Treatment Options for Gastroparesis

Oley Foundation Webinar
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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 treament
- 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!

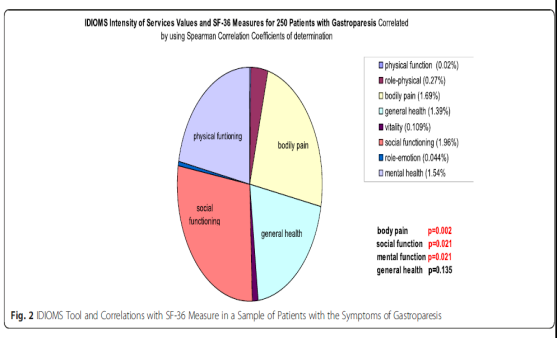

Fig. 2 IDIOMS Tool and Correlations with SF-36 Measure in a Sample of Patients with the Symptoms of Gastroparesis

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--

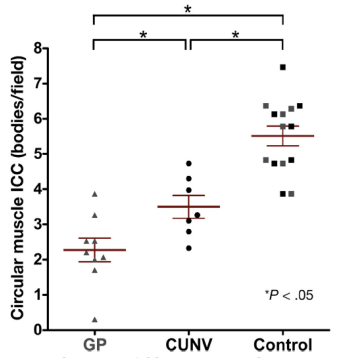

Figure 3. Comparison of ICC density between CUNV patients and healthy controls. Data from a recent gastroparesis cohort[9] (in grey) also are shown for comparison. GP, gastroparesis.

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)
- Prochloperazine (Compazine)
- Diphenhydramine (Benadryl)
- Ondansetron (Zofran)
- Other Drugs related to Ondansetron
- Scopolamine (TransdermScop)
- Drodabinal (Marinol)

Prokinetic drugs for Gp

- Metochlopromide (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
- 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!