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Original article

Changes in biochemical, hematological and immunological profiles after low-dose intravenous immunoglobulin administration in patients with hypogammaglobulinemia

Modifications des profils biochimique, hématologique et immunologique après faible dose d'immunoglobulines intraveineuses chez patients avec hypogammaglobulinémie

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Abstract

We assessed the immediate effect of intravenous immunoglobulins (IVIG) on the biochemical, immunological and hematological profiles in patients with hypogammaglobulinemia. Over a period of three months, patients with antibody deficiencies, who had been established on stable IVIG treatment as replacement therapy in our hospital, were enrolled in the study. Participants underwent pre-therapy determinations of their biochemical, immunological and hematological profiles. Laboratory determinations were repeated after completion of IVIG infusions. Over the study period, fourteen patients were enrolled and a total of 34 pre- and post-IVIG infusion determinations were performed and results compared. We found that low-dose IVIG treatment in patients with hypogammaglobulinemia results in post-infusion biochemical and hematological changes, as follows: an increase in total protein concentration and a reduction in albumin, total cholesterol, sodium and alkaline phosphatase concentrations as well as lymphocyte and platelet counts. All these biochemical and cellular changes seems to be transient, since they were not observed in the subsequent pre-infusion determination. However, in other patient populations, some of these changes might differ, depending on the dose of IVIG administered and the baseline condition and immunological status of the patient.

Résumé

Nous avons évalué l'effet immédiat des immunoglobulines intraveineuses (IVIG) dans les profils biochimique, hématologique et immunologique chez patients avec hypogammaglobulinémie. Dans une période de trois mois, des patients avec des déficits d'anticorps traités avec IVIG comme traitement de replacement, ont été inclus dans l'étude. Les profils biochimique, hématologique et immunologique ont été obtenus avant et après l'administration des IVIG. Pendant cette période, 14 patients ont été inclus, et un total de 34 déterminations pré- et postadministration des IVIG ont été obtenues et les résultats ont été comparés. Nous avons trouvé que les résultats des paramètres mesurés postadministration de faible dose d'IVIG ont changé significativement de la manière suivante : augmentation de concentration de protéine totale et une réduction d'albumine, de phosphatase alcaline, lymphocyte et aussi de plaquettes. Tous ces changements ont été temporaires car il n'y a pas eu de changement significatif des valeurs dans les déterminations prétraitement suivantes. Pourtant chez d'autres groupes de patients certains de ces changements peuvent différer dépendant de la dose d'IVIG administrées et des conditions de base et de l'état immunologique des patients.

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1. Introduction

Intravenous immune globulin (IVIG) is currently the most widely used plasma component in the world [1]. All commercially available IVIG preparations consist of intact IgG molecules with a distribution of IgG subclasses corresponding to that of normal human serum. Immunoglobulins provide the hypogammaglobulinemia patient with an important defense mechanism against infectious agents. Congenital syndromes involving hypogammaglobulinemia that can be treated with IVIG include X-linked agammaglobulinemia, common variable immunodeficiency (CVID), severe combined immunodeficiency, and X-linked immunodeficiency with hyperimmunoglobulinemia M [1–7].

The mainstay of therapy for hypogammaglobulinemia is still IVIG replacement therapy. IVIG requirements may vary, since baseline IgG and IgG catabolism rates differ widely among patients; hence, the dose and dosing interval need to be tailored to the individual patient.

Intravenous immunoglobulin is not only a replacement therapy for primary immunodeficiency, but also an immunomodulatory treatment for immune-mediated diseases and systemic inflammatory diseases [2,8–10].

Despite considerable advances in the safety of IVIG, its use is still associated with a variety of adverse effects, with an incidence ranging from 1 to 42% [1,11–14]. The symptoms complex, which includes headaches, fever, back pain, nausea, chills, and flushing, is typically mild and transient and is often related to the rate of IVIG infusion. Other minor symptoms that develop in the hours after the injection are fever, arthralgia, diarrhea, and urticaria. Although the etiology remains uncertain, IgG aggregates, IgG dimers, and complement activation appear to be involved in these reactions. Serious adverse effects have also reported, including dyspnea, circulatory shock, convulsions, a sudden fall in blood pressure, renal dysfunction and acute renal failure, thromboembolic events, severe hyponatremia, hemolytic anemia, pulmonary embolism, central retinal vein occlusion and cerebrovascular accidents [11–13,15–19].

Alterations have been reported in the hematological, immunological and serum chemistry profiles of patients with neuromuscular diseases treated with IVIG [16,20–22]). However, to our knowledge, there are few studies along this line in patients with hypogammaglobulinemia, and they have only reported the effect on hematological parameters, lymphocyte subsets, monocytes, and modulation of the cytokine network in small samples [23–25].

In this prospective, observational study, we assessed the immediate effect of IVIG on the biochemical, immunological and hematological profiles of patients with hypogammaglobulinemia.

2. Methods

Over a period of three months (from September to November 2001), adult patients with antibody deficiencies who had been established on stable IVIG treatment as replacement therapy in our hospital were enrolled in the study. The study was approved by our institution Ethics Committee and informed written consent for participation was obtained in all cases.

Participants underwent pre-therapy determinations (1/2 h prior or immediately before to IVIG infusion) of the biochemical, immunological and hematological profiles. Laboratory determinations were immediately repeated after completion of the infusion. Patients were followed during a period of three months; or until three serial pre- and post-treatment determinations for each patient were obtained.

The serum hematological and chemistry profiles included white blood cell count, automated white blood cell differential, hemoglobin, hematocrit, platelet count, sodium, potassium, creatinine, glucose, albumin, calcium, magnesium, alanine aminotransferase (ALT), alkaline phosphatase, total cholesterol, total protein, gamma-glutamyltransferase (GGT), urate, iron, ferritin, rheumatoid factor, and C-reactive protein (CRP).

The following lymphocyte phenotypic markers were also examined: CD25, CD2, CD19, CD5, and the CD3/CD4, CD3/CD8, and CD4/CD8 T cell ratios. Serum concentrations of IgG, IgA, IgM, and IgG subclasses were measured using standard automated methods.

Mean laboratory values before and after IVIG infusion were compared. Data are expressed as mean ± standard deviation (S. D.). To determine significant differences between mean values before and after IVIG infusion, statistical comparisons were made using paired *t*-tests. Stepwise linear regression analysis was used to analyze the determinants of variations in each laboratory determination. We chose the doses of body weight infused (dose/kg) as independent variables as well as the volume infused, age (years) and length of treatment before study IVIG infusion (months). A *P*-value below 0.05 was considered significant.

3. Results

Over the three-month study period, fourteen patients were enrolled and a total of 34 pre- and post-IVIG infusion determinations were performed. All patients received doses between 250 and 400 mg/kg of IVIG per month or every three weeks. Patient characteristics and composition of the IVIG commercial preparation used [Flebogamma® (Grifols, Barcelona, Spain)] are shown in Tables 1 and 2, respectively.

Evaluable data on ferritin, platelet count, hematocrit, red blood cells, hemoglobin, and leukocyte count were available