Ig Therapy: One Size Does Not Fit All

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Objectives

- Understand Rationale for Immunoglobulin Replacement Therapy
- Discuss Advantages and Disadvantages of IVIG vs SCIG Route of Administration
What Is Immunoglobulin Therapy?

- “Antibody concentrates” purified from large pools of human plasma.
- Immunoglobulins, aka antibodies, are proteins that bind specifically to antigens and may help destroy them.
- Large plasma pools contain antibodies directed against many different pathogens (bacteria, viruses, fungi, etc).
Immunoglobulin Replacement Therapy

- **1944**: Cohn develops ethanol fractionation of plasma
- **1952**: Bruton treats first patient diagnosed with agammaglobulinemia with SC injections of immune serum globulin (ISG)
- **1953-55**: Battery-powered pumps to slowly administer IM ISG by SC route
- **1969**: IVIG introduced and becomes standard therapy due to reduction of bacterial and non-bacterial infections
- **1970**: Janeway and Gitlin prefer IM injections, and this becomes standard of care in US
- **1979**: Plasma buddies
- **1980**: Janeway and Gitlin prefer IM injections, and this becomes standard of care in US
- **1990s**: Renewed interest in SCIG as alternative to IV therapy, especially for home use
- **2006**: First Sub-cu IgG
- **2010**: Licensed in US
- **Development**: New IVIG products
- **Development**: New SCIG products

**Timeline:**
- **1944**
- **1952**
- **1953-55**
- **1969**
- **1970**
- **1980**
- **1990s**
- **2006**
- **2010**

**Key Events:**
- 1944: Cohn develops ethanol fractionation of plasma
- 1952: Bruton treats first patient diagnosed with agammaglobulinemia with SC injections of immune serum globulin (ISG)
- 1969: IVIG introduced and becomes standard therapy due to reduction of bacterial and non-bacterial infections
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**Related Development:**
- IVIG in Europe
- Plasma buddies
- Battery-powered pumps to slowly administer IM ISG by SC route
- Development: New IVIG products
- Development: New SCIG products
Immunoglobulin Replacement Therapy: Why Is it Different from Other Infusions?

- Chronic vs. acute
- Lifelong vs. short term
- Impacts on quality of life
  - Missing days at work or school
  - Fatigue
  - Frequent infections
  - It affects physical, social, and economic aspects of the patient’s life
Creating a Positive Process for Therapy Management: The 5 Cs

- Chronic care approach
- Comprehensive treatment
- Collaborative partnership
- Communication
- Choice
Choices for Administration

- Intravenous IVIG
- Subcutaneous SCIG

What should you know to help you choose?
### Which Route to Use?

<table>
<thead>
<tr>
<th>Subcutaneous (SCIG)</th>
<th>Intravenous (IVIG)</th>
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<tbody>
<tr>
<td>No venous access required</td>
<td>Venous access required.</td>
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<tr>
<td>Convenient and well tolerated by most patients.</td>
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<tr>
<td>Slow administration and gradual absorption reduces severe headaches and other adverse events; Smaller volumes per infusion requires more frequent dosing (usually weekly)</td>
<td>Peak levels or rapid shifts in IgG level may result in adverse event; Patient may need medications to manage side effects before or after infusions; Ability to give large volumes per infusion allows intermittent dosing (every 21-28 days)</td>
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<tr>
<td>Maintains more consistent IgG levels and eliminates low troughs</td>
<td>Variability in IgG level or “Wear off “ effect may result in fatigue between infusions</td>
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<td>Facilitates self or home infusion, increasing patient autonomy – may improve patient’s self-image and sense of control</td>
<td>Patients may need to travel to receive infusion therapy or have trained healthcare professional in the home</td>
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Factors for Consideration of Therapy Options

IVIG vs. SCIG

- Right therapy for the patient
- Explain differences between therapies
- Discuss benefits of each therapy
- Discuss adverse events associated with each therapy
- Involve patient and/or family in the decision
- Discuss financial implications for each therapy
- Discuss lifestyle implications for each therapy

IVIG

YOU DOWN WITH IVIG?
IVIG

Pros

- Typically once a month dosing
- Quick reconstitution of new patients into therapeutic range
- Administer larger doses

Cons

- Time loss from school/work
- Infusion related reactions
- Wear off effect
Venous access

- Encourage oral hydration 24 hours prior to peripheral attempt

- Other needs for access
  - Broviac or Hickman catheters
  - Infusa-ports
  - Risk of surgical procedures for insertion & removal of in dwelling lines
  - Increased risk of infections with indwelling catheters
Infusion medications

- Timing
  - Pre-Infusion
  - During the Infusion
  - Post-Infusion
- “Less is best”
- Reconsider infusion medications at regular intervals
Selection of infusion setting

- Infusion centers
  - Social & community aspect
  - Comfort level of multiple providers close at hand
  - Proximity to the patients’ home
  - Impact on other family members

- Independence of patient
  - Interest in assuming self administration in the home
  - Support in the home
Selection of infusion setting

- Agency staffing
  - Availability of knowledgeable nursing staff
  - Privacy concerns with home health in the home

- Location of emergency services in relation to patient home

- Financial
  - Payer driven preference
  - Travel expenses
  - Loss of revenue due to days missed from work
  - Concerns over school / work absence
Prepare for an emergency

In clinical setting
- Infusion area free of clutter

In the home
- Epinephrine in auto-injectors
- Emergency medication box
- Emergency numbers posted
- Copy of updated clinical summary including current medications
Administration Reactions

- Renal Events
- Thrombotic Events
- Anaphylaxis is rare
- Phlogistic reactions most common (low grade fever, aches, malaise, chills)
AE Management

Mild: nausea, back pain

Stop infusion and assess
Restart @ 1/2 initial rate

Yes

Tolerated?

Increase to previous rate

No

Decrease rate again

Moderate to severe: fever, rigors, flushing, hypertension, nausea, change in VS, dyspnea

Stop infusion treat (antihistamine, steroids, antipyretics)
Allow symptoms to resolve

Yes

Resolution?

No

Wait to restart

Severe: significant VS changes, anaphylactoid reactions, urticaria, bronchospasm, angioedema

Stop infusion albuterol, epinephrine, supportive care
SCIG
What Is SCIG?

- Infusion of IgG into subcutaneous tissue using an ambulatory infusion pump or syringe driver
- Can be administered more frequently to meet patient needs
- Can be self-administered
SCIG Administration

Pros

➢ Convenient and well tolerated by most patients
➢ Venous access not required
➢ Gradual absorption decreases rapid large swings in serum IgG, reduces severe headaches and other adverse events, and maintains more consistent IgG levels
➢ Facilitates self- or home infusion

Cons

➢ Requires frequent dosing due to relatively small volume per infusion
➢ Ability to self-infuse requires reliable and adherent patient
Dosing and Administration of SCIG

- FDA approved products
  - 10% solution (100 mg/mL) or 20% solution (200 mg/ml)
  - Volume per site dependent on product

- Dosage and frequency can be tailored to meet the patient’s needs

- Subcutaneous sites: abdomen, thighs, flank, upper arms
92% of patients have local injection site reactions
- Decreases over time.
- Primarily puritis, burning, and erythema.
Assessing Site Reactions

- Assess reaction size: should be consistent with volume being infused and amount of subcutaneous tissue on patients; thinner patients may have more prominent raised area; decrease amount of volume per site if necessary
- Assess site location: may be too close to muscle
- Advise regarding rotation of sites
- Advise regarding contacting healthcare provider about use of topical anesthetic ointments
## Troubleshooting SCIG Site Reactions

| Injection-site reaction                  | • Assess for tape allergy; change to paper/hypoallergenic tape  
|                                        | • Assess size—choose a needle size that is consistent with volume being infused  
|                                        | • Assess length of catheter—may be too short and fluid may be leaking into intradermal layer  
|                                        | • Assess site location—may be too close to muscle  
|                                        | • Decrease rate of infusion or decrease volume per site  
|                                        | • Avoid tracking IgG through the intradermal tissue by not allowing drops of IgG on needle tip prior to needle insertion  
|                                        | • Assess appropriateness of rotating sites  
|                                        | • Consider use of topical anesthetic ointment  
| Leaking at catheter site               | • Assess catheter; ensure it is affixed securely and fully inserted  
|                                        | • Assess placement—may be in location that is subject to movement; advise regarding selection of site  
|                                        | • Assess length of catheter—may be too short; suggest change  
|                                        | • Assess infusion volume—amount per site may be too great; adjust volume  
|                                        | • Assess rate of infusion; adjust rate  
| Extreme discomfort with needle          | • Assess needle length—may be too long and irritating abdominal wall  
|                                        | • Try catheter that allows introducer needle to be removed, leaving indwelling flexible cannula catheter  
|                                        | • Try ice or topical anesthetic cream prior to insertion  
| Long infusion time                     | • Assess infusion preparation—Hizentra is ready to use at room temperature  
|                                        | • Assess volume per site, rate of infusion, and number of sites, or adjust infusion regimen  
|                                        | • Check equipment for pump setting, correct selection of tubing size and length to match infusion rates; check pump function, battery function, etc  
|                                        | • Arrange observation of patient technique (specialty pharmacy provider or office visit)  
|                                        | • Remove and discard catheter that demonstrated blood return; use new set (notify supplier of need for replacement)  
| Blood return observed                  | • Remove and discard catheter that demonstrated blood return; use new set (notify supplier of need for replacement)  

### Injection-site reaction
- Blanching
- Redness/Rash
- Itching
- Discomfort
- Swelling
Reminders at Home: Adequate Discharge Instructions

- What to expect
  - Side effects/adverse events
- Whom to call
  - Physician, nurse, clinic, or pharmacy
- When to call
  - Immediately or next day
  - Before infusion if not feeling well or running fever
- Other specifics
  - Next appointment
  - Methods to relieve side effects
  - Use of EpiPen®
  - Emergencies
Conclusion

- Immunoglobulin replacement therapy is lifelong treatment for management of PIDD
- Ig replacement therapy is not once size fits all
- Ig replacement therapy is not generic, differences in formulation should be considered in therapeutic decision making.
- Patients have a choice in treatment options
  - And should be part of the treatment plan discussion
  - And that choice can change as lifestyle changes
Questions

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