Guillain-Barre' Syndrome: A Clinical Summary

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Seminar Topic Lecture

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Oral Presentation

Honors College *Parker, CO*

Guillain-Barre' Syndrome is a neurological syndrome that impacts nearly 100,000 patients yearly. This disease is a severe neuropathy resulting in rapidly ascending paralysis. The presentation of Guillain-Barre' varies depending on the subtype and the region where it is contracted. Antecedent events for Guillain-Barre's Syndrome are not fully understood, but these are known to include bacterial or viral infections and rarely, immunizations. (Willison et al, 2016). Evidence suggests that molecular mimicry may be a component of antecedent event response, particularly in *Campylobacter jejuni* infections (Van Doorn, et al 2010). Pathophysiology of the condition differs between the axonal and demyelinating subtypes, as does length of recovery (Willison et al, 2016). Treatment is guideline-based and is centered around immunotherapy with either immune globulin administration or plasma exchange. (Hughes et al, 2003). Guillain-Barre' Syndrome presents a unique opportunity for pharmacists to educate patients and providers, lead evidence-based and patient-specific care, and to support patients in the recovery process through excellent symptoms management.

GUILLAIN-BARRE' SYNDROME

Hannah Belleau, PharmD Candidate 2019
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OBJECTIVES

At the completion of this presentation, participants should be able to:

- Review the proposed pathophysiology of Guillain-Barre' Syndrome
- Name the subtypes of Guillain-Barre' Syndrome and differentiate between them
- Know the diagnostic criteria and labs needed to identify Guillain-Barre' Syndrome
- Recommend appropriate treatment options for patients with Guillain-Barre' Syndrome
- Discuss the role of the pharmacist in Guillain-Barre' Syndrome

PATIENT CASE

David is a 56 year old male who has received his influenza vaccine two weeks ago. He presents to the emergency room today with his wife, complaining of tingling and numbness in his feet and legs. He states that the numbness is worsening, and he feels increasingly weak.

Vitals: BP= 137/82 Weight: 200 lbs Height: 6'2" RR: 16 HR: 96 bpm

PMH: Hypertension, Type II Diabetes mellitus

PSH: Wisdom teeth removal

Home medications: Metformin

What risk factors does David have for Guillain-Barre' Syndrome?

GUILLAIN-BARRE' SYNDROME

- Autoimmune polyradiculoneuropathy that is often life-threatening
  - Characterized by progressive weakness and paralysis
- Occurrence rate is 0.001-0.004%
- Mortality ranges from 3-7%
- Subtypes
  - Acute Inflammatory Demyelinating Polyneuropathy (AIDP)
  - Acute Motor Sensory Axonal Neuropathy (AMSAN)
  - Acute Motor Axonal Neuropathy (AMAN)
  - Miller Fischer Syndrome
  - Regional Variants

Hauser, S., Harrison's Principles of Internal Medicine, 20th edition, 2018, Chapter 439.
Willison, H. The Lancet, August 2016, 388(10045):717-727.
Misawa, S., *The Lancet Neurology, 17*(6), 519-529

DEMOGRAPHICS AND ASSOCIATED CONDITIONS

Males > Females

Adults > Children (in Western Countries)

More commonly seen in patients with HIV, systemic lupus erythematosus (SLE), or lymphomas

85% of patients make a full recovery in months to a year following their illness

Risk for developing GBS increases with age

Worse prognosis is associated with:

- Age >40 years
- Severe disability at most serious disease state
- Diarrheal episode prior to GBS presentation

Hauser, S., Harrison's Principles of Internal Medicine, 20th edition, 2018, Chapter 439..
Willison, H. The Lancet, August 2016, 388(10045):717-727.

SIGNS AND SYMPTOMS

Rapidly progressing, motor paralysis that is generally ascending

Legs that feel unstable or rubbery are an initial sign

Reflexes disappear or are greatly lessened

Diffuse pain in shoulders, neck, back/spine occurs in nearly half of patients

Deep or aching pain in muscles

Weakness progresses over hours to days

Lack of vasomotor control*

Dysesthesias in the limbs are common (tingling)

Lower extremities are more likely to be affected than are upper extremities

Facial diparesis is noted in 50% of cases

If lower cranial nerves are affected, patients may have trouble maintaining an airway and managing secretions

Hauser, S., Harrison's Principles of Internal Medicine, 20th edition, 2018, Chapter 439.
Willison, H. The Lancet, August 2016, 388(10045):717-727.

PATHOPHYSIOLOGY

Antecedent Event

- 70% of GBS cases occur between 1-3 weeks after acute infection
- Generally, respiratory or gastrointestinal infection
- 20-30% of cases in Europe, Australia, or the United States have been shown to be due to *Campylobacter jejuni*
- Other causes include cytomegalovirus, herpes simplex, and Epstein-Barr virus infections, human immunodeficiency virus (HIV), zika virus, hepatitis E, *Mycoplasma pneumoniae*, and *Hemophilus influenzae*
- Immunizations
  - 1976 swine influenza vaccine
  - Recent flu vaccines
  - Older rabies vaccines

Hauser, S., Harrison's Principles of Internal Medicine, 20th edition, 2018, Chapter 439.
Willison, H. The Lancet, August 2016, 388(10045):717-727.
van Doorn, P. *Journal of clinical immunology*, *30 Suppl 1*(Suppl 1), S74-8.

PATHOPHYSIOLOGY

1. Antecedent event occurs, stimulating immune response

→

2. An autoimmune response is triggered, which targets the peripheral nerves and their spinal roots

→

3. Beginning 1-2 weeks after the antecedent event, illness rapidly progresses and may worsen for a few hours to 28 days

↓

4. A clinical plateau is reached, after which patients begin to recover (takes months to years)

Hauser, S., Harrison's Principles of Internal Medicine, 20th edition, 2018, Chapter 439.
Willison, H. The Lancet, August 2016, 388(10045):717-727.

MOLECULAR IMPOSTERS

Auto-antibody attack on the axolemma of nerves is likely due to molecular mimicry of the pathogen and surface molecules on the nerve

The mimics are glycans on lipooligosaccharides (LOS) of pathogens which are structurally similar to glycans that reside on gangliosides of nerves

- However, only a small percentage of *C. jejuni* strains have glycans which mimic gangliosides on their LOS

In AMAN , neuronal damage is caused by subsequent recruitment of macrophages, complement changes, and addition of membrane attack complex to the axolemma

Nerve function is lost due to exposure of the nerve at nodes of Ranvier and nerve terminals

Willison, H. The Lancet, August 2016, 388(10045):717-727.

LOCATION OF ATTACK

The location of damage dictates what recovery will look like for patients

Acute Inflammatory Demyelinating Polyneuropathy (AIDP)

- Injury occurs at Schwann cells and the myelin sheath
- Recovery occurs via peripheral nerve remyelination

Acute Motor Axonal Neuropathy (AMAN)

- Main target is the axolemma (nerve axon membranes)
- Antibodies are produced against GM1 and GD1a (neuronal membrane gangliosides)
- Recovery may or may not occur, depending if the entire length of the nerve is damaged
- Slow recovery may occur via axonal regeneration

Willison, H. The Lancet, August 2016, 388(10045):717-727.

INFLAMMATION AND DEMYELINATION

There are more triggers for Acute Inflammatory Demyelinating Polyneuropathy (AIDP) than for other subtypes

Antibody biomarkers are unknown despite studies to pinpoint the specific nerve antigens

This type of GBS may have a wider range of auto-antibodies, that target both glycolipid and protein components of nerves

- Antibodies noted have been located near nodes of Ranvier
- Glycolipids expressed in the glial membranes are favored as antigens, and some findings support this

Some also suggest that this type of damage may be T-cell-mediated, although there is little evidence to show that T-cells respond to myelin proteins

Willison, H. The Lancet, August 2016, 388(10045):717-727.

VACCINATION: PREVENTION OR TRIGGER?

1976 vaccinations against H1N1 influenza virus: 1 in 100,000 chance of having GBS

2009 studies indicate that H1N1 vaccinations resulted in a 1.6 in 1,000,000 chance of having GBS

Despite concerns, it does not appear that influenza vaccinations have caused additional episodes of GBS in patients with a history of GBS

Vaccination is usually appropriate for patients with a history of GBS, with a few exceptions

- Those who had vaccination-related GBS
- Those who have recently had GBS (within 3 months)

Influenza vaccination may actually prevent GBS

- Infection with the influenza virus itself can be an precipitating event

Willison, H. The Lancet, August 2016, 388(10045):717-727.

LABORATORY VALUES

- Protein in Cerebrospinal Fluid (CSF): 100-1,000 mg/dl
  - Not seen if in early stages of disease (≤ 48 hours)
- Rarely, may see brief increase in lymphocytes (10-100/microL)
- Electrodiagnostic Signs
  - May not exist in early stages of GBS
  - Decreased amplitude of the compound muscle action potentials (CMAPs)
    - With no conduction slowing associated

Hauser, S., Harrison's Principles of Internal Medicine, 20th edition, 2018, Chapter 439.

DIAGNOSIS

Requires:

- Lack of fever or systemic symptoms
- Presence of an antecedent event
- Patient displays a disease pattern of quickly progressing weakness, loss of reflexes, and paralysis

Brighton Collaboration Criteria

- Break diagnosis into tiers of 'certainty'
- Validated by additional research

Electrodiagnostic Signs and CSF Labs

- Important in confirming, but recommend starting treatment if suspect GBS and unable to confirm via labs

Hauser, S., Harrison's Principles of Internal Medicine, 20th edition, 2018, Chapter 439.
Willison, H. The Lancet, August 2016, 388(10045):717-727.

Level 1 Diagnostic Certainty	Level 2 Diagnostic Certainty	Level 3 Diagnostic Certainty
Bilateral, flaccid limb weakness PLUS	Bilateral, flaccid limb weakness PLUS	Bilateral, flaccid limb weakness PLUS
Absent or decreased deep tendon reflexes in affected limbs PLUS	Absent or decreased deep tendon reflexes in affected limbs PLUS	Absent or decreased deep tendon reflexes in affected limbs PLUS
Electrophysiologic findings reflect GBS PLUS	CSF total white count <50 cells/microL (+/- protein elevation) PLUS	Monophasic pattern of illness and between 12 hours-28 days from onset to clinical plateau
Monophasic pattern of illness and between 12 hours-28 days from onset to clinical plateau PLUS	Monophasic pattern of illness and between 12 hours-28 days from onset to clinical plateau	No alternative diagnosis identified
No alternative diagnosis identified	OR, if CSF results unavailable or unable to be collected:	
Cytoalbuminologic dissociation	Electrophysiologic studies reflect GBS PLUS	
	No alternative diagnosis identified	

Hauser, S., Harrison's Principles of Internal Medicine, 20th edition, 2018, Chapter 439, based on table 439-3.

SUMMARY OF AMERICAN ACADEMY OF NEUROLOGY GUIDELINES

- Recommends IV immunoglobulin for non-ambulatory patients
  - Appropriate if patients are within 2 to 4 weeks of first experiencing GBS symptoms
- Recommends plasma exchange for non-ambulatory patients
  - Appropriate to treat within 4 weeks of onset of GBS symptoms
  - May also consider for ambulatory patients within 2 weeks of onset of GBS symptoms
- No recommendation can be made for corticosteroid use or combination regimens
- Plasma exchange and IV immunoglobulin are appropriate for use in pediatric patients

Hughes, R., Neurology, 61(6):736-740

SUPPORTIVE CARE

- Pain Management
  - No evidence is available to recommend a specific therapy
- Critical Care Support and Monitoring
  - Frequent turning and skin care
  - Venous Thromboembolism (VTE) Prophylaxis
  - Chest Physiotherapy
  - Regular range-of-motion exercises
  - Monitor for autonomic issues

Hauser, S., Harrison's Principles of Internal Medicine, 20th edition, 2018, Chapter 439.
Willison, H. The Lancet, August 2016, 388(10045):717-727.

SUPPORTIVE CARE: MECHANICAL VENTILATION

- Mechanical Ventilation
  - Required by nearly 1/3 of patients
  - Associated with
    - More rapid progression of illness
    - Increased severity of weakness
    - Bulbar/facial weakness
- Erasmus GBS Respiratory Insufficiency Score (EGRIS)
  - Should be used upon admission to see if the patient will likely need mechanical ventilation

Hauser, S., Harrison's Principles of Internal Medicine, 20th edition, 2018, Chapter 439.
Willison, H. The Lancet, August 2016, 388(10045):717-727.

GOALS OF THERAPY

Supportive care:

- Ensure that patient is carefully monitored during recovery
- Avoid in-hospital complications

Plasma Exchange

- Complete therapy within the first month after onset of symptoms
- Treatment should be completed in the first two weeks, if possible

IV Immunoglobulin

- Complete therapy within 2-4 weeks after onset of symptoms

Willison, H. The Lancet, August 2016, 388(10045):717-727.
Hughes, R., Neurology, 61(6):736-740

NON-PHARMACOLOGIC TREATMENT

Plasma Exchange

- Allows for removal of inflammatory factors, including complement and auto-antibodies
- 2-3 L of plasma should be exchanged, depending on bodyweight

The best-studied regimen is 5 plasma exchanges completed over a 2-week period for patients with GBS who cannot walk without assistance

2 plasma exchanges may be beneficial even in ambulatory patients

Anticoagulation is needed (generally heparin)

Replacement fluid may be albumin, albumin with saline or plasma expanders, or fresh frozen plasma

Willison, H. The Lancet, August 2016, 388(10045):717-727.
Lehmann H., *Arch Neurol.*2006;63(7):930–935.
Hughes, R., Neurology, 61(6):736-740

ADVERSE EFFECTS OF PLASMA EXCHANGE

- Hypocalcemia
  - Muscle cramps, arrhythmias
- Increased bleeding risk
- Increased susceptibility to infection
- Metabolic Acidosis
- Thrombosis
- Pneumothorax
- If use filtration method
  - Hypotension
  - Hemolysis

Lehmann, H., *Arch Neurol.*2006;63(7):930–935.

PHARMACOLOGIC TREATMENT

Multiple randomized clinical trials have demonstrated that immunotherapy using either plasma exchange or IV immunoglobulin is effective

Imperative that treatment be started quickly

- Unknown if immunotherapy has any effect after 2 weeks of illness

High-Dose Intravenous Immunoglobulin

- Recommended dose of 2g/ kg body weight in 5 divided doses over 5 days
- Some propose the mechanism of action is that IVIG anti-idiotypic antibodies help to destroy GBS autoantibodies
- Effective if started within 2 weeks of symptoms in patients unable to walk

Hauser, S., Harrison's Principles of Internal Medicine, 20th edition, 2018, Chapter 439.
Willison, H. The Lancet, August 2016, 388(10045):717-727.
Patwa, H., Neurology, 78(13):1009-1015

PHARMACOLOGIC AGENTS

IV Immunoglobulin

- A pooled serum product used to replace antibodies
- Designed to deliver human isotype G immunoglobulin

IV Ig can be used for numerous indications, in immunology, rheumatology, neurology, hematology, and more

Available products include:

- IV solutions--Bivigam, Flebogamma 10% DIF, Flebogamma 5% DIF, Gammagard Liquid, Gammaplex 5%, Gammaplex 10%, Octagam 10%, Octagam (5%), Privigen
- Powder for reconstitution
- Subcutaneous solutions
- Intramuscular solutions

van Doorn, *Journal of clinical immunology*, *30 Suppl 1*(Suppl 1), S74-8.
Jolles, S., *Clinical and experimental immunology*, *142*(1), 1-11.
Miller, M. "Intravenous Immunoglobulin (IV IG) *Internal Medicine: A Guid to Clinical Therapeutics.* IBM
Micromedex: "Immune Globulin". Micromedex Solutions [databaseonline] Truven Health Analytics, Inc.; 2018. Perez, E., J Allergy Clin Immunol, 139(1):S1-S46. Chaigne, B., Apheresis and Transfusion Science, 56 (1): 45-49.

MECHANISM OF ACTION

Multiple proposed mechanisms exist, but it is unclear how IV immunoglobulin treats GBS

- Anti-cytokine antibodies or anti-idiotypic antibodies in IV Ig may target autoantibodies and cytokines
- IV Ig might interfere with aspects of T-cell regulation and the complement cascade
- Downregulation of activating factors for B-cells
- Prevention of antibody attacks on Schwann cells via blockage of macrophage Fc receptors
- Upregulation of B-cell component Fc-gamma IIB
- Some also think that elevated levels of immunoglobulins help to speed the breakdown of immunoglobulin G

Miller, M. "Intravenous Immunoglobulin (IVIg)." *Internal Medicine: A Guide to Clinical Therapeutics.*
Hughes, R., Cochrane Systematic Review

IV IMMUNOGLOBULIN MONITORING PARAMETERS

- Hemolysis
  - Hct and Hgb
- Transfusion-related acute lung injury (TRALI)
  - Anti-neutrophil antibodies and/or anti-HLA antibodies
- Renal function
  - Watch urine output, blood urea nitrogen, and serum creatinine
- Signs of hyperviscosity
  - Increased triglycerides, presence of cryoglobulins and monoclonal gammopathies

Miller, M. "Intravenous Immunoglobulin (IVIg)." *Internal Medicine: A Guide to Clinical Therapeutics.* B
Micromedex: “Immune Globulin”. Micromedex Solutions [database online]. Truven Health Analytics, Inc.; 2018.
Octapharma USA, Inc. Octagam 10%[Package Insert]. FDA.gov.

ADVERSE EFFECTS

- Infusion Reactions
  - Usually mild, cease when infusion is stopped
  - Chills, fever, headache, flushing, tight chest, vomiting, diarrhea, tachycardia, blood pressure fluctuations
  - Anaphylaxis is possible
- Acute Kidney Failure
- Risk Factors for side effects:
  - First dose of IV Ig, high rate of infusion, elderly, dehydrated/volume depleted
- Prevention
  - Diphenhydramine (1mg/kg/dose), acetaminophen (15 mg/kg/dose), antiemetic
  - Decrease infusion rate
  - Keep epinephrine on hand

Miller, M. "Intravenous Immunoglobulin (IVIg)." *Internal Medicine: A Guide to Clinical Therapeutics.*

Octapharma USA, Inc. Octagam 10%[Package Insert]. FDA.gov. Perez, E., J Allergy Clin Immunol, 139(1):S1-S46.

ADMINISTRATION

Give infusion via a separate IV line

Do not combine IV immunoglobulin products from different manufacturers

Allow the product to reach room temperature prior to infusion

Administer at the slowest rate if concerns for kidney function or in elderly patients

Infusion Rate (Octagam 10%)	mg/kg/min	ml/min/kg
First 30 minutes	1mg/kg/min	0.01 ml/kg/min
Maximum rate	≤12 mg/kg/min	≤0.12 ml/kg/min

Miller, M. "Intravenous Immunoglobulin (IVIg)." *Internal Medicine: A Guide to Clinical Therapeutics.*
Lexi-Drugs Online™. " Immune Globulin" Lexi-Comp Online™. Hudson (OH): Lexi-Comp, Inc.; 2018
Octapharma, USA, Inc. Octagam10% [Package insert].

RELEVANT COUNSELING POINTS

Monitor for Transfusion-related Acute Lung Injury (TRALI)

Thrombosis may occur

Do not administer live vaccines within 3 months of the infusion

Aseptic Meningitis

- Headache, sore or stiff neck, photosensitivity

Hemolysis

- Elevated heart rate, yellow skin, fatigue

Renal Issues

- Shortness of breath, decreased production of urine, weight fluctuation/gain due to fluid

CSL Behring. Immune Globulin Intravenous (Human), 10% Liquid, Privigen [Product Insert]. FDA.gov

Octapharma USA, Inc. Octagam 10%[Package Insert].

"SAFETY AND EFFICACY OF ECULIZUMAB IN GUILLAIN-BARRÉ SYNDROME: A MULTICENTRE, DOUBLE-BLIND, RANDOMISED PHASE 2 TRIAL"

Japanese eculizumab trial for Guillain-Barre' Syndrome" (JET-GBS trial)

Purpose: To examine efficacy and safety of eculizumab in Guillain-Barre' Syndrome

Eculizumab-a humanized monoclonal antibody that prevents complement activation

Inclusion Criteria:

- ≥ 18 years of age
- First dose of eculizumab given within 2 weeks of symptoms, but after last IV immunoglobulin dose
- Not able to walk without assistance (>5 meters)
- Within 2 weeks of the start of GBS symptoms
- Receiving IV IG

Exclusion Criteria:

- Pregnancy or breastfeeding
- Patients receiving plasmapheresis
- Form of neuropathy other than GBS
- Immunosuppression 4 weeks prior to study
- History of eculizumab use for GBS
- History of meningococcal infection

Misawa, S., *The Lancet Neurology, 17*(6), 519-529
Yamaguchi, N.,JMIR Research Protocols, 5(4):e210

JET-GBS TRIAL CONTINUED

Subjects received either placebo or eculizumab 900 mg via a weekly IV infusion for 4 weeks (in addition to IVIG)

- The first dose of eculizumab had to be started before the last dose of IV immunoglobulin
- Nerve conduction tests and vital capacity tests were done during observation

Subjects also received antibiotic prophyaxis, due to increased risk of infection

N=34

Primary endpoint:

- Subjects able to walk by week 4 (functional grade 2 or lower)
- Not found to be statistically significant

Misawa, S., *The Lancet Neurology, 17*(6), 519-529
Yamaguchi, N.,JMIR Research Protocols, 5(4):e210

ECULIZUMAB (SOLIRIS)

Monoclonal, humanized Immunoglobulin G antibody designed to bind to complement protein (C5) to stop formation of membrane attack complex (MAC)

Meningococcal vaccination is necessary 2 weeks prior to treatment

- May use antibiotic prophylaxis if not possible to vaccinate

Guillain-Barre' Syndrome is not an FDA-approved use at this time

Adverse effects:

- Nausea, headache, back pain, nasopharyngitis

Contraindications to use:

- Unvaccinated against *Neisseria meningitidis*
- Active *Neisseria meningitidis* infection

Lexi-Drugs Online™. " Eculizumab" Lexi-Comp Online™. Hudson (OH): Lexi-Comp, Inc.; 2018.
Alexion Pharmaceuticals. Soliris™ (eculizumab) concentrated solution for intravenous infusion [prescribing information].

ECULIZUMAB: ADMINISTRATION AND COUNSELING POINTS

- Administration
  - Give over 35 minutes as an IV infusion
  - Dilute to 5mg/ml using NS, 1/2NS, D5W, or Ringer's solution
  - Let the solution reach room temperature prior to giving the infusion
- Monitoring
  - Lactate dehydrogenase (LDH), AST, serum creatinine, CBC (with differential)
  - Infusion reactions- watch for anaphylaxis
- Counseling
  - Educate regarding symptoms of meningococcal infection

Lexi-Drugs Online™. " Eculizumab" Lexi-Comp Online™. Hudson (OH): Lexi-Comp, Inc.; 2018.
Alexion Pharmaceuticals. Soliris™ (eculizumab) concentrated solution for intravenous infusion [prescribing information].

"A RANDOMIZED TRIAL COMPARING INTRAVENOUS IMMUNE GLOBULIN AND PLASMA EXCHANGE IN GUILLAIN-BARRE' SYNDROME"

Purpose: To determine if treatment with IV immune globulin is as effective as plasma exchange in Guillain-Barre' Syndrome

Exclusion criteria:

- Allergy to blood products
- Immunosuppressive therapy
- Selective IgA deficiency
- History of Guillain-Barre' Syndrome
- Pregnancy
- Immunosuppression
- Age less than 4

Multicenter, randomized trial

N=150 patients

Two Arms:

- Plasma Exchange over 1-2 weeks
- 0.4 g/kg Gammagard for 5 days

Inclusion Criteria:

- Able to participate in study within 2 weeks of onset of GBS
- Unable to walk independently
- Met diagnostic criteria for Guillain-Barre' Syndrome

Van der Meche',F., *The New England Journal of Medicine, 326(1)*, 1123-1129.

RESULTS OF TRIAL STUDYING IV IMMUNE GLOBULIN VERSUS PLASMA EXCHANGE

Primary outcome:

- 51% of patients treated with IV immunoglobulin had improved by 1+ functional grade 4 weeks after treatment, as compared to 30% of patients treated with plasma exchange (p=0.024)

Secondary outcomes:

- Median time to recovery of ambulation for patients treated with IV immunoglobulin was 55 days, compared to 69 days for patients treated with plasma exchange (p=0.07)

Patients receiving plasma exchange had more treatment-related complications compared to those receiving IV immunoglobulin (16 pts versus 5; p <0.01)

27% of patients receiving IV immunoglobulin needed mechanical ventilation, as compared to 42% of those receiving plasma exchange (P<0.05)

Van der Meche',F., *The New England Journal of Medicine, 326(1)*, 1123-1129.

TREATMENT-RELATED FLUCTUATIONS

Worsening of GBS after initial stabilization or treatment is referred to as a treatment-related fluctuation (TRF)

- 10% of patients experience a TRF

TFRs generally occur within two months of treatment

- Presentation varies-some have continued worsening after 4 weeks, while others have multiple episodes of worsening

Patients who respond this way may need longer treatment, as they may have permanent nerve damage or blockade

Repeated treatment with IV immunoglobulin does show benefit in these patients

- IV Ig 2g/kg (divided into 2-5 doses)

Willison, H. The Lancet, August 2016, 388(10045):717-727.
Thivakaran, T. *Journal of neurosciences in rural practice*, *2*(2), 168-70

RECOVERY AND SEQUELAE

Despite immunotherapy, patients with GBS often face long, painful recoveries

- Demyelination recovery
- Axonal damage

The majority of recovery occurs in the first 12 months, but may continue for 3+ years

GBS is costly: $100, 000+ for medical bills, and an estimated $300,000+ in lost productivity

Incomplete recovery, ongoing fatigue and pain are possible sequelae

- 20% of patients with GBS are unable to walk without help 6 months after the initial symptoms
- Persistent axonal loss contributes to pain and fatigue
- 67% of patients will have chronic fatigue
- Pediatric patients are less likely to have severe sequelae

Willison, H. The Lancet, August 2016, 388(10045):717-727.
Hughes, R., Neurology, 61(6):736-740

CONCLUSIONS: ROLE OF THE PHARMACIST

Reference available guidelines and recommend appropriate therapy

Help to answer questions about rate and administration of IV immunoglobulin products

Educate staff and patients about the risks associated with IV immunoglobulin

Ensure that patients receive any necessary pre-medications prior to IV immunoglobulin infusion

- Diphenhydramine
- Acetaminophen

Discuss data for eculizumab use, and be prepared to recommend appropriate antibiotic prophylaxis if this option is chosen

Being knowledgeable about costs associated with these therapies benefits your patients!

CONCLUSIONS

Guillain-Barre' Syndrome is an umbrella term for a number of demyelinating diseases or axonopathies

The cause and mechanism of damage is not clear, but may involve molecular mimicry resulting in autoimmune attack

Recovery may be complete or patients may have permanent sequelae

Supportive care is particularly important, including careful monitoring of vital signs and mechanical ventilation

Two treatment options are recommended:

- Plasmapheresis
- IV Immunoglobulin 2g/kg given in 2-5 divided doses on consecutive days
- Eculizumab may also be an option, but it has not yet been evaluated in the guidelines

PATIENT CASE WRAP-UP

No electrophysiology studies can be performed for at least 48 hours. Based on the pattern of disease and the Brighton Collaboration Criteria, the physician feels confident that this is Guillain-Barre' Syndrome.

Should treatment be recommended?

What do you recommend? Include dose and directions.

Name: _____

Guillain-Barre' Syndrome Quiz

1. CB is a 25 year old male who will be receiving Octagam 10% for treatment of GBS. He has no risk factors for an adverse reaction to IV immunoglobulin. What is the maximum infusion rate for this product, assuming that CB is able to tolerate the infusion?
    a. 4 mg/kg/min
    b. 1mg/kg/min
    c. ≤12 mg/kg/min
    d. ≤8 mg/kg/min

2. Based on the information presented, what are acceptable forms of Guillain-Barre' Syndrome treatment for pediatric patients?
    a. Plasma exchange
    b. Eculizumab
    c. IV immunoglobulin
    d. All of the above
    e. A and C

3. True or False: Receiving an influenza vaccine is contraindicated for ALL patients with a previous history of Guillain-Barre' Syndrome from any cause.

4. True or False: Both plasma exchange and IV immunoglobulin products are recommended by for use in sequence or together.

5. A 45 year-old patient with no past medical history presents with ascending weakness and loss of reflexes for the past 2 days. She does not take any medications. She notes that she had a "stomach bug" 3 weeks ago. CSF lab results are pending and electrodiagnostic studies are unable to be performed until the technician arrives tomorrow morning. The physician believes that this is Guillain-Barre' Syndrome. Should the patient be treated for probable Guillain-Barre' Syndrome?
    a. Yes, this patient should be treated.
    b. No, you should wait to confirm the diagnosis with labs.
    c. There are no medications or treatments that can help with GBS
    d. Tell the patient to go home, her weakness is likely just a symptom of the "stomach bug" that she had previously

Guillain-Barre' Syndrome Seminar References

Hannah Belleau, PharmD Candidate 2019

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