg administration may have a protective role. However, infusions can expose patients to an increased risk of contracting SARS-CoV-2 due to repeated access to Health Facilities. In this report we analyzed the short-term follow-up of CIDP patients who modified their chronic IVIg therapy during pandemic. About half of CIDP patients regularly treated with IVIg tried to stop treatment and about 10% shifted to SCIG. Forty-two percent of the patients who stopped the treatment reported a clinical deterioration after suspension and had to restart IVIg. This study demonstrated that in selected cases it is possible to successfully stop the chronic IVIg treatment, even in patients who have been treated for several years.

Keywords COVID-19 · CIDP · IVIg · SCIG · Pandemic

Introduction

Immune-mediated neuropathies include acute disorders, such as Guillain–Barré syndrome (GBS), which has several variants, or chronic disorders, such as chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multifocal motor neuropathy (MMN) polyneuropathies associated with monoclonal gammopathy, with or without anti-MAG antibodies, and neuropathies during vasculitis [1, 2].

CIDP is a clinically heterogeneous, immune-mediated, sensory-motor neuropathy typically characterized by symmetrical involvement [2].

SARS-CoV-2, a novel zoonotic coronavirus, originated as a human virus in China in December 2019; since then, the virus

has spread all over the world, causing a pandemic disease defined as coronavirus disease 2019 (COVID-19). COVID-19 primarily causes respiratory illness ranging from asymptomatic or mild infection to acute respiratory distress syndrome and death [3].

Patients with COVID-19 frequently manifest neurological symptoms, including acute cerebrovascular diseases, consciousness impairment, and skeletal muscle injury. Peripheral nervous system (PNS) involvement is reported in patients with COVID-19, but it is still unknown if and how SARS-CoV-2 can affect it [4].

Currently, there is no scientific evidence that immune-mediated neuropathies are associated with an increased risk of contracting COVID-19 [5].

Intravenous immunoglobulins (IVIg) are an established therapy for the treatment of chronic immune-mediated neuropathy, in particular CIDP and MMN [6]. For selected patients with immune-mediated neuropathies, subcutaneous immunoglobulins (SCIG) represent an alternative to conventional IVIg with an equivalent efficacy and safety [7].

Treatment with IVIg or SCIG does not increase the risk of contracting COVID-19 because immunoglobulins enhance the immune response or even the administration of IVIg may have a protective effect against SARS-CoV-2 infection [8].

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However, infusions can occur in the hospital, in an outpatient setting, or in an infusion center and patients may be exposed to an increase risk of contracting SARS-CoV-2 infection due to repeated access to Health Facilities. Furthermore, some patients during pandemic decided to voluntarily discontinue the treatment to avoid a possible contamination or postponed scheduled visit for safety reason. The clinician should discuss with the patient the option of switching the treatment to SCIG [5].

In this report we analyzed the short-term follow-up of patients with CIDP who modified their chronic IVIg therapy during COVID-19 pandemic.

Materials and methods

Patients with a diagnosis of CIDP fulfilling the diagnostic criteria of European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) [2] chronically treated with IVIg at March 2020 were included. IVIg were administered every 4 weeks at the standard dose of 2.0 g/kg.

Considering the risk during pandemic to periodic hospital admission for the infusion, patients were asked to shift to SCIG, according to guidelines, or to attempt to suspend the therapy [5].

The primary clinical outcome measure was change in motor function. Documentation of muscle strength was carried out by the same experienced neurologist using the Medical Research Council (MRC) rating scale. We considered a worsening > 2 point of MRC scale.

Results

Thirty-two patients (18 males; 14 females), all > 18 years old, were enrolled. Patients' mean age was 56 years (median 59, standard deviation 16.1), with mean disease duration of 11.52 years (median 11, standard deviation 8.5). Dose of IVIg per course was variable, ranging from 90 to 200 g. Mean treatment duration with IVIg was 9.1 years (median 7, standard deviation 5.4). All the patients included had a chronic progressive course and they have been treated continuously with IVIg.

Due to the pandemic, 14 (43.7%) patients tried to stop IVIg treatment in the month of March while 3 (9.4%) patients shifted to SCIG. Five of the 14 patients (35.7%) who stopped the treatment reported a clinical deterioration ranging from 1 to 3 months after suspension, and they had to restart the treatment. Nine patients who discontinued IVIg and all 3 patients who shifted to SCIG remained in remission after a 6-month follow-up. At a 9-month follow-up, 1 further patient of the 9 who suspended IVIg, presented a clinical worsening and shifted back to IVIg.

Hence, at the last follow-up, 8 patients definitely stopped IVIg and 3 patients shifted to SCIG.

Discussion

IVIg is a well-established treatment for chronic immune-mediated neuropathy as induction and maintenance. However, there is no evidence on how long IVIg maintenance treatment should be administered, potentially leading to an overtreatment that is frequently documented in clinical trial with a placebo group [9].

Some patients are reticent to try to lower the dose or to stop IVIg because it is an effective and well-tolerated treatment, so regimens with the highest dose tolerated and a short interval of administration of IVIg are frequently used.

Another issue is the treatment period; two retrospective studies investigating long-term prognosis in patients with CIDP showed that 26% of patients with CIDP reached sustained long-term remission without any treatment [10].

During pandemic it is important to reduce the exposure of people to healthcare environments and avoid gathering of patients in waiting rooms where SARS-CoV-2 can be transmitted.

Thus, we discuss with patients the possibility to discontinue IVIg or to switch the treatment to SCIG so that they can administer immunoglobulins at their convenience at home.

In our cohort, SCIG showed to be a safe and cost-effective treatment with a similar efficacy profile compared to IVIg, so we recommend this shift.

Considering patients that completely suspended therapy, we reported a relapse rate up to 42% but the majority of the patients has stabilized off-treatment, still maintaining a clinical stability at a 9-month follow-up. On the other hand, we cannot certainly exclude further relapses after longer-lasting follow-up.

Conclusion

This study demonstrated that in selected cases it is possible to stop the treatment with IVIg with a therapeutic success, even in patients who have been treated for several years. In case of clinical deterioration and consequent shift back to IVIg, it is important to evaluate the optimal IVIg maintenance regimen with the lowest effective dose and the longest tolerated interval.

SCIG remains a safe and efficacy alternative to IVIg and enables home administration that avoids the risk of additional exposure to SARS-CoV-2. The decision to switch from IVIg to SCIG treatment needs to be made on a case-by-case basis, but it could be strongly considered while dealing with COVID-19 pandemic, to reduce the movement of people and stop the spread of the novel coronavirus infection.

A long-term follow-up is required to establish how long a stable remission off-treatment can be achieved, and a cautious monitoring is required for patients undergoing IVIg withdrawal and for patients that are transitioned to SCIG.

Compliance with ethical standards

Conflict of interest Marina Romozzi has no potential conflicts of interest to be disclosed.

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Ethical approval None.

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