

Safety of Liquid Intravenous Immunoglobulin for Neuroimmunologic Disorders in the Home Setting: A Retrospective Analysis of 1085 Infusions

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Abstract

Objective:

To examine the overall safety of intravenous immunoglobulin (IVIG) administered according to a clinically defined, home-based therapeutic regimen in patients with neuroimmunologic diseases.

Methods:

A total of 1085 infusions of a new liquid IVIG 10% preparation were administered to 70 patients diagnosed with neuroimmunologic diseases over a 9-month period. These infusions were retrospectively reviewed for safety and tolerability.

Results:

A very favorable adverse effect (AE) rate (4.7%) was calculated over a wide range of doses (0.9–2.14 g/kg). There were no serious AEs reported, even among patients naive to IVIG therapy. Of 51 non-serious AEs, 53% occurred in 5 patients.

Conclusions:

The results of this review of 1085 high-dose liquid IVIG infusions using a closely monitored, yet highly flexible, home-based therapeutic regimen indicate a very favorable tolerability profile in patients with neuroimmunologic disorders, even in those who were new to IVIG therapy.

Key Words: intravenous immunoglobulin, IVIG, high-dose IVIG, neuroimmunologic disease, neuropathy, home infusion, IVIG home infusion, immunoglobulin home infusion

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INTRODUCTION

An accepted approach to the treatment of patients with neuroimmunologic disorders is high-dose intravenous immunoglobulin (IVIG) therapy.^{1,2} The term “high-dose” refers

to the typical therapeutic dose used for neuroimmunologic disorders (>1–2 g/kg) versus that used for replacement therapy (0.1–0.4 g/kg) in primary immune disorders.³ IVIG can be associated with adverse effects (AEs) at both standard and high-dose regimens.^{4–6} Fortunately, most AEs are mild, transient, and nonserious. Reported rates range from 12% to 23%.⁴ In a survey of more than 1000 patients with primary immune disorder, it was found that 34% of AEs occurred during the first infusion of IVIG and 23% after multiple infusions.⁶

The purpose of this study was to retrospectively review the overall safety of high-dose IVIG administered according to a well-defined, supervised, home-based IVIG clinical policy (Crescent Healthcare, Inc, Anaheim, CA) in both previously treated patients and previously untreated patients (PUPs) with neuroimmunologic disorders. Although home-based, high-dose IVIG therapy is an option for these patients, there is a paucity of data concerning its safety. A recent study was conducted that conveyed positive patient-reported efficacy outcomes and pharmacoeconomic benefits related to home-based, high-dose IVIG therapy in patients with systemic autoimmune disease; however, no safety data were collected or reported.⁷ In this study, the safety data of 1085 home infusions are reported to enhance therapeutic decision making in this patient population.

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METHODS

From September 2005 to November 2006, the patient database maintained by Crescent Healthcare, Inc, was retrospectively reviewed for all patients with a diagnosis of a neuroimmunologic disorder receiving a specific liquid IVIG product (GammaGard Liquid 10%, Baxter Healthcare Corp.). Representative samples (10%) of hard copy charts were also reviewed to substantiate the accuracy of the database.

Crescent has rigorous guidelines in place for the evaluation, treatment, and disposition of patients experiencing AEs both during and after every IVIG infusion. Regardless of causality, all AEs during or up to 72 hours after an IVIG infusion are recorded in their database and in the patient's chart.

Per the Crescent policy, the standard infusion rate of IVIG began at 25 mL/h and increased incrementally every 15 minutes to a maximum of 100 mL/h. A qualified nurse, trained by Crescent in the administration of IVIG, was present during all the infusions studied, with the exception of 1 patient who was given permission to self-monitor infusions in the presence of a caretaker. Vital signs were obtained every 30 minutes or sooner if necessary. Per the Crescent policy, referring physicians may, however, modify the standard therapeutic regimen for individual patients with respect to dose, infusion rate, and additional medications (eg, acetaminophen, diphenhydramine).

RESULTS

There were 70 patients identified (36 men and 34 women) with a diagnosis of a neuroimmunologic disorder from their referring physician (chronic inflammatory demyelinating polyneuropathy, $n = 44$; myasthenia gravis, $n = 8$; peripheral neuropathy unspecified, $n = 4$; polymyositis, $n = 4$; "other" inflammatory neuropathy, $n = 4$; dermatomyositis, $n = 2$; stiff person syndrome, $n = 1$; multiple sclerosis, $n = 1$; Guillain-Barré syndrome, $n = 1$; and demyelinating neuropathy, $n = 1$). Of

these patients, 23 were PUPs and 47 previously treated patients. The median patient age was 65 years (range: 15–95 years).

The 70 patients studied received a total of 1085 individual infusions (median = 11, range: 1–66). The mean monthly dose of IVIG was 1.6 g/kg per patient. The overall rate of nonserious AEs was 4.7% ($n = 51$); the rate of serious AEs such as aseptic meningitis, thrombosis, hemolysis, or renal dysfunction was 0%. Of the 51 nonserious AEs, 5 could not be definitively linked to the infusion by the physician reviewer and were therefore classified as "possibly infusion related" (non-serious AE rate was 4.3% if these are excluded) (Figure 1).

Due to high levels of variability within IVIG total doses and dosing intervals studied, the authors defined a standard "course" (total dose) of IVIG as that received by a patient within a 1-month period. In this way, the 1085 infusions could be further grouped into 283 distinct courses. Of the 283 studied, there were 27 (9.5%) in which 1 or more AEs were reported.

The most common AE reported was headache, followed by rash. None of the headaches were reported as serious, severe, or prolonged, and 53% (8/15) occurred in just 2 patients. Overall, 53% of all 51 AEs reported occurred in 5 patients. Of the 70 patients studied, 23 (33%) experienced 1 or more nonserious AEs. Only 1 patient with an AE classified as "infusion related" was sent to an emergency room for evaluation but was discharged home the same day without sequelae. Notably, even during the initial infusion courses of the 23 PUPs (median dose: 1.96 g/kg, range: 0.9–2.14 g/kg), no serious AEs were recorded, and only 2 patients experienced minor transient effects (headache and rash).

IVIG administration rates for all 1085 infusions were compared with rates received by patients who experienced AEs. The median (maximum) infusion rates were 100 and 90 mL/h, respectively. These rates are on the low side of what is considered standard in this patient population (100–200 mL/h) and may

Patient's with AEs				Infusion-Related Adverse Effects																TOTALS
Age	Diagnosis	Total Patient Infusions	Headache	Rash	Muscle Pain	Nausea	Infusion Site Inflammation	Increased Blood Pressure	Fatigue	Chills	Infusion Site Pain	Flushing	Decreased Blood Pressure	Rigor	Diarrhea	Shortness of Breath	Pulmonary Congestion			
1	76	CIDP	15							2								2		
2	74	CIDP	35				1		1		1							3		
3	73	CIDP	39	1														1		
4	72	CIDP	11	1														1		
5	70	CIDP	26	1														1		
6	64	CIDP	12				2											2		
7	62	CIDP	14	1														1		
8	62	CIDP	9	2		2			2									6		
9	47	CIDP	18	4		3	3		1									11		
10	45	CIDP	13	1														1		
11	32	CIDP	27		2													2		
12	15	CIDP	3	1				1						1				3		
13	63	PM	14							1								1		
14	35	PM	25										1					1		
15	74	PN	2		2													2		
16	68	PN	21									1						1		
17	67	AIP	16	1														1		
18	61	MGE	6	4														4		
19	79	OIN	29				1	1										2		
20	49	SPS	1			1												1		
Subtotal				15	6	5	4	3	3	3	2	2	2	1	1	0	0	0	47	
				Possibly Infusion-Related Adverse Effects*																
21	75	CIDP	7												1			1		
22	64	CIDP	66		1													1		
23	45	CIDP	13													1	1	2		
Subtotal				0	1	0	0	0	0	0	0	0	0	0	1	1	1		4	
				TOTAL AEs															51	
				TOTAL OVERALL INFUSIONS															1085	
				TOTAL INFUSION-RELATED AE RATE															4.3%	
				TOTAL OVERALL AE RATE**															4.7%	

AIP, acute inflammatory polyneuropathy; CIDP, chronic inflammatory demyelinating polyneuropathy; MGE, myasthenia gravis exacerbated; OIN, other inflammatory neuropathy; PM, polymyositis; PN, peripheral neuropathy; SPS, stiff person syndrome.

*Possibly related to infusion-indefinite relationship.

**Including possibly infusion-related AEs.

FIGURE 1. Adverse effects in 1085 infusions studied.

be a factor in the low number of AEs reported. In addition, although the role of premedication was not studied (due to variability based on prescribing physician preference and the retrospective nature of data examined), this may also be a contributing factor to the low rate of AEs.

CONCLUSIONS

The results of this review of 1085 high-dose liquid IVIG infusions of a specific product, using a closely monitored yet flexible, home-based therapeutic regimen, indicate a very favorable tolerability profile in

neuroimmunologic patients, even in those who are naive to IVIG therapy. The low rate of AEs recorded suggests that this treatment option is well tolerated in this patient population. Although outside the scope of this retrospective analysis, further clarification as to the role of IVIG infusion rate and premedication on the incidence of AEs in patients receiving home infusions warrants further study.

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