Long Term Follow-up and Correlates of Success in Patients on Immune Globulin for Antibody Deficiency

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Abstract

Antibody deficiencies range from mild deficits of antibody subclasses to more severe deficiencies of all immune globulins. Patients with deficiencies of immune globulin G (IgG) are predisposed to recurrent sinopulmonary infections, often necessitating multiple courses of antibiotics and frequent hospitalizations and provider visits. Treatment with intravenous immune globulin (IVIG) replacement therapy is currently indicated for patients with severe primary immune deficiencies but is less well studied in patients with more mild deficits that nonetheless experience recurrent infections.
A retrospective chart review was conducted on 71 patients from the Temple University Infectious Disease Department (15 transplant recipients) with varying levels of antibody deficiency that had been treated with monthly IVIG for at least six months. Available patients (N=49) were interviewed by phone about their experiences on IVIG, side effects, and quality of life changes on therapy.
Mean age sx onset was 40 y, 68% were women, 87% Caucasian, 49% had pneumonia, 65% purulent bronchitis, 65% sinusitis. Patients reported a mean reduction in infection frequency of 78% and average patient-reported improvement in quality of life was 4.7/5.0. Antibody deficiency levels at baseline were not correlated with infection reduction (R=-.05, p=0.71), and neither was response to pneumococcal polysaccharide vaccine (vaccine responder median infection reduction 83%; non responder 87%, p= 0.60) Adverse events on treatment were experienced by 59% of patients and caused 9 patients (13%) to stop treatment. There was no difference in incidence of adverse events between men and women (p= 0.076), but women had a 50% higher rates of severe headache than men (p= 0.038); 10% pts required a port or PICC, 32% IV fluids, 48% IV steroids, 31% IVIG brand change; 17% changed to subcutaneous IG.
Even patients with relatively mild immunoglobulin deficiencies can experience a significant reduction in recurrent infections and improved quality of life when treated with immunoglobulin. IVIG is usually well tolerated for many years but may require adjunctive steroids, IV hydration, or brand change to limit adverse side effects.

Background

Deficiencies in immune globulins or in IgG subclasses can predispose patients to recurrent sinus and lung infections[1,2]. Patients with such deficiencies are often treated with multiple courses of antibiotics, experience frequent hospitalizations and provider visits, and have a diminished quality of life. Intravenous immune globulin (IVIG) replacement therapy is indicated for patients with severe hypogammaglobulinemia and poor vaccination response but has not been well studied for its efficacy in patients with more mild antibody deficiencies[3]. Small prospective studies have been conducted examining the use of IVIG replacement therapy in patients with IgG and subclass deficiencies[4], but more research is needed on larger cohorts of patients with longer follow up periods.

Methods

A retrospective chart review was conducted on 71 patients (56 with frequent infections, 15 transplant recipients – 2 with frequent infections) receiving IVIG therapy for at least six months seen in the infectious disease department at Temple University Hospital. Patients were also called and asked to take part in a survey about their experiences on IVIG therapy. If a patient was unable to be contacted, they were considered lost to follow up. Transplant recipients without frequent infections were excluded from analyses of infection reduction
Data were entered into REDCap and analyzed using Epi info (CDC) and SysStat (San Jose, CA). Fisher's exact, Chi square, and Mann-Whitney two sample tests were used for statistical analysis.

Results

Patients were followed for a median of 3.0 years on IVIG (0.5-18 years). Fifty-two patients were contacted by telephone. Infections included sinusitis, bronchitis, pneumonia, and adult otitis media. Twelve patients switched from IV to subcutaneous immune globulin (and 6 then switched back). Twenty-six non-transplant patients discontinued therapy. Of those 10 patients then restarted and continued it, and 16 did not.

- 71 patients had varying degrees of IgG deficiency and pneumococcal vaccine response (Table 1)

Deficiency	Number of Patients (%)
Total IgG	46 (64.8%)
Total IgG less than 400	18 (25.4%)
IgG1	42 (59.1%)
IgG2	49 (69.0%)
IgG3	25 (35.2%
IgG4	20 (28.2%)
Abnormal pneumococcal vaccine response* (n=53)	32 (60.4%)

Table 1: Antibody Deficiency Status
*A normal vaccine response is defined as having a level of 1.3 mg/dl or greater for at least 70% of serotypes

- On average, patients experienced a 78% reduction in infections per year, and 25 patients (43% of pts with frequent infections) also reported a reduction in the severity of sinopulmonary infections (Table 2).
    - In patient telephone surveys, patients reported fewer hospitalizations and taking less medication (i.e., antibiotics or steroids) while on therapy (Table 2).

Average number of respiratory infections per year before IVIG	8.8	
Average number of respiratory infections per year after IVIG	2.1	
Average reduction in infection frequency	78.3%	
Reported reduced in infection severity	25 patients (43%)	
Reported improved energy	13 patients (23%)	
Survey Results (n=49)	Perceived benefit of IVIG	Number of respondents (%)
	Fewer hospitalizations	11 (22%)
	Taking less medication	5 (10%)
Average quality of life improvement (0-5 scale) – phone survey	4.7	

Table 2: Outcomes

Results

- The degree of infection reduction did not correlate with the extent of underlying antibody deficiency or presence of abnormal vaccine response.
    - There was an equivalent reduction in infection frequency for patients that had a normal pneumococcal vaccine response and those that had an abnormal response (Figure 1, p= 0.5981) and there was no difference in reduction in infection severity (p=0.33).
    - Degree of antibody deficiency, as measured by a patients lowest total IgG or IgG subclass was not correlated with infection reduction (Figure 2, r= -0.05, p=0.71) or reduction in infection severity.

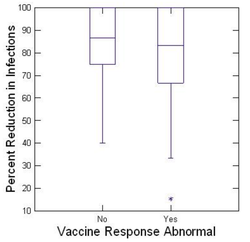

Figure 1: Pneumococcal polysaccharide vaccine response and reduction in infection

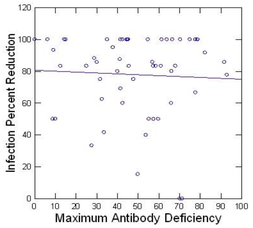

Figure 2: Infection Reduction and Antibody Deficiency (as a percent reduction from normal)

- Adverse events on treatment were experienced by 59% of patients (Table 3) and caused 9 patients (13%) to stop treatment. There was no difference in incidence of adverse events between men and women (p= 0.076), but women had a 50% higher chance of having a severe headache than men (p= 0.038). IVIG dose was, paradoxically, inversely correlated with risk of adverse events (p=0.049). In order to mitigate adverse events of treatment, 10% pts required a port or PICC, 32% IV fluids, 48% IV steroids, 31% IVIG brand change; 17% changed to subcutaneous IG.

	Number of Patients (%)
Any adverse reaction	42 (59%)
Stopped treatment due to adverse reactions	9 (13%)
Incidence of severe headache	29 (41%)
Changed brand due to adverse reaction	19 (27%)

Table 3: Adverse Events

Summary

- Degree of antibody deficiency and pneumococcal polysaccharide vaccine response were not correlated with infection reduction indicating that even patients with relatively mild antibody deficiency can experience significant benefit in terms of improved quality of life and infection reduction on monthly IVIG.
- IVIG is a generally well tolerated and effective treatment, but may require pre-treatment with IV hydration or steroids in order to limit adverse effects.

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