Clarifying the Use of Immunoglobulin Treatment in Primary Immunodeficiency

EDUCATIONAL OBJECTIVES
1. Describe the normal immune processes;
2. Identify common primary immunodeficiencies;
3. Recognize the clinical presentation associated with common primary immunodeficiencies;
4. Identify the primary immunodeficiencies for which immunoglobulin (IG) is a treatment modality;
5. List the differences among IG products that can result from manufacturing methods;
6. Describe the product and patient factors that should be considered when selecting an IG product;
7. Understand the comparative efficacy and safety between intravenous and subcutaneous IG; and
8. List the advantages and disadvantages of intravenous and subcutaneous IG.

Learning Assessment Questions

1. Which immunoglobulin plays the most important role in antibody-mediated immunity?
   A. IgA
   B. IgD
   C. IgG***
   D. IgM
   **Correct Answer: C**
   IgG plays the most important role with regard to the development of antibody-mediated immunity.
2. What is the most frequent and symptomatic primary immunodeficiency disorder (PID)?
A. Severe combined immunodeficiency (SCID)
B. Common variable immune deficiency (CVID)***
C. Wiskott-Aldrich syndrome (WAS)
D. X-linked agammaglobulinemia (XLA)
Correct Answer: B
CVID is the most frequent and symptomatic PIDs with a prevalence estimated at between 1 in 25,000 and 1 in 50,000.

3. Patients with severe combined immunodeficiency (SCID) typically present with severe opportunistic infections. Which system do these infections commonly involve?
A. Respiratory tract***
B. Urinary tract
C. Bloodstream
D. Joints
Correct Answer: A
Patients with SCID generally present with severe opportunistic infections at the age of 3 to 6 months. The most common infections are of the respiratory system, such as Pneumocystis jiroveci, and the gastrointestinal tract.

4. Hematopoietic stem cell transplantation (HSCT) is the treatment of choice for patients with severe combined immunodeficiency (SCID). However, intravenous (IV)IG is a treatment modality after HSCT in patients that have inadequate function in which cell line?
A. T-cells
B. Plasma cells
C. Macrophages
D. B-cells***
Correct Answer: D
Without treatment, all forms of SCID are universally fatal. HSCT therapy remains the treatment of choice for SCID. In addition to serving as a temporizing measure prior to HSCT, IVIG is a standard treatment option for patients with inadequate B-cell function following engraftment.
5. In an effort to decrease osmolarity of IG preparations, manufacturers may use which of the following as a stabilizer:
A. Glycine***
B. Glucose
C. Sorbitol
D. Maltose

**Correct Answer: A**
To decrease osmolarity, which can become elevated with sugars, the amino acids glycine and L-proline have been added to the 4th-generation formulations.

6. Which of the following stabilizers should be used with caution when treating patients with renal impairment:
A. Maltose
B. Sucrose***
C. Glucose
D. Sorbitol

**Correct Answer: B**
It is practical to exercise caution when treating patients with a sucrose stabilized product that have mild renal impairment, even when the treatment only requires a low dose of IG. Avoidance of products that contain sucrose is the standard for mitigating adverse renal events in high-risk patients and, when possible, products containing low solute loads should be considered the preferred agents.

7. Patients with which untreated PID are more likely to have a severe anaphylactic reaction?
A. Severe combined immunodeficiency (SCID)
B. Hyper IgM syndrome (HIGM)
C. Wiskott-Aldrich syndrome (WAS)
D. Congenital agammaglobulinemia***

**Correct Answer: D**
More serious anaphylactoid reactions occur most frequently in previously untreated individuals with agammaglobulinemia. In these individuals, IG treatment may lead to acute complement activation with the production of anaphylatoxins C3a and C5a. Anaphylatoxins with acutely formed antigen/antibody complexes can trigger mast cells and polymorphonuclear granulocytes to release histamine and cytokines. These events are relatively rare in those who do not meet this profile.
8. The risk of what type of reaction is more common with subcutaneous IG (SCIG) versus IVIG?
A. Anaphylaxis
B. Headache
C. Swelling at injection site***
D. Hemolysis
Correct Answer: C
The risk for local adverse reactions is higher with SCIG than with IVIG. Patients receiving SCIG commonly experience swelling and redness at site of infusion.

9. What is a disadvantage of traditional SCIG administration?
A. More systemic adverse effects
B. Longer time commitment
C. Multiple infusion sites***
D. Decreased quality of life
Correct Answer: C
SCIG, however, requires multiple infusion sites, ranging from 4 to 8, and sessions because of volume capacity limitations in the SC tissue. The selection of an IG formulation of a higher concentration, such as 20%, may reduce the volume of the required dose for SC administration.

10. What is an advantage of IG infusion 10% with recombinant human hyaluronidase?
A. Improved safety profile as compared with SCIG
B. Similar peak-to-trough variation as compared with subcutaneous SCIG***
C. Higher peak levels compared with IVIG
D. Less frequent administration compared with IVIG
Correct Answer: B
IG infusion 10% with recombinant human hyaluronidase (IGHy) administered at a similar dose and frequency as IVIG provides similar trough levels and the area under the curve (AUC) to IVIG, while achieving a lower peak concentration of IG than IVIG and a peak-to-trough variation more similar to conventional SCIG.