

Immunodeficiency and other clinical immunology

Slow subcutaneous human intravenous immunoglobulin in the treatment of antibody immunodeficiency: Use of an old method with a new product

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Human intravenous immunoglobulin (IVIG) is a valuable therapeutic agent for antibody immunodeficiency and certain immunoregulatory disorders. However, for some patients, intravenous administration is not feasible because of poor venous access, severe side effects, or rapid IgG catabolism. This report demonstrates that the slow subcutaneous infusion of IVIG is a suitable alternative in these patients.

Berger et al.¹ first reported the use of 16.5% intramuscular immunoglobulin given by slow subcutaneous infusions for antibody replacement in immunodeficiency. Gardulf and associates^{2, 3} have used the subcutaneous route in immunodeficient adults in Scandinavia for many years, and they report that it is less expensive, better tolerated, and preferable to intravenous infusions by most patients. Abrahamsen et al.⁴ report a similar experience in eight children with primary immunodeficiency.

Because mercury-free 16.5% intramuscular immunoglobulin is not available in this country, we used preservative-free 10% IVIG in eight antibody-deficient patients, all of whom tolerated subcutaneous infusions

Abbreviation used

IVIG: Intravenous immunoglobulin

well, including three patients with prior severe adverse reactions to IVIG infusions.

METHODS

The subcutaneous infusions were usually given weekly or biweekly by using a battery-operated pump and a 20 ml syringe connected to a 1 cm × 24-gauge needle (Sof-Set; Minimed Technologies, Sylmar, Calif.) that is fitted with a stylus and is inserted perpendicularly into the subcutaneous tissue. The usual site was the abdominal wall 2 inches from the umbilicus in any direction (rotated 90° at each visit), and the rate is adjusted to complete the infusion in 3 hours. The inner thigh or arm can also be used. The usual dose is 100 mg/kg/wk (e.g., 1 ml/kg of a 10% solution). We have used doses as high as 250 mg/kg (2.5 ml/kg) given every 3 weeks. Three commercial brands of 10% IVIG were used (Table I) without discernible difference in their reactivity.

In some patients, particularly those with prior anaphylactic reactions, oral aspirin or acetaminophen (10 mg/kg/dose), oral diphenhydramine (1 mg/kg/dose), and/or intravenous hydrocortisone (6 mg/kg, with a maximum 100 mg) are given 1 hour before infusion. Most infusions were given at outside hospitals or by home infusion services. These infusions were deemed necessary for the patients' own good and thus not considered experimental.

RESULTS

Four patients (numbers 1, 2, 4, and 8; Table I) were given subcutaneous IVIG because of poor venous access. One of these patients had stopped IVIG because of this problem. Nursing personnel find this route easier, with less risk of needle-stick injury.

Two patients (numbers 3 and 7) were given IVIG subcutaneously because of prior anaphylactic reactions to IVIG. One of these patients had repeated severe anaphylactic reactions but was able to tolerate subcuta-

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TABLE I. Summary of patients receiving 10% IVIG by subcutaneous route

Patient no.	Age (yrs)/sex	Diagnosis	Reason for subcutaneous use	Product, Dose, and Duration	IgG levels before and after IVIG (mg/dl)
1	2/M	AIDS	Poor venous access	10% Gamimune N (125 mg/kg/wk) for 5 mos	1602* → 1650
2	8/M	X-linked agammaglobulinemia	Poor venous access	10% Gammagard (140 mg/kg/wk) for 14 mos	508* → 906
3	9/F	Common variable immunodeficiency	Anaphylaxis to intra-venous infusions	10% Gamimune N (100 mg/kg/wk) for 3 mos and 10% Gamimune N (120-140 mg/kg/week) for 2 mos	33 → 406 and 482
4	10/F	Common variable immunodeficiency	Poor venous access, fever, diarrhea with infusion	10% Venoglobulin S (150 mg/kg/wk) for 2 mos	1000* → 1140
5	14/F	Common variable immunodeficiency	Aseptic meningitis	10% Gamimune N (100 mg/kg/wk) for 2 mos and 10% Gamimune N (120 mg/kg/2 wks) for 2 mos	407* → 665 and 645
6	17/F	Intestinal lymphangiectasia	Rapid gastrointestinal protein loss	10% Gamimune N (125 mg/kg/wk) for 4 wks	233* → 444
7	37/F	Common variable immunodeficiency	Anaphylaxis to intra-venous infusions	10% Gamimune N (250 mg/kg/3 wks) for 2 mos	583* → 1060
8	40/F	Common variable immunodeficiency	Poor venous access	10% Venoglobulin S (185 mg/kg/2 wks) for 14 mos	94 → 518

*Prior IVIG therapy.

neous infusions with the simultaneous use of prednisone, albuterol aerosols, diphenhydramine, and acetaminophen.

Patient number 5, a 14-year-old girl with common variable immunodeficiency, was given subcutaneous IVIG because she had developed aseptic meningitis after her initial IVIG infusion of 400 mg/kg. Subcutaneous IVIG was started 4 weeks later at a dose of 100 mg/kg. Except for slight headache, she has tolerated the subcutaneous infusions well and is receiving them at home.

Patient number 6 was given subcutaneous IVIG because of rapid loss of immunoglobulin. She has protein-losing enteropathy caused by intestinal lymphangiectasia with hypogammaglobulinemia and recurrent respiratory infections. Her trough IgG level was 233 mg/dl 4 weeks after an intravenous infusion of 600 mg/kg IVIG. After five subcutaneous IVIG infusions of 125 mg/kg, her IgG trough level was 444 mg/dl 1 week after the infusion.

DISCUSSION

The successful use of the subcutaneous route for administration of IVIG in these eight patients parallels the safety and efficacy reported by European physicians in immunodeficient subjects.²⁻⁴ Intramuscular immunoglobulin for intramuscular use (16.5%) is in short supply in the United States, and it contains thimerosal, a mercury preservative. Accordingly, we have used preservative-free IVIG by clysis with minimal local or systemic effects. Three different brands of 10% IVIG were used without discernable differences. Cost savings are not achieved because the same 10% IVIG product and dose

is used for both intravenous and subcutaneous routes. This could change if preservative-free 16.5% solutions of immunoglobulin become available.

The IgG concentration area under the curve after subcutaneous IVIG is equivalent to that of intravenous administration; however, peak serum levels are usually not obtained for 4 days.⁵ This slow release of intramuscular immunoglobulin into the blood stream is advantageous when there has been prior anaphylaxis, aseptic meningitis, or rapid IgG catabolism.

In summary, subcutaneous IVIG permits selective patients to continue immunoglobulin therapy in a safe and effective fashion. In patients with rapid IgG catabolism, it is ideal because of the slow release from the injection site.

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