

Correspondence

Immunoglobulin replacement therapy: Is there a role for IgA and IgM?

To the Editor:

In an article in this Journal, Rachid and Bonilla¹ reviewed immunoglobulin-associated anaphylaxis in IgA-deficient patients since 1968. In total, 27 IgA-deficient patients with anti-IgA antibodies were reported with anaphylaxis or moderate reactions to immunoglobulins. In response to this problem, the immunoglobulin manufacturing industry has developed a range of low-IgA products. The main active immunoglobulin isotype in such products is IgG, trough levels of which are used for adjusting the dose of immunoglobulin replacement therapy (IGRT) in antibody deficiency states. The other isotypes, IgA and IgM, are not normally considered in treatment efficacy. Two cohort studies of patients with common variable immunodeficiency (CVID) showed contrasting results on the association of IgG levels and pretreatment frequency of infections.^{2,3}

In our unit, a 21-year-old patient receiving IGRT for CVID with bronchiectasis suffered from increased frequency of infective exacerbations. She was placed on multiple trials of different prophylactic antibiotics and her immunoglobulin dose was increased to achieve IgG trough levels above 10 g/L. Oral prednisolone and intensive physiotherapy marginally improved her lung function that had deteriorated dramatically over a 1-year period.

Despite the above, she had to be admitted for intravenous antibiotics 10 times, over an 18-month period and once a month for the last 4 months (Fig 1). Subsequently, her IGRT was changed to an IgA- and IgM-rich preparation (IgA, 6 mg/mL; IgG, 38 mg/mL; and IgM, 6 mg/mL). In the 28 months after switching the immunoglobulin preparation, she required only 3 admissions for intravenous antibiotics to treat infections (Fig 1). In this patient, the use of an IgA- and IgM-rich product was associated with a significant reduction in infective exacerbations ($P = .006$, Spearman correlation).

In another article in this journal,⁴ a detailed analysis of 90 patients with CVID over a 22-year period demonstrated that despite a rise in the mean IgG levels after IGRT over the last 3 decades, the

mean number of infections per patient-year has plateaued. Cunningham-Rundles⁵ suggests that factors other than IgG levels may also be implicated in susceptibility to infections, such as memory B-cell subtypes and pathogen-specific antibody levels. A recent study of a cohort of 473 patients has demonstrated that low baseline IgA, IgM, and IgG levels all correlated independently with chronic lung disease.⁶ In a multicenter prospective study of 201 patients with CVID over a 5-year period, the mean IgA and IgM levels were significantly lower in patients who had more than 1 episode of pneumonia compared with patients with only 1 episode or no pneumonias.⁷ This study also identified age and IgA trough levels (<0.07 g/L), but not IgG, as independent predictors of developing bronchiectasis. Although these observations do not demonstrate causation, they raise a compelling question about the possible outcome of IGRT if IgA and IgM were also replaced in addition to IgG. Rachid and Bonilla¹ concluded that IgA-associated anaphylaxis is not common, and measures can be taken often to help patients tolerate the IgA content. Our case raises the possibility that IgA and IgM in IGRT preparations might offer an additional benefit to IgG to protect against infections.

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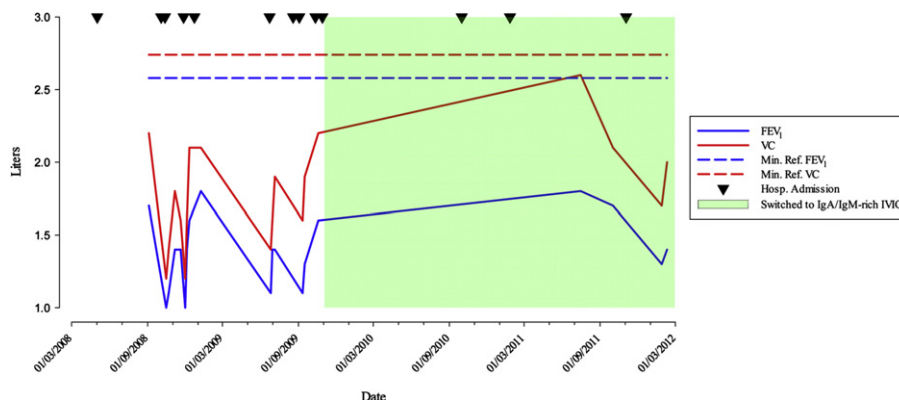


FIG 1. The frequency of hospital admissions is reduced after patient is switched to a preparation of IVIG that is rich in IgA and IgM (shaded area). Hospital admissions (solid triangles) for intravenous antibiotics treatment of infective exacerbations of bronchiectasis are plotted over a period of 4 years. The patient's FEV₁ and VC are shown (solid lines) with the minimum reference values (dashed line). Hosp., Hospital; VC, vital capacity.

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