Norovirus A to Z

(How to Look Forward to Seeing Gastro Cases)

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Goals

- Review Epidemiology
- Discuss Clinical Evaluation and Differential Diagnosis
- Review Current Recommendations for Treatment of Gastroenteritis and Dehydration
- Describe a (relatively) new class of antiemetics (Disclaimer)

EPIDEMIOLOGY

Burden of Disease

- URI and Gastro—Most Common Infectious Diseases World-Wide
- 5 Billion Cases Gastro World-Wide Each Year
- Over 23 Million Cases in US yearly
- Illness Most Severe in Infants & Elderly

Etiologic Agents

- Viruses predominate
  - Rotoviruses
  - Caliciviruses—includes Norovirus
  - Astroviruses
  - Adenovirus
- Parasitic
  - Giardia
  - Cryptosporidium
- Bacterial
  - Camphylobacter
  - Clostridium difficile
  - Salmonella
  - E coli

Epidemiology

- Norovirus & other Caliciviruses
  - Norwalk Like Virus predominated for years
  - Norovirus became predominant in 2006
- Genetic Diversity of Norvirus
  - Emergence Novel Genotypes (2006, 2012) → Higher Intensity Outbreaks
  - New strains mean no sustained immunity over life
- Individual Susceptibility
  - People w certain blood group types more susceptible to some strains

Pathogenesis

- Infection of Intestinal Lining Cells
- Fluid and Salt Lost into GI Tract
- Inability to Digest Food, Absorb Sugars
- Slowed Gastric Emptying

Definition of Gastroenteritis

- Clinical Syndrome Caused by Enteric Pathogens
- Inflammation of the Gastrointestinal Tract Including Stomach and Intestines
- Associated Systemic Symptoms

CLINICAL EVALUATION

Clinical Syndrome

- Gastro = Norovirus = Stomach Flu = The Throw-Ups
- Norovirus Illness Characterized by
  - Abrupt Onset
  - Vomiting > Diarrhea
  - Systemic Symptoms
  - Wide Variability in Sx
  - Incubation Period 1-2 days
  - Disease Lasts 2-4 days

History

- Time course of sxs
- What are stools like
- Urination
- Degree of dizziness
- Travel
- Illness contact
- Other symptoms
- ?What was last eaten?

Differential Diagnosis

- Differential Diagnosis
  - ?
  - ?
  - ?
  - ?

Differential Diagnosis

- Bacterial Gastroenteritis/Traveler's Diarrhea
- Appendicitis
- Inflammatory Bowel Disease
- Kidney Stone
- H pylori
- C difficile
- Gallbladder Disease
- Intracranial mass
- Meningitis

Red Flags (Hospitalization/Alternative dx)

- ?
- ?
- ?
- ?
- ?

Red Flags (Hospitalization/Alternative Dx)

- Bloody stools
- Severe abdominal pain
- Prolonged symptoms (> 1 week)
- Antibiotic use in past 3-6 months
- Severe dehydration
- Elderly, Pregnant
- Comorbidities (eg diabetes, colitis)

PE

- Postural VS

Postural VS

- So lets talk about Postural VS!
- How do you do it?
- What is abnormal?
- What do you think it means?

Its Not So Clear Cut!

- No consistent definition found
- Used to assess fall risk in elderly
- How applicable this is to young adults with strong CV compensatory mechanisms→ Unclear!

What does Literature Show?

- Harrison's "Principles of Internal Medicine"
  - Measure Supine and Standing
  - Does not define how long lying down
  - Take standing measurements "within 3 min"
  - Significant
    - "Sustained" drop in Systolic ≥ 20 mm OR
    - Diastolic ≥ 10mm
    - Pulse increase > 15 beats/min

Definition of Orthostatic (con't)

- Mayo Clinic
  - Lie down for 10 min
  - Take standing measurements "within 3 minutes"
  - Significant
    - Systolic drop of ≥ 20 mm
    - Diastolic drop of ≥ 10 mm
    - Pulse not addressed
- CDC (on caring for elderly)
  - Lie down for 5 min
  - Take BP & Pulse, 1 and 3 min after standing
  - Significant
    - Systolic > 20 mm
    - Diastolic > 10 mm
    - Pulse not addressed

Definition of Orthostatic (con't)

- British Medical Journal 2001
  - "No information is available on optimal time that a subject should remain in a particular position, but 3 min suggested for lying and 1 min for standing."

Definition of Orthostatic (con't)

- Geriatric Nursing 2004; "The Importance of Accurately Assessing Orthostatic Hypotension"
  - Reviews the wide range of standards used in many studies
  - Suggests lying down for 5-10 min
  - Standing for 2-3 min
  - Symptoms of dizziness may be most important

A Word About the Pulse

- What causes a significant orthostatic change in pulse?
  - Intravascular volume depletion
    - Excessive fluid loss from vomiting or diarrhea
  - Exercise
  - Hot Temperature
  - Medication
    - Anti depressants
    - Etoh

What Can We Agree On

- Length of Time Lying
  - Ranges from 2-30 min, 5-10 min most common
- Length of Time Standing
  - 1-3 min most common
- Significant Change
  - Drop of > 20 mm Systolic AND/OR
  - Drop of > 10 mm Diastolic
  - Pulse increase > 15 beats/min
- If Student Experiences Dizziness

Orthostatics in Summary

- Need a consistent protocol
- Time consuming
- Meaning is not as clear as we might hope
- Symptoms as important as the measurements
- "Positive" is one piece of information, but not the whole story

Back to the PE

- Postural VS
- Degree of toxicity
  - Most consistent finding
  - Students look miserable
- "Hydration"
  - Wet Mucous Membranes
  - Tears
  - Capillary Refill
- Abd Exam
  - Bowel Sounds
  - Tenderness

More About Dehydration

- Dehydration most likely with large stool losses
- Norovirus more a vomiting illness
- Unlikely to get significantly dehydrated in first 24 hours unless lots diarrhea

Testing

- Generally no tests for acute diarrhea of short term duration
- Public Health might do testing in outbreaks

TREATMENT

Treatment Modalities

- Symptomatic Management
  - Fluids/Dietary Management
  - Time
  - Medication

Fluids

- Rehydrating orally preferred
  - Oral Rehydration Solution (ORS)
  - Fruit juice, Soda, too high in sugar
  - Sports Drinks, Broth, Water usually sufficient
- Controlling Vomiting
- IV fluids if severely dehydrated
  - 1-2 L NS or Ringers Lactate, quick pace

A Word About "Diet As Tolerated"

- What dietary advice should we give?
- Vomiting
  - Low Fat
  - Small amounts frequently
- Diarrhea
  - BRAT Diet
  - Avoiding dairy products
  - Balanced diet w protein
  - Gastro-colic Reflex

Antiemetic Treatment

How Vomiting Works

- What causes vomiting?
- Humoral Stimuli
  - Toxins
  - Drugs
  - Neurotransmitters
- Neuronal Stimuli
  - Motion Sickness
  - Vagal nerve stimulation

How Vomiting Works

- Vomiting mediated in several areas of brain
  - Area Postrema, floor of 4th ventricle→ Chemoreceptor Trigger Zone recognizes humoral stimuli
  - Vagus nerve carries neuronal stimuli
  - Area in Medulla "Central Pattern Generator" for vomiting, receives signals from Area Postrema & Vagus nerve

Classes of Antiemetics Old Fashion Drugs

- Muscarinic Receptors Antagonists
  - Scopolamine
  - Work on Vagal Nerve
  - Limited use—Motion Sickness
  - Side effects: sedation, anti-cholinergic effects
- Histamine Receptors Antagonists
  - Benadryl, Meclizine, Dramamine, Phenergan
  - Work on Vagal Nerve
  - Limited use—Motion Sickness
  - Side effects: sedation

Classes of Antiemetics
More Old Fashioned Drugs

- Dopamine Receptor Antagonists
- Compazine, Thorazine, Metaclopramide
  - Antagonize Dopamine Receptors in Area Postrema
  - First drugs to demonstrate efficacy w chemotherapy
  - Mildly to Modestly effective
  - Side effects: Sedation, Dystonia

Classes of Antiemetics
The New Generation

- 5-HT3 Serotonin Receptor Antagonists
- Ondansetron (Zofran) prototype
- Most useful class of antiemetics for chemo induced emesis
- Chemo→release of serotonin from small intestine→stimulates Area Postrema
- FDA Approved Indications
  - Antiemetic prevention for chemotherapy or radiation
  - Post Op nausea and vomiting
- Use for other causes of N & V off label

Other Classes of Antiemetics

- Neurokinin Receptor Antagonists
- Glucocorticoids
- Cannabinoids

Antiemetics for Gastroenteritis

- No high quality studies in adults examining efficacy of different drugs for acute gastro
- "Antiemetic treatment for acute gastroenteritis in children: an updated Cochrane systematic review." BMJ Open. 2012; 2(4); e000622.

Cochrane Review Children 2012

- 10 trials and 5 treatments: dexamethasone, dramamine, metaclopramide, granisetron, and ondansetron
- Clear evidence that compared w placebo, ondanseton increased proportion of pts who stopped vomiting, decreased hospitalization, and decreased need for IV
- Ondansetron most likely treatment to stop vomiting
- 90/90 US ER docs, 107/136 British ER docs frequently prescribe ondansetron to children
- Urged future updates to AAP guidelines for tx of gastroenteritis.

Ondansetron

- First Licensed for Use 1991
- Mechanism of Action
  - 5-HT3 Serotonin Receptor Antagonist
  - Blocks signals to Area Postrema that cause N & V

Ondansetron

- Multiple Forms and Strengths
  - 16-24 mg/day for chemotherapy
  - No data on best dosing in our setting
  - 4 and 8 mg ODT in our setting
  - Oral Dissolving Tablet that dissolves on tongue
  - Rapidly absorbed and quickly effective (mins)
  - Usually one dose effective. Max 16 mg/day
- Common Side Effects—Minimal
  - Generally very well tolerated
  - Headache
  - Constipation

Safety Warning

- 2011 Safety Alert for Pts w Long QT Syndrome
- "Rarely and predominantly with IV use, transient EKG changes including QT interval prolongation"
- "Mostly small and clinically insignificant"
- "However potentially fatal cardiac arrhythmias have been reported in association with QT prolongation."
- 32 mg IV dose taken off market

Safety Warning

- FDA recommends EKG monitoring
  - Electrolyte abnormalities: hypokalemia, hypomagnesemia
  - Heart failure
  - Bradyarythmias
  - Concomitant medications that prolong QT interval

Safety Advice for College Health Ambulatory Setting

- Screen for personal or fam hx of Long QT
- Contraindication*/Caution w certain drugs
  - Fluconazole *
  - Erythromycin class
  - Quinilone class

What do ER Docs Do?

- Standard of care: Ondansetron

Old Way of Managing Gastro

- Watching people for hours
- Tying up exam rooms
- Trying to get them to take sips
- Giving them pep talks—trying to get them to tough it out
- Going back and forth to bathroom (spreading virus)
- IV's
- ER visits

New Way: Gastro Greatly Simplified

- Quick eval, limited PE (wearing gloves!)
- Quick screen for ondansetron contraindications
- Provide one dose (sometimes another to go)
- Quickly back to dorm/apt
- Limit time in medical facility
- Students feel dramatically better
- Rarely need to use IV, because student can hydrate orally
- Very rare ER referrals
- Back to class quickly

Bottom Line

- Treatment often based on clinical experience, costs, safety
- When I talk to ER docs, use of ondansetron is considered standard of care for adult w gastro
- Personal experience has been compelling

More About Epidemiology

Contagiousness

- Transmission
  - Fecal-Oral
  - Airborne Droplets
  - Food/Water—Traveler's Diarrhea, shellfish
  - Contaminated Environmental Surfaces
- Readily Transmissable
  - Median Infectious Dose 18 viruses
  - Over 1 Billion virus in 1 gm stool
- Very High Secondary Attack Rate
- Most contagious at time of sx

Prevention

- Alcohol based disinfectants ineffective
- Prevent aerosolization when cleaning up
  - PPE: Gloves, Masks, Gowns
  - Chlorine based disenfectants
  - Emesis bags
- Personal Hygiene
  - Hand Sanitizers not effective
  - Gloves when examining patients
  - Soap and Water always in bathroom

Advice For Students

- Soap and Water Handwashing
  - Self and Roommates, Hallmates
  - Esp after going to bathroom
- Stress infectiousness
- Have chlorox wipes in bathroom—use regularly
- Do not cook, go in kitchen or dining hall
- Stay home while sick

Community Issues

- Weekly report on # GI illness
- Generally 2-3% of visits
- When cases spike:
  - Campus wide message about hygiene
  - Staying home
  - Record residence—if ≥ 2 cases on one floor, small residence hall, institute twice daily bathroom cleaning
- Have done table tops w Emergency Planners

Summary

- Review Epidemiology
  - High prevalence, antigenic drift, highly contagious
- Reviewed Diagnosis
  - History, Diff Dx, PE w focus on Postural VS
- Current Concepts in Management
  - Types of fluids, dietary advice
- Reviewed New Class of Antiemetics
  - 5-HT3 Serotonin Antagonist Ondansetron, effectiveness, rare side effect, greatly simplifies tx, Students feel remarkably better

Thank You!

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