

Subcutaneous immunoglobulins: Alternative for the hypogammaglobulinemic patient?

Javier Chinen, MD, PhD,^a and William T. Shearer, MD, PhD^b

Bethesda, Md, and Houston, Tex

Key words: Subcutaneous immunoglobulins, IVIG, primary immunodeficiencies, quality of life, hypogammaglobulinemia

In this issue of the Journal, Gardulf et al¹ report on the advantages of home-based subcutaneous immunoglobulin (SCIG) administration over intravenous immunoglobulins (IVIGs) administered in the hospital, as perceived by 15 pediatric and 32 adult patients. By using standardized questionnaires to assess quality of life, the authors found that all patients who switched from hospital-based IVIG to home-based SCIG reported improvement of their quality of life when evaluated after 6 and 10 months. The areas of significant perceived advantage were those related to greater independence, less emotional distress, and availability of time for family activities.

The chronic use of immunoglobulins to help immunodeficient patients with poor antibody production is a therapeutic measure usually reserved for the clinical immunologist. Patients with inherited deficiencies leading to impaired humoral immunity are highly susceptible to a wide range of infections, most commonly bacterial infections of the respiratory tract.² The administration of parenteral immunoglobulins has helped to prevent severe invasive infections in these patients since 1952, when Colonel Bruton³ reported that the use of serum globulin fraction could reduce the frequency of infections in 1 patient with agammaglobulinemia. Although Bruton used subcutaneous injections of immune serum globulins,

Abbreviations used

IVIG: Intravenous immunoglobulin

SCIG: Subcutaneous immunoglobulin

intramuscular preparations were initially favored and became standard of care. The amount of immunoglobulin given by intramuscular route was limited and involved painful injections; therefore, only children and a few adults benefit from this therapy. In the 1980s, intravenous and pump-delivered SCIG preparations were developed. Because higher doses could be administered with IVIG, this route became more popular than SCIG for antibody replacement therapy.⁴

In the last few years, there has been a renewed interest in investigating SCIG as an alternative for antibody replacement therapy, especially for patients who have intravenous access problems or develop adverse effects with IVIG administration, such as headache or myalgias, which are attributed to high immunoglobulin concentration peak or osmolality.⁵ It has also been advocated for patients who cannot maintain therapeutic concentrations of immunoglobulins for more than 2 weeks because of shortened immunoglobulin half-life.⁴ Protocols for SCIG involving rapid infusions and in multiple sites have been developed, allowing the delivery of as much as 6.4 g of immunoglobulin per day.⁴ Although SCIG requires more frequent injections than IVIG, experience shows that SCIG is well tolerated, can be self-administered, and has fewer reported side effects, except for local skin inflammation. These studies have also shown similar rates of infection and hospital admissions to those reported with IVIG.⁶⁻⁹ SCIG preparations of 16% immunoglobulins are not available in the United States; therefore, studies in this country have been limited to small trials using products imported from Europe or using the 10% IVIG solution.^{4,5,10} These trials have confirmed the ability of SCIG to maintain therapeutic serum IgG levels. In addition, it has been suggested that SCIG is preferred by patients and less expensive than IVIG.¹¹ It is not clear whether these last 2 advantages are actually a result of the method of

From ^athe Genetics and Molecular Biology Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda; and ^bthe Department of Pediatrics, Allergy and Immunology Section, Baylor College of Medicine, Houston.

The expressed views do not necessarily represent the views of the National Human Genome Research Institute or the National Institutes of Health.

Received for publication July 22, 2004; revised July 23, 2004; accepted for publication July 26, 2004.

Reprint requests: Javier Chinen, MD, PhD, Genetics and Molecular Biology Branch, National Human Genome Research Institute, 49 Convent Dr, Building 49, Room 4A18, Bethesda, MD 20892. E-mail: jchinen@nhgri.nih.gov.

J Allergy Clin Immunol 2004;114:934-5.

0091-6749/\$30.00

© 2004 American Academy of Allergy, Asthma and Immunology

doi:10.1016/j.jaci.2004.07.045

administration or the convenience of receiving treatment at home. Ochs et al¹² have previously reported that receiving IVIG at home is less expensive and preferred by patients than receiving IVIG at the hospital. In addition, to define better the safety profile and the disadvantages of SCIG, more clinical trials are needed to assess whether the improvement of quality of life observed by Gardulf et al¹ and others is related to the location where the immunoglobulins are administered—at home or at the hospital—or whether there is an actual preference of the subcutaneous route over the intravenous route.

Although home-based SCIG appears to be an alternative for patients with impaired antibody production and significant problems with receiving IVIG, there are some considerations that need to be addressed in these fragile patients with regard to self-administration of a parenteral medication, including verification of a high level of patient compliance. Close medical follow-up and frequent serum IgG level measurements are mandatory, and home health care services should monitor the patient at their homes at least until assurance of patient compliance is obtained. In addition, the patients and the caretakers of pediatric patients should be willing to administer the medication, requiring adequate training and dealing with needle phobia. Patients who opt for receiving home-based SCIG should undergo a stepwise transition from IVIG, with a period when SCIG is administered in the hospital under direct medical supervision. Not a few clinical immunologists may view this method of immunoglobulin treatment with a jaundiced eye because it represents interference in their treatment of complex patients with serious underlying disorders. After being used to a routine of monthly IVIG treatments with trained personnel and close medical observation for possible side effects, it is not easy for physicians to decrease their level of supervision of sophisticated therapy and incur some risks to their patients, for whom they

are morally and legally responsible. Hopefully, sufficient consideration of the continuing need for physician supervision of SCIG-treated patients will ensure protection of the long-term best interests of patients with immunodeficiency.

REFERENCES

1. Gardulf A, Nicolay U, Asensio O, Bernatowska E, Bock A, Costa-Carvalho BT, et al. Children and adults with primary antibody deficiencies gain quality of life by subcutaneous IgG self-infusions at home. *J Allergy Clin Immunol* 2004;114:936-42.
2. Bonilla FA, Geha RS. Primary immunodeficiency diseases. *J Allergy Clin Immunol* 2003;111:S571-8.
3. Bruton OC. Agammaglobulinemia. *Pediatrics* 1952;9:722-8.
4. Berger M. Subcutaneous immunoglobulin replacement in primary immunodeficiencies. *Clin Immunol* 2004;112:1-7.
5. Stiehm ER, Casillas AM, Finkelstein JZ, Gallagher KT, Groncy PM, Kobayashi RH, et al. Slow subcutaneous human intravenous immunoglobulin in the treatment of antibody immunodeficiency: use of an old method with a new product. *J Allergy Clin Immunol* 1998;101:848-9.
6. Chapel HM, Spicken GP, Ericson D, Engl W, Eibl MM, Bjorkander J. The comparison of the efficacy and safety of intravenous versus subcutaneous immunoglobulin replacement therapy. *J Clin Immunol* 2000;20:94-100.
7. Abrahamsen TG, Sanderson H, Bustnes A. Home therapy with subcutaneous immunoglobulin infusion in children with immunodeficiencies. *Pediatrics* 1996;98:1127-31.
8. Gardulf A, Hammarston L, Smith CIE. Home therapy of hypogammaglobulinemia with subcutaneous gammaglobulin by rapid infusion. *Lancet* 1991;338:162-6.
9. Gaspar J, Gerritsen B, Jones A. Immunoglobulin replacement treatment by rapid subcutaneous infusion. *Arch Dis Child* 1998;79:48-51.
10. Radinsky S, Bonagura V. Subcutaneous immunoglobulin infusion as an alternative to intravenous immunoglobulin. *J Allergy Clin Immunol* 2003;112:630-3.
11. Gardulf A, Andersen V, Bjorkander J. Subcutaneous immunoglobulin replacement in patients with primary antibody deficiencies: safety and costs. *Lancet* 1995;345:365-9.
12. Ochs HD, Fisher SH, Lee ML, Delson ES, Kingdon HS, Wedgwood RJ. Intravenous immunoglobulin home treatment for patients with primary immunodeficiency diseases. *Lancet* 1986;1:610-1.

Receive tables of contents by e-mail

To receive the tables of contents by e-mail, sign up through our Web site at

<http://www.mosby.com/jaci>

Choose *E-mail Notification*

Simply type your e-mail address in the box and click the *Subscribe* button

Alternatively, you may send an e-mail message to majordomo@mosby.com.

Leave the subject line blank and type the following as the body of your message:

subscribe jaci_toc

You will receive an e-mail message confirming that you have been added to the mailing list.

Note that TOC e-mails will be sent out when a new issue is posted to the Web site.