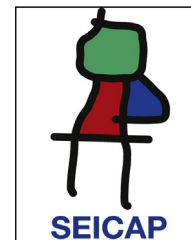


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RESEARCH LETTER

Audit of the use of intravenous immunoglobulin for antibody deficiencies in a Clinical Immunology Unit

To the Editor,

Intravenous immunoglobulin preparations (IVIG) are indicated as the treatment of choice in a number of primary and secondary antibody deficiencies.¹⁻³ There are many options for IgG replacement, and the choice is an individual one based on many factors.⁴ The present audit was developed to examine the current hospital practice of IVIG use for replacement therapy of antibody deficiencies in a Clinical Immunology Unit.

A two-month (February–March 2013) prospective audit of all IVIG use for replacement therapy of antibody deficiencies in two Immunology Day Hospitals was conducted at the Clinical Immunology Unit in the Gregorio Marañón Hospital in Madrid. Patients receiving subcutaneous immunoglobulin were not included in this study. Medical files and dispensing records were prospectively examined. A questionnaire was used. Solid organ transplantation recipients receiving IVIG therapy because of IgG hypogammaglobulinaemia and severe infections were not included in this audit as they were receiving replacement IVIG therapy in other facilities of the hospital.

Ninety-seven patients were included during the study period. The main four groups of distinct antibody deficiencies using IVIG at the time of the study were: Group 1: Common variable immunodeficiency (CVID, $n=36$); Group 2: agammaglobulinaemic patients ($n=3$, X-linked agammaglobulinaemia [$n=2$], Good's Syndrome [$n=1$]); Group 3: other primary antibody deficiencies ($n=22$, including specific antibody deficiencies with normal IgG levels [$n=12$], IgG subclass deficiency [$n=6$], hyper IgM Syndrome [$n=1$], other [$n=3$]); and Group 4: secondary antibody deficiencies ($n=36$, including IgG hypogammaglobulinaemia and recurrent infections secondary to lymphoma [$n=14$], chronic lymphocytic leukaemia [$n=2$], immunosuppressive therapy [$n=9$], rituximab [$n=2$], asthma or COPD using corticosteroids [$n=5$] and other [$n=4$]).

Mean age was 57, interval 19–87 years, 67 women, 30 men. Patients with secondary antibody deficiencies were significantly older (69 ± 14 years) than CVID patients (50 ± 17

years, ANOVA, $p < 0.01$) and agammaglobulinaemic patients (44 ± 17 years, ANOVA, $p = 0.012$). Baseline mean serum IgG concentrations at the time of indication of IVIG replacement therapy (before commencement of IVIG) were as follows: Group 1, CVID: 349 ± 166 [47–570 mg/dL]; Group 2, agammaglobulinaemic patients: 208 ± 25 [180–230 mg/dL]; Group 3, specific antibody deficiencies with normal or high IgG levels: 1360 ± 595 mg/dL [706–2800 mg/dL], IgG subclass deficiencies with normal total IgG levels: 1084 ± 380 [762–1600 mg/dL]; and Group 4: secondary antibody deficiencies: 380 ± 151 [111–673 mg/dL].

Three preparations were available in the hospital at the time of the study: preparation A (5% concentration, $n=45$, 46.4%), preparation B (10% concentration, $n=38$, 39.2%) and preparation C (5% concentration, $n=14$, 14.4%). The distribution of preparations in the four groups of patients was similar.

Overall, the protocol used followed current guidelines for IVIG replacement therapy including a dose of 200–800 mg/kg/month with an interval between doses of 3–4 weeks. Individual adjustments in the administered doses and intervals were performed taking into account the maintenance of IgG levels reached by each patient in combination with the clinical efficacy. The catabolic rate, tolerability of each product and logistic issues also affected the doses and interval between administrations of IVIG infusions.

Mean total prescription of IVIG was of 2695 g per month. Mean individual dose was of 28 ± 12 g/patient/month, interval 7–60 g/month (mean 465 ± 195 mg/kg/month [111–1110 mg/kg/month]).

Mean pre-infusion IgG serum concentration was 917 ± 402 mg/dL with an interval of 287–2720 mg/dL. Pre-infusion IgG levels obtained with distinct preparations were as follows: preparation A 873 ± 413 mg/dL, preparation B 885 ± 289 mg/dL and preparation C 1145 ± 560 mg/dL (ANOVA, $p = 0.07$). The ratio IgG/dose was as follows: preparation A 41 ± 28 , preparation B 43 ± 29 and preparation C 69 ± 44 mg/dL/g infused of IVIG (ANOVA, $p = 0.012$).

CVID patients used similar doses of IVIG (477 ± 210 mg/kg/month) to patients with secondary antibody deficiencies (451 ± 124 mg/kg/month, ANOVA, $p = 0.59$) to maintain similar pre-infusion IgG levels (766 ± 239 vs 814 ± 276 mg/dL, ANOVA, $p = 0.47$). Agammaglobulinaemic patients tended to require higher IVIG doses (656 mg/kg/month) than CVID and secondary hypogammaglobulinaemic patients (ANOVA, $p = 0.12$ and $p = 0.11$,

respectively) to maintain similar IgG concentrations (698 ± 24 mg/dL).

The mean infusion interval of time between IVIG doses was of 3.7 weeks. Distribution: 2 weeks: 13.5%, 3 weeks: 31.3%, 4 weeks: 42.7%.

Maximum IVIG infusion rate: 5% preparations: 159 ± 50 mL/h, interval 40–250 mL/h; 10% preparation: 133 ± 69 mL/h, interval 40–430 mL/h. Maximum IVIG infusion rates were significantly lower in those patients who referred to have adverse reactions (128 ± 57 mL/h vs 158 ± 58 mL/h, Student's *t* test, $p=0.026$).

Mean total time of IVIG infusions was of 2.4 ± 1.2 h with an interval of 1–6.5 h. 20% of patients required more than 3 h to receive their IVIG doses.

Prevalence of adverse reactions: headache 19%, asthenia 4%, malaise 5%. No adverse reactions were reported by 72% of patients at the time of the study. Prevalence of patients with adverse reactions with the distinct preparations: preparation A 33%, preparation B 26%, preparation C 21% (Chi-square, $p=0.63$). The prevalence of adverse reactions at the time of study was similar in the distinct indications (Chi-square, $p=0.94$).

This audit emphasizes the variability in distinct parameters related with the administration of IVIG products for replacement therapy in clinical practice. Wide range of ages of the patients, heterogeneous conditions within different antibody deficiencies, patients requiring different doses according to their distinct IgG catabolic rates and higher pre-infusion IgG levels obtained with some preparates are also part of this variability. IVIG requires well-trained personnel to deal with this variability. On the other hand these characteristics should be taken into account when patients are scheduled in Day Hospitals and for the selection of potential candidates for switching to SCIG or IVIG-home-therapy. The availability of more than one preparation (with distinct concentrations) in the hospital offers an advantage to deal with this variability.

Ethical disclosures

Patients' data protection. Confidentiality of data. The authors declare that they have followed the protocols of

their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

Protection of human subjects and animals in research. Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

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L. Arriaran, J. Gil, E. Fernandez-Cruz, J. Carbone*

Clinical Immunology Unit, Immunology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain

*Corresponding author.

E-mail address: javier.carbone@salud.madrid.org (J. Carbone).