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Review

Long-term subcutaneous immunoglobulin use in inflammatory myopathies: A retrospective review of 19 cases

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ABSTRACT

Subcutaneous immunoglobulin (SCIg) therapy is indicated in primary and secondary immunodeficiency diseases. Its use in practice is being extended to autoimmune diseases. Few studies investigated the feasibility and safety of SCIg in these rare conditions. The aim was to describe the use of SCIg in inflammatory myopathies including polymyositis (PM), dermatomyositis (DM) and inclusion body myositis (IBM), in real-life settings. This case series was based upon a retrospective data collection. The primary objective was to assess the feasibility of the SCIg injections for the treatment of autoimmune diseases and adherence to high doses. Secondary objectives included safety and efficacy. Nineteen cases were identified: 7 patients were diagnosed with PM, 7 with IBM, 2 with DM, and 3 with myositis associated with connective tissue disease. Patients were treated and followed-up for a mean duration of 18.8 months (range 4.5–42). They received a median of 64 SCIg infusions and a total of 1215 infusions. Out of 14 patients, 10 showed an improvement in muscle strength, and 7 out of 11 showed an improvement in muscle disability scale. Two patients were lost to follow-up. Few slight adverse reactions were reported including mainly mild headaches and local skin reactions. Any serious adverse event was reported. These results suggest that the use of high-dose SCIg is feasible, beneficial and safe in patients with inflammatory myopathies. SCIg could be an alternative of IVIg in patients with difficult venous access or with insufficient response, and in patients preferring home care setting.

Contents

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1. Introduction

Immunoglobulin replacement therapy is the first-line treatment for primary immune deficiencies. The use of intravenous immunoglobulin (IVIg) is now extended, as an immunomodulatory therapy, to autoimmune disease including peripheral neuropathies, autoimmune thrombocytopenia, Kawasaki disease and inflammatory myopathies. Many studies showed the benefit of IVIg in autoimmune diseases [1–7]; however, the immunomodulatory effects of immunoglobulin therapy are still not fully understood.

IVIg therapy is recommended for patients presenting myositis refractory to corticosteroids and/or immunosuppressive agents [8]. It is also recommended for patients with myositis who are unable to continue immunosuppression due to adverse events, as well as for whom such agents are contra-indicated [3–5,9]. However, this long-term IVIg therapy is associated with a risk of systemic adverse effects, and is also associated with high costs due to the need of intravenous access, surveillance and hospitalizations [10]. Therefore, an alternative route of administration, subcutaneous immunoglobulin (SCIg) was recently made available [11,12]. SCIg are indicated in primary and (some) secondary immunodeficiency diseases [13]. Danieli et al.were the first to describe the feasibility and safety of SCIg in polymyositis (PM) and dermatomyositis (DM) in 2011 [14]. Recently, the use of SCIg in clinical practice for the treatment of inclusion body myositis (IBM) was also described [15,16].

For the majority of patients, IVIg and SCIg are equally efficacious [13]. However, there are differences between the therapies, particularly in the mode of administration (single large infusion every 3 to 4 weeks for IVIg, smaller doses once or twice a week for SCIg). Fractionating the total dose into smaller portions decreases the changes in serum IgG levels and maintains sustained serum IgG levels. This fractionation offers a favorable safety profile and may prevent some of the systemic adverse effects associated with IVIg infusions [17,18]. However, the use of SCIg in autoimmune diseases is actually not indicated and particularly uncommon because of the large quantities of IgG required for the immunomodulation in autoimmune diseases, compared with the substitution in primary immunodeficiencies.

Because inflammatory myopathies including polymyositis (PM), dermatomyositis (DM) and inclusion body myositis (IBM) are uncommon disorders, few studies with limited number of patients have investigated the feasibility and safety of SCIg in myositis [14,19]. These reports showed that SCIg was effective in myositis, with no increased safety concerns. Here, we report 19 cases of inflammatory myopathies treated with SCIg and with a long-term follow-up in clinical practice in France.

2. Methods

2.1. Patients and study design

This case series was based upon a retrospective data collection; therefore this was deemed exempt from ethics review. However, it was approved by the National Advisory Committee on Information Processing in Material Research in the Field of Health (CCTIRS) and the National Commission on Informatics and Liberty (CNIL).

The primary objective was to assess the feasibility of SCIg for the treatment of autoimmune diseases and the adherence to high dose of SCIg treatment. Secondary objectives were to assess the reasons for SCIg prescription, and to evaluate the efficacy and safety. The efficacy was evaluated using clinical assessment (including muscle power and functional scale) and laboratory tests including creatine phosphokinase (CPK). Inclusion criteria were: adult patient (>18 years) with autoimmune muscle disease, having received SCIg (Gammanorm®, Octapharma) and having consented to participate.

2.2. Patient's evaluation

Muscle power was assessed using a simple modification of the British Medical Research Council grading system, which assigns grades ranging for 0 (no contraction) to 5 (normal power) to describe the muscle state. To provide more precision, grades from 0 to 5 were subdivided into 2 grades, resulting in a score ranging between 0 and 11, as previously described [1,6,7,20]. The following muscles were provided a grade ranging for 0 to 11 each: neck flexors, trapezius, deltoid, biceps, psoas, maximus and medius gluteus, and quadriceps. The final muscle strength is evaluated by the sum of the eight grades, and thus the theoretical maximum score is 88 points (normal muscle power).

The muscle disability scale (MDS) score, as previously described [1,2,20], measures both proximal strength, and axial and pharyngeal strength in myositis. The MDS contains 18 items: 4 items for the proximal upper limbs, 7 items for the proximal lower limbs, and 7 items for the axial and pharyngeal musculature. Each of the 18 items is scored on a 4-point Likert scale: for the limbs, 4 ratings ranging from 0 (no difficulty) to 3 (impossible), whereas the ratings for axial muscles are ranging from 0 to 6, giving double weight to these ratings. Global score (sum of all items) is ranging from 0 (no disability) to 75 (maximum disability).

2.3. Data collection

All patients' records since July 1, 2011 were reviewed and patients meeting the study criteria were identified. The patients were evaluated at treatment initiation and at each subsequent routine visit, as per clinical practice. At treatment initiation, the following data were collected: demographics, the indication for SCIg treatment, prior and concomitant treatments, and comorbidities. Muscle weakness score, myositis activity scale (MDS) and biological parameters were collected at treatment initiation and at each visit, when recorded. Information about SCIg administration was collected during the whole duration of the study. Treatment modifications and withdrawal were also reported with the underlying reason. The type and severity of any adverse events were recorded.

2.4. Statistical analyses

Parameters were expressed as mean ± standard deviation (SD). Baseline value was defined as the value measured less than 100 days prior to treatment initiation. Endpoint values were defined as the last value measured during the treatment with SCIg. Paired tests were performed to evaluate the change from baseline.

3. Results

Eight centers for internal medicine and neurology participated in this study. Between July 2011 and May 2014, 19 patients received SCIg for the management of an inflammatory myopathy.