Treatment Options for Gastroparesis

Oley Foundation Webinar
Thomas L Abell
20 June 2017

Disclosures: Thomas L Abell
- Primary Funding: NIH GpCRC & NIH DiaComp
- Investigator: Rhythm, Theravance, Vanda
- Consultant: Theravance
- GI/GI Stim/GES Editor: Med Study, Neuromodulation, WikiStim
- Reviewer: UpToDate
- Holder of IP from U of MS on GES and related
- Will discuss some off-label drugs and devices

Organization
- Introduction and Personal Statements
- Current Status of Patients with Gastroparesis
- Gastroparesis & Gastroparesis Like Disorders
- NIH, FDA and Medicare Involvement
- Pathophysiology of Gastroparesis Syndromes
- Options for Treatment for Gastroparesis
- Related Discussion of Team Related Care
- Concluding Comments

Personal Perspective
- 69 Y/O Physician: GI Motility & other areas
- Working on Nausea/vomiting for ~ 50 years
- Perspective: Bad, Good, Mixed, Now, Future
- How I got interested:
  - Migraine related nausea and vomiting
  - Told (1968) these were all psychosomatic
- This presentation: Just my own opinions—
- No one else: U of L, NIH, any support group

Symptoms of Gastroparesis (Gp)
- Main/Common Symptoms:
  - Nausea *
  - Vomiting *
  - Abdominal Pain *
  - Bloating/Distension
  - Loss of Appetite/Anorexia
  - May be associated with other symptoms--

Associated Symptoms of Gp
- Lower Symptoms:
  - Constipation and/or
  - Diarrhea
  - Fecal Incontinence
  - May also have:
    - Urinary Hesitancy and/or
    - Urinary Frequency
    - Some patients have interstitial cystitis
Other Symptoms in Gp

- Autonomic Symptoms—such as dizziness...
- Many patients have—Migraine headaches
- Muscle pains—often Dx: Fibromyalgia
- May have Diagnosis—autoimmune disease
- Some patients have overly flexible joints
- Some patients have cyclic symptom pattern
- Many patients have a family history of Sx
- Other patients have seizures ....

Variety of Sx with Gp

- Raises question—what are all these Sx from?
- Many symptoms are seen with acute illness:
  - Such as viral infections, and then resolve
  - But Gp have recurrent or chronic symptoms..
- Most Providers have never learned about Gp
- Either in school, training, or practice
- And thus may not ‘value’ these symptoms
- OR value the illnesses and thus the patients:

History of Patients with Gastroparesis (Gp)

- The M’s/Mis’s:
  - Miserable
  - Misunderstood
  - Misdiagnosed
  - Mismanaged
  - Mistreated
  - Hopefully these days are (almost) past us !

What I have Learned from Patients

- First all of the above on Hx of Gp treatment
- Second, with nearly 100 focus groups over 25 years
- Third, how little we have known about Gp
- Fourth, how much patients are trying to tell us
- Fifth, how much suffering—called disease burden—exists
- Sadly, this is the history of much in medicine!

Data from Gp Focus Groups

- Team approach crucial for helping patients
- Autonomic nervous system is part of illness and may not be just the GI tract involved
- Providers often underestimate effect of illness on quality of life
- Increase levels of anxiety and depression in some likely due to the trauma of the illness
- Well intentioned providers may make things worse
Federal Involvement in Gp

- The NIH GpCRC—in response to patient needs
- Was started due to feedback from many patients
- www.gpcrc.us site—recommend looking at
- Many items & Much effort with publications:
- US FDA has been very helpful in defining what is measured and reported in trials for Gp.
- Medicare has not covered many home therapies—Only some congressional action

What the NIH GpCRC has done:

- Disease Burden
- Descriptions
- Diagnosis
- Details of illness
- Distinctive pathophysiology
- Concomitant Interest in Gp at FDA
- Related proposals on Medicare coverage

Gp / Gastroparesis Like Syndrome

- From GpCRC—comparison:
- Patients with no delay in gastric emptying (GE)
- Gp and GLS are identical except for GE testing
- Thus GE may not be the best way to differentiate patients
- Related ancillary work from GpCRC has shown Gp and GLS identical except for GE
- These finding may influence how Gp is viewed

Gp and GLS

- Full thickness gastric biopsies from patients
- Related ancillary work from GpCRC has shown that:
- Measures like ICC are decreased in all patient with SX of GP
- But as the ICC numbers get lower, the GE becomes (more) delayed
- Example shown below--

What does this mean

- My own (and others) view: Gp and GLS can be viewed as part of a spectrum
- But many others would not agree with us, especially outside of the US
- So no general agreement or consensus on this
- What is not widely circulated is some new work and
- These are My Opinions from this new work:
NIH: Diabetes Complications Consortium
- Related to the NIH and submitted to Clinical Trials.gov
- Small groups of Diabetic & Non-Diabetic patients studied:
  - Inflammation—common systemically abnormal by whatever method
  - Autonomics—may be abnormal in many patients

New NIH Diabetes Gp work, cont’d
- From same two groups of patients:
  - Enterics—confirmed what GpCRC has shown with some additional measures
  - Electrophysiologic—confirmed what is known
  - Hormones—many abnormal even if not diabetic
  - So—that Gp can be look at as a systemic disease with variable presentations of symptoms

Additional Comments on new data
- We also looked at the mechanism of one therapy for Gp—Gastric Stimulation (GES)
- And showed several possible mechanism of action (But will not emphasize this here....)
- The rest of this talk: related to therapies
- As in title—and I will use the letters--
- “COPS” for Care/Chronic Disease, Options for Therapy, Particulars and Searches

Chronic Illnesses Care —The C’s
- Home Care/ Primary Care
- Internet Care
- Acute Care
- Chronic Care
- Hospital Care
- All important to be integrated
- So providers work as a team
- Ongoing communication essential !!

Options for therapy—the D’s
- Diet/ Nutritional Support
- Drugs
- Devices
- Disrupt/Divert
- Detoxify
- Will discuss each separately.
- But first, why are there not more treatments?
- The Particulars next regarding treatments

Why Not More Treatments for GP?
- 1. Belief that Gp not a Real Disease
- 2. Belief that Gp not a Biologic Problem
- 3. Lack of Understanding the Mechanisms
- 4. Limited Resources for New Drugs
- 5. Narrow View of Range of Treatments
- All of these contribute to the current--
- Lack of Great Treatment Options for GP
Diet/Nutritional Support for Gp

• Traditional Approach:
  • Frequent, Small portion meals
  • Of Limited ‘Digestibility’
  • The problem is:
  • This only works with certain patients.
  • Also the MAJORITY of Gp patients
  • Never seen by a Nutritionist…..
  • Even in Referral Centers!

More on Nutritional Support for Gp

• Enteral Nutrition Best
  • But not everyone can eat
  • For those that can’t eat by mouth:
  • Small bowel feeding an option
  • Trial of an NJ tube then permanent tube
  • But limited expertise IF problems with tubes
  • Not everyone can have successful SB feeds
  • MOST with tubes never have a SB Bx!!

Even more on Nutritional Support-

• TPN—only option for some patients
  • Full discussion of TPN beyond today’s talk
  • Can be wonderful
  • But not easy, inexpensive, or risk free
  • Expertise on TPN varies widely
  • Although many excellent TPN Pharmacies
  • And support groups like Oley help greatly

Drugs for Gp

• Can be discussed by class
  • Anti emetics
  • Prokinetics
  • Other
  • Many available worldwide
  • But not all in US
  • Some investigational
  • Renewed interest by Pharmaceutical Cos

Anti-emetic Drugs for Gp

• Examples: chemical/generic & (Brand) names
  • Promethazine (Phenegran)
  • Prochlorperazine (Compazine)
  • Diphenhydramine (Benadryl)
  • Ondansetron (Zofran)
  • Other Drugs related to Ondansetron
  • Scopolamine (TransdermScop)
  • Drodabinal (Marinol)

Prokinetic drugs for Gp

• Metochlorpromide (Reglan)—
  • Only approved drug fro Gp in US
  • Many ways to deliver
  • A number of therapy issues
  • Short and Long term safety a concern
  • Recommended for short term use
  • Some help but has a lot of limitations
Other Sx/ Prokinetic Drugs for Gp

- Aprepitant (Emend) —
  - Expensive
  - Has documented efficacy
  - Erythromycin —
  - May not work long term
  - Other drugs —
  - Most not studied systematically

More on Drugs for GP

- Investigational — not approved in US by FDA
- Domperidone —
  - Safer than Metochlopromide
  - Some complexity in obtaining
  - Other Investigational drugs —
  - In Clinical trials
  - All under FDA guidelines

Even More on Drugs

- Above are (almost) all oral drugs (Most are tablets)
- Some as capsules, suppositories, liquids
- Some can be given intravenously (IV)
- IV therapies — beyond the scope of talk today
- Have real risks but some benefits
- Coverage issues by insurers
- Need dedicated team to administer

Drugs for Pain in Gp

- VERY Complex issue
- Difficult for most patients and providers
- Beyond the scope of this presentation
- One approach — all Gp Patients with pain:
  - Need to see a pain specialist
  - Pain should be able to be treated
  - But often does not happen in practice

Devices for Gp

- Limited availability
- Only one approved device
- Many regulatory, insurance, other issues
- Will have limited discussion today
- The one available device (GES) for Gp
- FDA HUD approval in 2000 — Enterra
- Recommended for compassionate use by ACG Gp Guidelines 2013

Divert/Disrupt

- Stomach has inlet, upper, lower and outlet
- Increased interest in Pyloric= outlet function
- Clear that this is an issue for many patients
- Especially those with delayed gastric emptying
- Many new approaches, some endoscopic
- None yet conclusively shown to always help
- Needs to be discussed with all patients
Detoxify

- Many Gp Patients have systemic issues
- Not only generalized symptoms
- But disordered physiology
- Some Gp Patients have neuro-muscular issues
- Measured by blood and/or tissue=inflammation
- Some therapies like Immunoglobulin (IVIG) are immune/anti-inflammatory and can help

Particulars for Therapy—more Ps

- Patient and Protectors
- Providers
- Partnerships
- Pharmacies/Professional Companies
- Processes—working together
- Comes back to having a true team
- As with any Chronic Illness

 Searches—The Future

- Searches—not just internet--
- PreSearch—Talking about issues, like today
- ReSearch—formal work like GpCRC & others
- ProSearch—education of providers
- FuSearch—How we can get to the future
- Support groups Crucial
- Knowing Federal resources: NIH, FDA, Medicare and Others Are Very Important

Summary Comments

- Most things in Medicine are Opinions vs. Facts
- And Thus I have Given my own opinions
- Perspective: over 50 years (as I see it going): Bad, Good, Mixed, Now, Future
- I have tried to focus on therapies
- But especially teams, and supports
- In the context of the illness we call Gp
- Which, when severe, is Gi Tract Failure

Concluding Comments

- My bottom lines:
  1. Gp has been misunderstood—not unusual in the history of medicine
  2. May illnesses take decades (or longer) to be understood
- 2. Now accepted as a ‘legitimate’ illness
- Although STILL Not everyone agrees!!

Conclusions, Cont’d

- 3. US NIH and FDA are engaged in work on this problem. Medicare/gov’t can be ‘lobbied’.
- 4. Much has been learned esp. over the last decade about Gp and Gut Failure
- But Much More Work need to be Done!!
- 5. Partnerships of Patients Protectors and Providers may be the key to making this happen !!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!
Contacts & Follow Up

• Web access very important:
• www.grpcrc.us and many related sites on Gp
• Support groups like Oley and Many Others!
• See on-line info, esp. about FDA & Medicare
• Questions: will try to answer any and all
• Please send questions to Oley Foundation:
  • Roslyn Dahl-----dahlr@mail.amc.edu
• We will try to answer in a timely manner!