Subcutaneous Immune Globulin: Alternative Therapeutic Pathway for Patients With Primary Immunodeficiency

EDUCATIONAL OBJECTIVES
Upon completion of this program, participants should be better able to:
1. Recognize uses for subcutaneous immunoglobulin (SCIG) therapy
2. Summarize safety data for use of SCIG in special populations
3. Summarize comparative efficacy and safety data for the use of intravenous immunoglobulin (IVIG) and SCIG in patients with primary immunodeficiency
4. Identify advantages and disadvantages of SCIG compared with IVIG
5. Identify advantages and disadvantages of self-administration of SCIG
6. Compare and contrast the pharmacokinetics of IVIG and SCIG
7. Describe hyaluronidase-facilitated SCIG administration
8. Describe rapid-push SCIG administration

Post-test/Rationale:

1. Which of the following is an advantage of intravenous immunoglobulin therapy compared to subcutaneous administration of immunoglobulin for patients with primary immunodeficiency?
   A. Fewer infections per year
   B. Increased quality of life
   C. Lower risk for anaphylaxis
   D. Reduced swelling at injection site***

Correct answer: D.

Rationale: Local adverse reactions, such as pain, bleeding, and bruising at the infusion site, are rare for patients receiving IVIG but common with SCIG; only patients with difficult venous access experience significant pain and swelling at the infusion site with SCIG.

2. Which of the following conditions can be treated with immunoglobulin administered via the subcutaneous route?
   A. Idiopathic thrombocytopenia purpura
   B. Common variable immune deficiency***
   C. Kawasaki syndrome
D. Multifocal motor neuropathy

Correct answer: B.

Rationale: Common variable immune deficiency (CVID) is the most frequent and most symptomatic type of primary immunodeficiency, with a prevalence estimated to be between 1 in 25,000 and 1 in 50,000. The hallmark of CVID is primary hypogammaglobulinemia, which necessitates life-long immunoglobulin maintenance therapy.

3. Conversion to which of the following products would require a dosage adjustment in a patient who had been receiving intravenous immunoglobulin (IVIG) 10% stabilized with glycine?

A. Conventional subcutaneous immunoglobulin (SCIG) 20% stabilized with proline***
B. SCIG 10% with recombinant human hyaluronidase
C. IVIG 10% stabilized with maltose
D. IVIG 6% stabilized with sucrose

Correct answer: A.

Rationale: Data supporting the recommendation for using higher immunoglobulin doses when administering conventional SCIG are derived from several studies comparing SCIG to IVIG. For example, the product labeling for Hizentra (Immune Globulin Subcutaneous [Human], 20% Liquid, CSL Behring AG, Bern, Switzerland) recommends increasing the dose by 137% when converting from IVIG to conventional SCIG and IGHy.

4. Which of the following commonly used methods of immunoglobulin administration requires the most injection sites?

A. Intravenous immunoglobulin
B. Conventional subcutaneous immunoglobulin***
C. Intramuscular immunoglobulin

D. Subcutaneous immunoglobulin with recombinant human hyaluronidase

Correct answer: B.

Rationale: Intravenous immunoglobulin requires the fewest monthly infusion sites (1) and subcutaneous immunoglobulin with recombinant human hyaluronidase requires a similarly low number of sites (typically 1–2); conventional subcutaneous immunoglobulin requires substantially more injection sites (16 [range 12–20]).

5. Which of the following comorbid conditions is a contraindication to a patient receiving immunoglobulin via the subcutaneous route?

A. Migraine headaches
B. Congestive heart failure
C. Diabetes mellitus
D. Idiopathic thrombocytopenia purpura

Correct answer: D.

Rationale: Patients being treated for both primary immunodeficiency and idiopathic thrombocytopenic purpura should not receive immunoglobulin by the subcutaneous route due to the risk of hematoma development.

6. Which of the following patients would not be a candidate for self-administration of rapid-push subcutaneous immunoglobulin?

A. A 50-year-old male with common variable immune deficiency (CVID) and hypertension
B. A 60-year-old female with CVID and rheumatoid arthritis that causes significant pain and swelling in the wrists and fingers
C. A 30-year-old male with Wiskott–Aldrich syndrome (WAS) and diabetes

D. A 25-year-old male with WAS and hyperlipidemia

Correct answer: B.

Rationale: One disadvantage of rapid-push administration is the fact that it requires dexterity to manually compress the syringe. Therefore, this method may not be appropriate for patients with limitations to joint function or dexterity, including a condition such as rheumatoid arthritis that affects the hands. The other comorbid conditions listed may affect the occurrence of adverse reactions to immunoglobulin therapy, but they do not affect the utility of rapid-push administration.

7. Patients with primary immunodeficiency are most likely to have a severe anaphylactic reaction when treated with which of the following types of therapy?

   A. Intravenous immunoglobulin***
   B. Conventional subcutaneous immunoglobulin
   C. Intramuscular immunoglobulin
   D. Subcutaneous immunoglobulin with recombinant human hyaluronidase

Correct answer: A.

Rationale: Trace amounts of non-immunoglobulin (Ig) G proteins are also known to impact patient tolerance. For example, trace amounts of IgA, or the presence of anti-IgA antibodies in patients with selective IgA deficiency, may elicit anaphylactic or anaphylactoid reactions during intravenous immunoglobulin (IVIG) administration. Patients with anti-IgA antibodies or anaphylactic reactions to IVIG may have a lower risk of these events with conventional subcutaneous immunoglobulin.
8. The risk of which of the following reactions is more common with subcutaneous immunoglobulin administration than with intravenous immunoglobulin administration?
   A. Anaphylaxis
   B. Headache
   C. Swelling at injection site***
   D. Hemolysis

Correct answer: C.

Rationale: Compared with intravenous administration of immunoglobulin, the incidence of local adverse effects is more frequent with the 2 methods of subcutaneous administration. Patients receiving subcutaneous administration of immunoglobulin often experience swelling and redness at the infusion site.

9. Which of the following is a disadvantage of traditional subcutaneous immunoglobulin administration?
   A. More systemic adverse effects
   B. Longer time commitment
   C. Multiple infusion sites***
   D. Decreased quality of life

Correct answer: C.

Rationale: Conventional subcutaneous immunoglobulin (SCIG) requires substantially more injection sites than intravenous administration or subcutaneous administration of immunoglobulin with recombinant human hyaluronidase. However, SCIG requires a lower time
commitment and offers improved quality of life compared to the other methods of administration. Systemic adverse effects are more likely to occur with intravenous administration of immunoglobulin, not SCIG.

10. Which of the following is an advantage of immunoglobulin infusion 10% with recombinant human hyaluronidase?

A. Improved safety profile over subcutaneous immunoglobulin (SCIG)

B. Similar peak-to-trough variations compared to SCIG***

C. Higher peak levels than intravenous immunoglobulin (IVIG)

D. Less frequent administration than IVIG

Correct answer: B.

Rationale: Immunoglobulin with recombinant human hyaluronidase (IGHy) administered with the same dose and frequency as IVIG generates similar trough levels and areas-under-the-curve compared to IVIG. IGHy also reaches lower peak immunoglobulin concentrations than IVIG, which results in peak-to-trough ratios that more closely match those observed with conventional SCIG.