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BRIEF COMMUNICATION

Intravenous and Subcutaneous Immunoglobulin Replacement: A Two-Way Road. Optimizing Healthcare Quality in Patients with Primary Immunodeficiencies

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Abstract
Purpose To evaluate the alternate use of subcutaneous immunoglobulin (SCIG) and intravenous immunoglobulin (IVIG) in patients with primary immunodeficiencies (PID) in a third-level Pediatric University Hospital.
Methods Retrospective study of all patients receiving SCIG from 2006 to 2012. Data collected included demographics, date SCIG was started, date of switch to IVIG and reasons, administration tolerance, and related adverse events. Effectiveness was defined as the lack of severe infections.
Results Twenty-three patients (15 male, 8 female) with PID were studied. SCIG was initiated at a median age of 14.2 years (8.4 months-25.7 years) and median duration on SCIG treatment was 41 months (4-68). Nine patients (39.1%) temporarily switched from SCIG to IVIG for the following reasons: vacation (8), administration issues (1), and transient need for immunomodulatory therapy (1). A mean of 5.2 IVIG infusions/patient (SD=2.86) was administered while on SCIG. IVIG-related adverse events were documented in 3 patients with 6 infusions. Eight (34.8%) patients definitively discontinued SCIG use for the following reasons: convenience (5), adverse effects (1), coagulopathy (1), and autoimmune thrombocytopenia (1). There were no severe infections requiring hospital admission in any patient during the study period.
Conclusions Alternating SCIG and IVIG use in patients with PID was associated with considerable advantages in terms of convenience for the patients and their caregivers, while maintaining the effectiveness and safety of this therapy. Healthcare units treating these patients should show flexibility with this dual therapy in order to optimize patients' quality of life.

Keywords Intravenous immunoglobulins · primary immunodeficiency · quality of life · subcutaneous immunoglobulins

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Introduction

Since the 1990s, subcutaneous IgG (SCIG) administration for replacement therapy in patients with primary immunodeficiencies (PID) became an increasingly more common practice in some Scandinavian countries [1–3]. However, the use of SCIG has not been uniformly incorporated into clinical practice in all countries although a gradual increase in the percentage of SCIG use has taken place in the last years (in Spain, it is around 25 %) [4, 5]. The European Society for Immunodeficiencies registry for 2013, reported that 33.84 % patients recorded in the registry received intravenous IgG (IVIG) and 16.39 % SCIG [6].

With the continuing improvements in both IVIG and SCIG preparations actually showing a comparable efficacy and a well-defined adverse events (AE) pattern [7–12], specialists in PID can now devise effective and safe therapeutic plans that are adapted to the individual needs of each patient.

Several studies have shown that SCIG administration results in better health-related quality of life (HRQoL) in both children and adults with PID, in comparison with IVIG [7, 10, 13–22]. In our center, SCIG use has been used since 2006 and

there is a possibility to change the administration route temporarily depending on the circumstances, or to definitively switch to IVIG for medical reasons or the wishes of the patient or family.

The aim of this study is to evaluate the intermittent use of SCIG and IVIG in pediatric PID patients treated in our unit, in order to determine the frequency of this practice, to analyze the reasons for changing the administration route, and to assess the clinical results in terms of efficacy and safety.

Methods

Retrospective, observational study including all pediatric PID patients who received treatment with SCIG between November 2006 and August 2012 in our centre.

The IVIG pharmaceutical products evaluated included Endobulin (Baxter SL, Valencia, Spain), Flebogamma (Instituto Grifols SA, Barcelona, Spain), Kiovig (Baxter AG, Vienna, Austria), and Privigen (CSL Behring GmbH, Marburg, Germany), whereas the SCIG product was Vivaglobin 16 % (CSL Behring GmbH, Marburg, Germany).

The statistical study was performed with SPSS Statistics for Windows, version 17.0 (SPSS Inc, Chicago, IL).

Results

The study included 23 patients with PID, 15 boys and 8 girls, who received SCIG treatment. Seventeen patients were diagnosed of common variable immunodeficiency, 3 of agammaglobulinemia and 3 of T-cell deficiencies. All these patients started IgG replacement therapy with IVIG. SCIG use accounted for 47.9 % of IgG treatments given during the study period in our unit (23 of 48 PID patients). Median age at the beginning of SCIG therapy was 14.2 (0.7–25.7) years and median time under SCIG treatment was 41 (4–60) months.

In 9 out of the patients (39.1 %), SCIG was temporarily changed to IVIG due to greater convenience during vacation time in 8 patients (80 %), administration issues in 1 and immunomodulation needs in 1 other patient (1 patient with 2 different reasons). These 9 patients received a mean of 1.85 (SD=0.98) temporary IVIG infusions per patient and year. The SCIG dose prescribed was 100 mg/kg/week and the IVIG dose was 400 mg/kg/3–4 weeks in 88.9 %. A single patient received 1 g/kg of IVIG.

Eight of the 23 patients (34.8 %) receiving SCIG, with a duration of 27 months (12–37), chose to definitively switch to IVIG. The following reasons led to the switch: convenience (5 patients: 2 patients changed to IVIG since his brother did not tolerate SCIG, 1 patient moved to another city where SCIG was not available, and 2 due to changes in family lifestyle), systemic AE, coagulopathy, and autoimmune thrombocytopenia in 1 patient each. There were no severe infections requiring hospital admission in any patient during the study period. Systemic AE occurred in 3 patients during 6 infusions. Only one of these patients needed premedication with antihistamines. The commercial preparations implicated in the IVIG AE were Kiovig® in 3 infusions and Privigen® in 3 infusions. The patients' registries of home administration documented 2 cases of mild AE and 1 of severe systemic AE (generalized rash and tremors).

Discussion

Various authors have indicated that the patients' preference is a fundamental factor to take into account in addition to clinical criteria when choosing the administration route for IgG therapy [23, 24].

Thus, following an evaluation in our center to assess the patients' and families' satisfaction with SCIG in 2009, which brought to light the perception that this treatment was associated with better quality of life [25], we decided to take a step ahead in establishing an IgG replacement regimen that would be as suitable as possible for the medical, personal, and social needs of our PID patients. More than a third of these patients chose an intermittent use of SCIG and IVIG, which proved to be an effective strategy, as no severe infections occurred during the study period. These data are in keeping with those from other studies that have evaluated the efficacy of switching from IVIG treatment to SCIG [13, 17, 25–27]. Similarly, alternative use of the two routes was found to be safe. Although notification of side effects and tolerance in SCIG administration was voluntarily performed and conceivably may have been underestimated, there was only one severe AE requiring corticosteroid treatment and support measures.

In most patients who temporarily changed the treatment routes, the change was mainly based on personal preference, with the main reasons being convenience and adapting treatment to the vacation period and summertime activities (80 % of cases). This option was particularly applied when the patient had planned a trip, a long voyage, or a lengthy stay away from home.

Although several studies have reported that SCIG improves the patients' quality of life while displaying an efficacy and safety profile comparable to IVIG [18–22], some patients continue to prefer definitive IVIG administration, as was seen in our study. In 50 % of these patients, the reason was convenience and patient preference whereas in the remainder, it was used because intercurrent clinical situations required high IgG doses with the aim of immunomodulation or there were contraindications to SCIG because of thrombocytopenia or severe systemic AE.

Conclusions

We consider that intermittent use of SCIG and IVIG in IgG replacement therapy for PID patients offers a step ahead in adapting this treatment to the patient's lifestyle, specific needs, clinical situation, and even personal preferences without reducing effectiveness or increasing undesirable effects. The attending physician has the challenge of informing patients and helping them decide which administration route will best suit their circumstances at any given time.

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Conflict of Interest All the other authors declare that they have no conflict of interest.

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