Subcutaneous Immune Globulin Therapy for Neuromuscular Diseases

By Michelle Greer, RN

THE FIRST SUBCUTANEOUS

immune globulin (SCIG) treatment (Vivaglobin immune globulin subcutaneous [human] 16% liquid) was approved by the U.S. Food and Drug Administration (FDA) for the treatment of primary immune deficiency disease (PI) in 2006 (and removed from the market in 2011). Since then, several other SCIG preparations have been approved to treat PI (Table 1). Yet, while SCIG is not approved for conditions other than PI, it is frequently prescribed off-label, and it is being explored in clinical trials and prescribed in clinical practice by some neurologists for certain neuromuscular conditions.

SCIG Dosing for Neuromuscular Conditions

SCIG has many benefits, including lower incidence of systemic side effects, elimination of the requirement for venous access, and patient convenience and independence. When PI patients have problems infusing IG intravenously (IVIG), switching them to SCIG is usually the next step. However, for those with neuromuscular conditions, physicians typically take other steps first, such as a brand change, additional pre-medications, central venous access placement and/or adjusting the duration of the infusion.

When the decision is made to prescribe SCIG or IVIG for neuromuscular conditions, volume and dosing are the main factors. Volume, or the amount of the IG preparation being infused, is a consideration whether administered intravenously or subcutaneously. With IVIG, any patient health condition that may involve volume restrictions must be considered. With SCIG, volume impacts site reactions and, in turn, the number of SC sites and needles necessary to successfully infuse.

IG is dosed by weight. For the treatment of PI, IG is considered a replacement therapy. When administered intravenously, it is usually dosed around 400 mg/kg and, on average, given monthly. For example, the dosing for an individual who weighs 75 kg would equate to 30 grams (or 300 milliliters) of fluid. When administered subcutaneously, however, a dose conversion is recommended that will result in additional volume (although, in some instances, one-to-one dosing can be used, which is determined by the physician and the severity of the condition).

For the treatment of autoimmune conditions, IG is considered immunomodulation therapy. With autoimmune conditions, the immune system malfunctions and creates an autoantibody that attacks some part of the body. In neuromuscular disease, the attack occurs on some part of the nerve, muscle or neuromuscular junction. Immunomodulation is used to prevent the immune system from making the autoantibody. How this works is complex and multifaceted, and in many cases, it is not clearly understood. Dosing for an immunomodulatory effect requires more grams than for PI. A typical dose may be as high as 2 grams/kg administered monthly. So, for a 75 kg individual, the dose would be 150 grams (or 1,500 milliliters) of fluid.

When SCIG is prescribed, the physician and/or dispensing pharmacist will determine the rate of infusion and the number of sites needed to infuse. The total volume to be infused determines the number of sites, because only a certain amount of fluid per minute can be infused into any one site. Frequency of infusion is typically weekly, and patients are taught to self-administer.

Clinical Trials of SCIG for Neuromuscular Conditions

Currently, there are several clinical trials underway that are examining the efficacy of SCIG treatment for neuromuscular conditions.

The PATH (polineuropathy and treatment with Hizentra) study is currently active and recruiting in 98 centers in the U.S. and many other countries. This prospective three-arm study is investigating

Table 1. SCIG Products Currently Available

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<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Concentration</th>
<th>Year Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gammagard Liquid</td>
<td>Baxalta</td>
<td>10%</td>
<td>2011</td>
</tr>
<tr>
<td>Gammaked</td>
<td>Kedrion</td>
<td>10%</td>
<td>2010</td>
</tr>
<tr>
<td>Gamunex-C</td>
<td>Grifols</td>
<td>10%</td>
<td>2010</td>
</tr>
<tr>
<td>Hizentra</td>
<td>CSL Behring</td>
<td>20%</td>
<td>2010</td>
</tr>
<tr>
<td>HYQVIA</td>
<td>Baxalta</td>
<td>10% plus hyaluronidase</td>
<td>2014</td>
</tr>
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two different doses of subcutaneous IgPro20 compared with placebo for maintenance treatment of patients with chronic inflammatory demyelinating polyneuropathy (CIDP). During the trial, patients stabilized on IVIG will be randomized to receive weekly infusions of one or two SCIG doses (0.2 or 0.4 g/kg body weight) or placebo for 24 weeks to measure the proportion of patients who experience a relapse in their CIDP over a period of 52 weeks.2

Another study completed a few years ago showed some promise with patients with multifocal motor neuropathy (MMN). The multicenter trial examined eight patients who were stable with IVIG and transitioned to SCIG, seven of whom remained stable with SCIG. The study suggests that MMN patients with stable clinical course on regular IVIG can be switched to SCIG at the same monthly dose without deterioration and with a sustained overall improvement in health-related quality of life.3

Another active trial is evaluating the efficacy and safety of SCIG (Hizentra) in patients with dermatomyositis (DM). At present, patients with steroid-resistant DM can be treated only with IVIG. This study will look at whether SCIG is a suitable replacement by exerting an immunomodulatory effect on complement antibodies.4 It is being led by Dr. Marinos Dalakas, director of the neuromuscular disease program at Thomas Jefferson University in Philadelphia, who previously conducted studies that show the efficacy of IVIG treatment for DM via complement inhibition. Dr. Dalakas wants to explore how SCIG works in this disease state. In the trial, skin biopsies to look at complement and other inflammatory mediators are being performed to determine whether SCIG is as effective as IVIG, if it is preferred by patients and how it works. There are currently three patients enrolled.

There are many challenges to conducting clinical trials for rare conditions such as these, including getting patient participation and FDA approval for the headache, fever and nausea. In addition, some patients with clotting or renal problems may do better with SCIG than IVIG. However, larger studies to prove these differences still remain to be completed.”

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The SCIG Alternative
SCIG appears to be a viable route of administration for some patients with neuromuscular conditions. While it is currently being prescribed off-label, many other therapies are also prescribed for conditions before being approved by FDA, including SCIG for PI. SCIG can offer alternatives when there are difficult side effects, challenges with venous access or simply the desire to be more independent with treatments. It is hoped, then, that the positive outcome of the clinical trials investigating the efficacy of SCIG for neuromuscular conditions will lead to FDA approval.

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References

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