INTRAVENOUS IMMUNE globulin (IVIG) can play an important role in solid organ transplants, both in preparation to enhance successful grafting and posttransplant to treat potential complications. Here, we take a look at some of the uses of IVIG in transplants.

Pretransplant

Much success has been had using IVIG in kidney transplantation over the last 20 years. IVIG may be used as part of a protocol prior to transplantation in both living and deceased kidney donors. When someone becomes a candidate for a kidney transplant (host), the workup includes a blood test called a panel reactive antibody (PRA). This test measures the amount of alloantibodies produced by the host immune system. Alloantibodies are antibodies produced when there is exposure to the tissue of another person. This may occur when pregnant, when receiving a blood transfusion or during a transplant.

The PRA tests host cells against various samples of other people, and the result may range from 0 percent to 100 percent. Zero percent means there are no alloantibodies, and the risk of rejection is low. One hundred percent means there would be a reaction to all potential donors, significantly decreasing the chance of a successful transplant. Higher PRA scores can have a significant impact on wait times for a compatible donor. However, highly sensitized patients may be eligible for desensitization therapy with IVIG to improve their chances of successful transplant.

Research over the last several years has shown that although IVIG has been extensively used in most desensitization protocols, use of IVIG alone is not sufficient to sustain low levels of alloantibodies. Therefore, desensitization therapy may vary depending on the transplant center, and may involve steroids, plasma exchange, high- and low-dose IVIG and/or other drugs (Table 1).

IVIG is used to suppress the immune response, known as immunomodulation. The mechanism of action of IVIG in this manner is not clearly understood. However, it is believed that because IVIG consists of antibodies from a large variety of human donors, the antibodies suppress the immune response and, ultimately, lower PRA levels.

Although there is much documented

**IVIG in Solid Organ Transplantation**

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success using IVIG as part of desensitization prior to kidney transplant, there is currently little data to support similar success in other organs. There is one recent Canadian study, though, which designed a protocol that included IVIG, plasma exchange, anti-thymocyte globulin and mycophenolic acid given during the transplant operation to patients with a PRA of 30 or more. The researchers concluded that by applying this perioperative treatment, lung transplantation can be safely performed in donor-specific HLA antibodies/PRA-positive patients, with similar outcomes to nonsensitized recipients.2

Posttransplant

Rejection is a potential complication after transplantation, so very close monitoring of various lab values and use of immunosuppressants that deplete B and/or T cells to keep a patient from rejecting the transplanted organ are required. Rejection can be acute, occurring in the first few months posttransplant, or chronic, happening slowly over time, and can be caused by cells or antibodies. Rejection caused by circulating antibodies is known as antibody-mediated rejection (AMR). If AMR is suspected, a treatment regimen is implemented to suppress the immune response and save the organ.

In kidney transplants, IVIG and other drugs used in a desensitization protocol pretransplant are also utilized posttransplant. In a series of studies over the last 10-plus years, graft survival was enhanced using IVIG in conjunction with rituximab and other medications.3 Additionally, IVIG in combination with other treatments and medications have been used to treat AMR in lung, cardiac and liver transplants.

Another potential complication posttransplant is secondary hypogammaglobulinemia resulting from the use of potent immunosuppressants in transplant recipients, a trend that appears to be increasing. When this occurs, patients present with recurrent or multiple infections similar to those seen in patients with primary immunodeficiencies.4 IgG levels are part of lab monitoring after transplant, and if levels are low and/or infections occur, Ig replacement therapy, either IV or subcutaneous, is implemented.

Use of IG products in the liver transplant population is a little different than other organs. Liver transplants have some unique challenges. Special IG formulations are used specifically for liver transplantation. One is hepatitis B hyperIG, which has made transplantation for hepatitis B-related liver cirrhosis not only possible, but successful. It has also opened up a potential new pool of donors who have been previously exposed to the hepatitis B virus. The introduction of specific hyperIGs against cytomegalovirus (CMV) infection approximately two decades ago resulted in a significant reduction of viral infection rates posttransplant.5 Various trials suggest a lower incidence of rejection and improved long-term survival using CMVIG.

The use of IVIG in highly sensitized liver transplant recipients is currently undefined, since comparative trials are still lacking.6

Great Success, Yet More Studies Are Needed

The No. 1 issue in organ transplantation is lack of appropriate donors, both living and deceased. IVIG formulations have played a major role in broadening the population of donors, making solid organ transplants more successful, decreasing wait times, improving long-term survival rates and preventing complications. As always, more studies in all solid organ transplants utilizing IVIG in combination with other therapies are needed to further improve outcomes.

References


Table 1. Drugs Used in Desensitization Therapy

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<thead>
<tr>
<th>Intravenous Immune Globulin</th>
<th>Rituximab</th>
<th>Obintuzumab</th>
<th>Bortezomib</th>
<th>Carfilzomib</th>
<th>Tocilizumab</th>
<th>IgG Endopeptidase</th>
<th>Belimumab</th>
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