Intravenous Immunoglobulin for Infectious Diseases: Tailor-Made or Universal?

To the Editor—Intravenous immunoglobulin (IVIG) is prepared from pools of plasma samples obtained from at least 3000–10,000—or, in some cases, as many as 100,000—healthy blood donors; thus, it can be assumed that IVIG covers the entire array of variable regions of antibodies that would be present in normal human serum. IVIG comprises a broad range of immune antibodies directed against pathogens, a quality that is critical for maintaining normal levels of IgG in patients with humoral immunodeficiencies. The results of Ben-Nathan et al. [1] and various other groups support the use of IVIG as a treatment for infectious diseases [2–4]. Their results are not surprising, however, when one considers the beneficial effects of IVIG in patients with primary immunodeficiency who have viral infections. Here, we discuss some practical issues that require attention before randomized clinical trials of IVIG are conducted.

First, the dose of IVIG must be considered. Recent studies have highlighted the need to obtain normal residual levels of IgG (8 g/L), to reduce the number and severity of bacterial infections in patients with primary immunodeficiency. Therefore, the first step toward the use of IVIG as a treatment for patients with viral infections would be fine-tuning of the dose regimen by clinical trials. This step is critical in considering distinct dose regimens of IVIG for inflammatory conditions and immunodeficiencies. For example, at high therapeutic doses, in patients with autoimmune diseases and other inflammatory conditions, IVIG was found to inhibit the function of different arms of the immune system; it inhibits the maturation and function of dendritic cells, blocks the proliferation of T lymphocytes, and attenuates the production of proinflammatory cytokines [5–7]. Therefore, high therapeutic dose regimens may not necessarily be beneficial for treatment of some infectious diseases.

Second, the source of IVIG must be considered. The results of Ben-Nathan et al. [1] indicate that IVIG from Israeli, but not US, blood donors conferred protection against West Nile virus infection. Thus, preparing IVIG from pooled plasma samples of thousands of healthy donors from the entire world, rather than from a particular country or region, may be advantageous. Because certain diseases are endemic to specific regions of the world, this approach might help in the preparation of a “universal” IVIG that contains antibodies against a broad range of pathogens. An alternative approach would be the preparation of a “tailor-made” pathogen-specific IVIG enriched with antibodies against specific infectious agents. Such pathogen-specific enrichment may be achieved either by using plasma from vaccinated donors or by complementing with humanized mouse monoclonal antibodies, and the latter approach would potentially reduce the risk of contamination with viral particles.

Jagadeesh Bayry, Sébastien Lacroix-Desmazes, Michel D. Kazatchkine, and Srinivasa V. Kaveri
INSERM U430 and Université Pierre et Marie Curie, Institut des Cordeliers, Paris, France

References

Reply
To the Editor—The points raised in the letter by Bayry et al. [1] suggest that the dose of intravenous immunoglobulin (IVIG) used for treatment of infectious diseases should be fine tuned because of potential adverse reactions to high doses of IVIG. We certainly agree. The fine-tuning will have to be tailored to the disease in question and cannot be a generic regimen or a “universal” preparation, as suggested by Bayry et al.

The essence of our article [2] was that treatment of West Nile fever with an IVIG preparation containing West Nile virus (WNV)—specific antibodies manufactured from plasma obtained from Israeli donors (Omr-IgG-am; OMRIX Biopharmaceuticals) is more effective than a polyclonal