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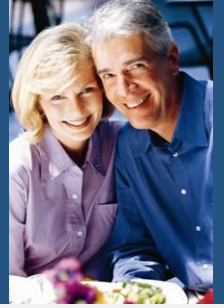


IVIG Therapy

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Objectives

- The basics of the Immune System
- What is IVIG?
- Why is it used for Myositis?
- How does it work?
- How is it administered?
- What are the risks associated with IVIG?
- How will I know it is working for me?
- What about insurance coverage?
- Q & A

The Immune System

- Elaborate and dynamic communication network comprised of organs, tissues, cells and their products
  - Provide the body with defense against foreign invaders (microbes): bacteria, fungi, viruses and parasites
    - Keep microbes out when possible
    - Seek out and destroy if they get in
  - Able to differentiate between self and non-self.
  - Differentiate between normal, healthy cells and infected, cancerous or malfunctioning cells

Dual Nature of Immune System

- Self / Non Self
  - The bodies own cells (self) / Foreign cells (non self)
  - Recognition of self is via distinctive self marker molecules carried on cell surfaces
  - Non self cells carry markers recognized as foreign which result in an attack by the immune system
  - Cells which trigger this immune response are called antigens
  - Miscue in recognition of self can result in autoimmune disease

What is IVIG?

- IVIG = Intravenous Immunoglobulin
- "Antibody concentrates" purified from large pools of human plasma.
- Immunoglobulins, also known as antibodies, are proteins that bind to specific antigens
  - Aid in destroying antigens
  - Protect the body from bacteria, viruses, fungi, etc. – anything foreign.

IVIG Therapy

- There are 5 types of Immunoglobulins: IgG, IgA, IgM, IgE and IgD.
- Current IVIG preparations are highly concentrated IgG (90% to 98%)
- There are small amounts of IgA, IgM and IgE in current IVIG products
- Preparations are screened for HIV, HTLV and hepatitis (B and C) before pooling
- Large donor pools appear to maximize the effect of IVIG

Immunoglobulins

- IgG – Most common in serum (75%), coats microbes speeding their uptake by other cells in the immune system. Secondary production by B cells. Crosses placenta and confers immunity to newborn
- IgA – Second most common in serum, concentrates in body fluids (tears, saliva, respiratory and digestive secretions). Plays a role in local immunity
- IgM – Third most common in serum, effective at killing bacteria. The first Ig produced by B cells in response to antigen
- IgE – Least common in serum, protects against parasitic infections, binds to basophils and mast cells and is involved in allergic reactions
- IgD – Low concentrations in serum, remains attached to B cells and functions as a receptor for an antigen

Are all IVIG Products the Same?

- IgG Immune Globulins
  - >90% Monomeric – Single IgG molecule
  - Intact IgG (Normal Distribution of Four Subclasses)
  - Different Plasma Sources and Antibodies
  - Different Viral Inactivation Methods
  - Different Stabilizing Agents
  - Different pH
  - Different Adverse Event Profiles

Auto Immune Diseases

- Immune system fails to recognize "self" and autoantibodies are produced
- Autoantibodies may "attack" and damage different body systems
- Examples include:
  - *Myositis - Muscle*
  - *Pemphigus/Pemphigoid - Skin*
  - *Guillain-Barre Syndrome – Peripheral Nervous System*
  - *CIDP – Chronic Inflammatory Demyelinating Polyneurophathy – Peripheral Nervous System*
  - *Myasthenia Gravis – Peripheral Nervous System*

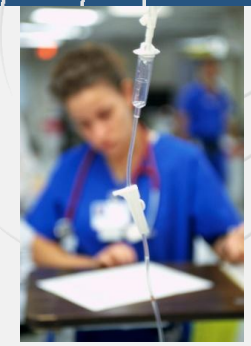
IVIG as Immunomodulation

- The exact mechanism of action for IVIG in autoimmune disease is unknown
- *Immunomodulation* means adjusting the level of an immune response.
- In autoimmune diseases there are many theories as to how IVIG provides an *immunomodulatory* effect.

IVIG as Immunomodulation

- Common theories are antibodies in the IVIG products may do one of the following:
  - Complement fixation – leads to cell destruction
  - Neutralization – binding to specific sites on the antigen to prevent it attaching anywhere else
  - Agglutination – clumping
  - Precipitation – forces the antigen out of solution
  - Suppress the level of cytokines released in immune mediated disorders.
  - An excessive amount of antibodies may cause a down regulation of self antibodies
- Result is a decreased attack on self and presenting symptoms subside.

Infusion of IVIG



- IVIG is administered intravenously
- Dosages and administration rates vary by product, dependent on individual's weight and diagnosis
- The infusion is started at a slow rate and gradually increased to a maximum rate tolerated by each patient
- The infusion may take several hours depending upon the dose and pre-treatment requirements, and most importantly, how it is *tolerated*.
- A nurse will monitor vital signs and assess and manage any side effects or reactions.
- Typical dosing is 0.4gm/kg over 5 days every 4 – 6 weeks

Potential Adverse Reactions and Side Effects

- Adverse reactions are rare, but must always be considered
- Adverse Reactions differ from Side Effects.
- Both Adverse Reactions and Side Effects can be minimized with thorough prescreening and pre infusion precautions
  - Side Effects are more common.
    - Often rate-related.
    - May resolve after a few treatments as patients start to tolerate treatment.
    - Vital Sign monitoring is important in helping to minimize side effects: baseline and prior to increasing rate.

Adverse Events

- Anaphylaxis
- Thrombotic Events
- Acute Renal Failure
- Aseptic Meningitis Syndrome

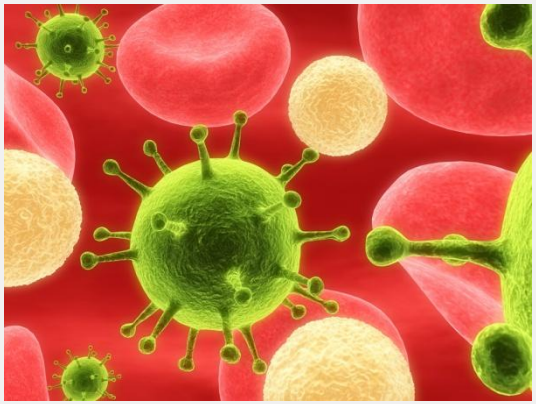
Anaphylaxis

Prescreen including:

- Allergy history
- IgA levels
- Pre-medication recommendations: Tylenol, Benadryl.
- Anaphylaxis protocol and meds in home.
- Appropriate brand selection.

Thrombotic Event

- Stroke, heart attack, blood clots



- Prescreen for other disease states that further increase risk for thrombotic event.
- May recommend premed with ASA or hydration.
- Education on S/S to report to MD/911.

Acute Renal Failure

- Prescreen for:
  - Lab values assessing current kidney function:
    - BUN (Blood Urea Nitrogen) – waste product of protein metabolism that is cleared by the kidneys.
    - Creatinine – waste product created by muscle breakdown that is cleared by the kidneys.
  - Other disease states: diabetes, kidney problems.
  - Appropriate concentration and rate of infusion.
  - Product selection: sucrose
  - Education on S/S of renal dysfunction and when to call MD.

Aseptic Meningitis Syndrome

- Infrequent, shown to be associated with higher dosing and history of migraine
- Prescreening:
  - Migraine history: appropriate pre-meds as needed.
- If IVIG discontinued, AMS remits within several days without residual effects.
- Does not necessarily mean someone cannot restart IVIG on another brand, different premeds, slower infusion.

Potential Side Effects

- Headache
- Fever
- Fatigue
- Chills
- Flushing
- Dizziness
- Urticaria
- Chest Tightness
- N/V
- Muscle cramping
- Blood Pressure changes
- Rash
- Back Pain

- During infusion:
  - Assess vital signs: baseline and before increasing rate of infusion.
  - Ensure premeds are given as ordered.
  - Slow infusion back to previous rate.
  - Education on potential SE's and home safety, positional changes, and adequate rest and hydration prior to and on day of infusion.
  - Call infusion provider or MD for any non life-threatening symptoms.
  - Call 911 for life-threatening symptoms.

IVIG for Myositis

- Multiple studies have shown IVIG is most effective in Dermatomyositis and Polymyositis.
- There have been a few studies in Inclusion Body Myositis showing IVIG is not effective in treating the disease itself, but may have some effect on people with difficulty swallowing.

Is IVIG Working?

- Assess patient specific baseline symptoms
- Track improvement of baseline symptoms over time
- Symptoms should start to subside / improve several days after the first course of therapy
- Continued improvement with additional courses of therapy
- Discontinuation of therapy
  - After 6 to 9 months of therapy with symptom resolution
  - If no improvement after two to three courses, myositis may be unresponsive to IVIG

Insurance Coverage for IVIG

- Most insurance companies have IVIG medical policies outlining IVIG coverage.
- Guidelines are based on peer reviewed published studies: evidence-based medicine.
- PM and DM have coverage guidelines:
  - History of disease
  - Muscle biopsy
  - Lab results
  - Other meds tried and failed: steroids, immunosuppressants
- IVIG for IBM is considered investigational at this time; studies are not conclusive enough to warrant coverage.
- Continued coverage may depend on *response:*
  - Symptoms diminish and/or resolve.
  - IVIG is NOT about *not getting worse.*

In Conclusion

- IVIG is a viable treatment option for dermatomyositis and polymyosotis.
- Just because a patient has a side effect, doesn't mean the infusion needs to be discontinued.
- ***Who administers IVIG is more important than where it is administered.***
- Prescreen, instruct, assess, monitor, intervene as needed.

QUESTIONS?