

GI Disorders

Peptic Ulcer Disease
GERD
Nausea/Vomiting

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PEPTIC ULCER DISEASE PATIENT CASE #1

- ◆ B.S. - 64yo w/epigastric pain, worse at noc, relieved by food & antacids, recurrent, no weight or bowel changes
 - * ? S/S c/w PUD
 - * ? Gastric vs Duodenal Ulcer
 - * ? NSAID vs H. Pylori
 - * Treatment Goals
 - * Non-pharmacological strategies

EPIDEMIOLOGY Peptic Ulcer Disease

- ◆ 10% U.S. Lifetime Incidence, 1% annual
- ◆ DU > GU
- ◆ Men = Women
- ◆ Age DU - 25 - 55 (avg. 40)
- ◆ GU - Peak Incidence 60-70 Female, 70-80 male

PRESENTATION FEATURES GU vs. DU		
Feature	GU	DU
Epigastric Pain	2+	3+
Episodic Pain	0	2+
Pain at Night	2+	3+
Pain Relieved by Food	1+	2+
Pain Assoc. w/ Eating	1+	0
Anorexia	3+	2+
Nausea/Vomiting	3+	2+
Bloating/Belching	2+	2+
Ulcer Recurrence	2+	3+

0	Rare
1+	Infrequent
2+	Frequent
3+	Consistent

- CLINICAL COURSE**
Peptic Ulcer Disease
- ◆ Periods of exacerbations and remissions
 - ◆ May become asymptomatic w/o tx
 - ◆ Treatment accelerates healing
 - ◆ GU heals more slowly
 - ◆ 50% - 90% recurrence rate in 1 year
 - ◆ Factors influencing recurrence

- GOALS OF THERAPY**
- ◆ Decrease acid secretion & enhance defense
 - ◆ Eradicate *H. pylori*
 - ◆ Promote ulcer healing
 - ◆ Relieve ulcer pain
 - ◆ Prevent complications
 - ◆ Prevent recurrences

GENERAL TREATMENT MEASURES

- ◆ Stop smoking!
- ◆ Eliminate ulcerogenic medications
- ◆ Minimize alcohol
- ◆ Avoid exacerbating foods
- ◆ Drug therapy . . .

**PATIENT CASE #2
RECURRENT PUD**

- ◆ JM 56yo, presents to your clinic w/complaints c/w PUD; h/o several recurrences over past couple of years, noncompliant w/ evening H2
 - * ? What is likely etiology of her PUD
 - * ? Diagnostic work-up
 - * ? Treatment plan

RECURRENT ULCERS

- ◆ PUD is chronic and recurrent by nature
- ◆ Up to 90% recur within 1 year
- ◆ Factors: *H. pylori*, smoking, NSAIDS, hypersecretion, noncompliance
- ◆ Focus on *H. pylori*
- ◆ Maintenance therapy -- is there a role??

Helicobacter pylori

◆ NIH Consensus Conference (Feb 94)

* Role of H. pylori, Dx, who to treat

◆ Findings

* PUD + H. pylori - tx w/H2s + antibiotics

* Nonulcer dyspepsia + HP = ???

* Interesting relationship w/gastric malignancy

Helicobacter pylori
Diagnosis

◆ Endoscopy - Antral biopsy - 1-24 hr result

◆ Histology - allows evaluation of the gastritis

◆ Culture - difficult, time consuming, \$\$

◆ Serologic - measure IgG antibodies to HP

◆ Office based whole blood - simple, cheap

◆ Breath test for urease (Meretek, TriMed)

◆ Presumptive - good argument if DU (or GU)

Helicobacter pylori
Treatment

◆ Amox or TCN +Flagyl + Bismuth

* 1st generation - 15 pills/d

* Eradication rate around 90%

◆ 2nd generation - not an option, need 3

* Omeprazole +Amox or Clarithromycin

* Still 2 weeks - 70%-90% response

◆ One week regimen - 3rd generation

* MOC or MOA (OK to sub. Prevacid)

SUGGESTED HP REGIMENS

- ◆ MOC - BID X 14 days
- ◆ MOA - BID X 14 days
- ◆ **Tritec + Biaxin + Amox or Metro or TCN**
BID x 14 days
- ◆ **Pepto QID + Metro TID + TCN QID + PPI**
QD x 14 days
- ◆ **Pepto + Metro + TCN x 14 days + H2 x 28 d**

Helicobacter pylori
Issues

- ◆ **1 week vs. 2 week regimens**
 - * Similar efficacy?, increased compliance
 - * Better tolerated, lower cost - 10 day maybe OK
- ◆ **Inclusion of H2-RA or PPI**
 - * Effect on symptoms, healing
 - * Duration
- ◆ **Resistance - Metro high, Biaxin low**
- ◆ **FDA Approved regimens - non issue**
- ◆ **Cost**

H₂ Receptor Antagonists

- ◆ **Competitive and reversible binding**
- ◆ **Historically - #1 PUD class --> PPIs??**
- ◆ **Potency varies but all equally effective**
- ◆ **Regimens: multidose vs. nighttime**
- ◆ **Dosing Schedules: healing vs. maintenance**
- ◆ **Renal insufficiency adjustment**

H₂ Receptor Antagonists

- ◆ Ideal duration of treatment
- ◆ Adverse effects of H₂-RAs
 - * Subtle differences; all well tolerated
- ◆ Drug interactions
 - * Cimetidine >> Ranitidine > Famotidine = Nizatidine

Cost of H₂-RAs 1 month supply

<u>Agent</u>	<u>Dosage</u>	<u>AWP (\$)</u>
Cimetidine (Tagamet)	300 mg QID	\$78 (gen)
	400 mg BID	\$101 (brand)
	800 mg HS	
Famotidine (Pepcid)	20 mg BID	\$102 (brand)
	40 mg HS	
Nizatidine (Axid)	150 mg BID	\$104 (brand)
	300 mg HS	
Ranitidine (Zantac)	150 mg BID	\$89 (gen)
	300 mg HS	\$105 (brand)

CHOICE OF AN H₂

- ◆ Experience: C = R > F > N
- ◆ Efficacy: All equal
- ◆ Potency: Not an issue!
- ◆ Adverse effects: C >= R = F = N
- ◆ Drug Interactions
 - * Affect few patients. Careful w/ Cimet
- ◆ Dosing Convenience
- ◆ Cost: all similar, generic less, OTC cheapest

ANTACIDS

- ◆ Neutralize gastric acid
- ◆ Disadvantages: side effects, dosing schedule
- ◆ Intermittent Use: CaCO_3 , NaHCO_3
- ◆ Frequent Use: Limit to Mg, Al, & Combo
- ◆ Drug Interactions
- ◆ Place in therapy: PRN symptoms

SUCRALFATE

- ◆ Cytoprotective: topical barrier
- ◆ Similar efficacy to H2-RAs
- ◆ Regimen: 2 g BID vs. 1 g QID
- ◆ Typical Rx: 1 tab AC & HS
- ◆ Combination with H2-RAs
 - * No clear advantage; doubles cost

SUCRALFATE

- ◆ Adverse effects: nonsystemic
- ◆ Drug Interactions
 - * May impair absorption of some drugs
- ◆ Cost: 1 g QID = \$85-\$106/mo (AWP)
- ◆ Sucralfate vs. H2-RAs
 - * Comparable efficacy and cost
 - * Non-systemic may be beneficial
 - * No effect on gastric pH
 - * Less convenient dosing

OTHER CYTOPROTECTIVE AGENTS

- ◆ **Misoprostil**
 - * NSAID-induced GU
 - * No real role in PUD
- ◆ **Bismuth salts (Pepto-Bismol)**
 - * Combination tx in *H. pylori*
 - * Dose: 525 mg (2 tabs) QID
 - * Cautions: neuro, salicylate
 - * Role in PUD linked to *H. pylori*

PROTON PUMP INHIBITORS

- ◆ **Drugs**
 - * Omeprazole (Prilosec)
 - * Lansoprazole (Prevacid)
 - * Rabeprazole (Aciphex)
 - * Pantoprazole (Protonix)
- ◆ **Dramatic reduction in gastric acid**
- ◆ **Long acting - up to 3 days**
- ◆ **Multiple Indications**

PROTON PUMP INHIBITORS

- ◆ **Dose / Duration:**
 - * Omeprazole: 20/day, up to 40/day - 4-8 wks
 - * Lansoprazole: usually 30 mg/day - 4-8 wks
 - * Rabeprazole: 20mg/d - 4-8 wks
 - * Pantoprazole: 40mg/d - 4-8 wks
- ◆ **Potency L30 > O20 > L15 = R20 = P40**
- ◆ **Slightly faster healing than H2-RAs**
- ◆ **Short & long-term safety similar to H2RAs**

PROTON PUMP INHIBITORS

- ◆ **Drug Interactions**
 - * Inhibits hepatic enzymes -- omeprazole
 - * pH effect on absorption -- all agents
- ◆ **Cost: \$110-\$120/month (P < R < L < O)**
 - * May decrease overall costs (6 vs 4 weeks)
- ◆ **Role in PUD**
 - * Potentially first line agent
 - * DON'T combine with H2- RAs

COMPARISON OF PPI'S

- ◆ **Experience: O > L > R > P**
- ◆ **Potency: not really an issue except for cost**
- ◆ **Drug intxns: O slightly greater risk**
- ◆ **Efficacy: likely no real difference**
- ◆ **Ability to give via tube or as liquid - L**
- ◆ **Cost: some advantage for P**

MANAGEMENT OF PUD
Recommendations

- ◆ **Focus on HP - combine antibiotic and acid inhibition**
- ◆ **Limit usual options to PPI , sucralfate, and 1 H2-RA**
 - * PPI active against HP and quicker healing
 - * H2's role becoming more limited
 - * Sucralfate ideal for pregnancy (nonsystemic)
 - * Antacids - no role in active Rx
- ◆ **NSAIDs ?**

**MANAGEMENT OF NSAID
INDUCED ULCERS**

- ◆ Can NSAID be d/c'd ?
 - * NO - consider maintenance Rx
 - * YES - treat ulcer in usual fashion
- ◆ Misoprostol 200 mcg QID for prevention
- ◆ COX-2 Inhibitors are important options
- ◆ H2 blockers - may work
- ◆ PPI's - some data suggests may be DOC - treatment and prophylaxis (see NEJM 3/12/98)

**MANAGEMENT OF PUD
Monitoring**

- ◆ Cautious work-up of young or old
- ◆ Be aware of renal adjustments for H2s
- ◆ Watch out for CNS side effects w/H2s
- ◆ Review regimens for drug interactions
- ◆ Follow-up lifestyle modifications
- ◆ Investigate for *H. pylori*
 - * Endoscopy
 - * Serology or breath tests

**PATIENT CASE #3
GERD**

- ◆ JH, 51 yo F, severe retrosternal burning, frequent, usually at noc, assoc w/ large meal, relieved by antacids
 - * ? Factors in history which contribute to problem
 - * ? Potential complications
 - * ? Lifestyle changes
 - * ? Stepwise approach to drug therapy

**GASTROESOPHAGEAL
REFLUX DISEASE (GERD)**

- ◆ GERD: condition or histological alteration resulting in reflux.
- ◆ Reflux Esophagitis: Inflammation of esophagus secondary to reflux

**DEFENSIVE MECH vs.
AGGRESSIVE FACTORS**

- | | |
|------------------------------|----------------------|
| ◆ Normal defense | ◆ Aggressive Factors |
| * Lower esophageal sphincter | * Acid |
| * Esophageal clearing | * Pepsin |
| * Mucosal resistance | * Bile acids |
| * Gastric emptying | * Pancreatic enzymes |

**PRESENTATION AND
EVALUATION**

- ◆ Heartburn is hallmark
 - * Waxing and waning
 - * Activities may aggravate it
- ◆ Other: regurgitation, dysphagia, bleeding, chest pain
- ◆ Evaluation
 - * Classic sx: don't require endoscopy
 - * Endoscopy if uncertain dx, tx failure, or sx include dysphagia, bleeding, weight loss, choking, chest pain

THERAPY OF GERD

◆ **Goals**

- * Alleviate symptoms
- * Decrease GE reflux
- * Promote healing of injured mucosa
- * Prevent complications

◆ **Aims of Treatment**

- * Increase LES pressure
- * Improve gastric emptying
- * Decrease acidity and volume

THERAPEUTIC APPROACH TO GERD

- ◆ **Phase I:** Elevate bed, change diet, stop smoking, avoid certain meds, antacids or gaviscon, OTC H2-RAs
- ◆ **Phase IIa:** H2-RAs, prokinetic agents, bethanechol, sucralfate
- ◆ **Phase IIb:** Hi-dose H2-RAs, PPI
- ◆ **Phase III:** Antireflux laparoscopic surgery

ANTACIDS & ALGINIC ACID

- ◆ **Antacids aimed at neutralizing acid**
- ◆ **Alginic Acid (Gaviscon)**
 - * Viscous foam floats on acid secretions
 - * Mechanical barrier, mucosal protectant
- ◆ **Antacids and Gaviscon equally effective**

H2-RAs in GERD

- ◆ Mainstay of therapy although PPI's rising
- ◆ Probably superior to antacids
- ◆ Response depends on severity, duration of tx, dose
- ◆ Prolonged tx often required
- ◆ Doses: C 400 QID or 800 BID, R 150 BID, F 20 BID or 40 HS, lower OTC dose Phase I
- ◆ Continuous acid suppression

PPIs IN GERD

- ◆ Greater acid inhibition
- ◆ Superior results over H2RAs at 4 & 8 weeks
- ◆ Effective if refractory to H2s
- ◆ Dose: same as for PUD, often longer
- ◆ Severe cases may require higher doses

BETHANECHOL IN GERD

- ◆ Cholinergic agonist - increases LES tone
- ◆ Results: reduced sx, less antacid use, healing
- ◆ Dose: 25 mg QID
- ◆ Cost: Urecholine \$115/mo, generic \$6/mo
- ◆ Side effects
- ◆ Avoid in asthma, COPD, PUD

PROKINETIC AGENTS
Metoclopramide

- ◆ Increase LES tone and gastric emptying
- ◆ Reduces sx but no healing
- ◆ Dose: 10 mg QID
- ◆ Cost per month
 - * Reglan \$100/mo vs. generic \$38/mo
 - * Cisapride (Propulsid) - available only through investigational protocol

METOCLOPRAMIDE vs.
CISAPRIDE

- ◆ Side effects
 - * Significantly limits Reglan - EPSE
 - * Cisapride - no dopaminergic activity --- NO EPSE, but has serious drug interactions
 - * Clinically: Cisapride ≥ Metoclopramide
- ◆ Choice of Prokinetic
 - * Metoclopramide first line
 - * Cisapride not marketed after 7/00 - "limited access" program available - "investigational"

TREATMENT GUIDELINES
GERD

- ◆ Stepwise approach
 - * Mild - lifestyle changes, antacid or low dose H2
 - * Moderate - H2-Ras or PPI
 - * Refractory - PPI best option usually
- ◆ Bethanechol and Reglan adjunct Rx
- ◆ Multiple combinations increase cost
- ◆ Monitor: Reglan toxicity
- ◆ Laparoscopic Surgery

**PATIENT CASE #4
DIABETIC GASTROPARESIS**

- ◆ KR, 74yo M, poor control of NIDDM since age 40, 2-d h/o persistent vomiting. Vomit contains undigested food, sick stomach, putrid belching, 12# wt loss, barium --> gastric dilation, diminished peristalsis. PMH Parkinson's, HTN, high cholesterol
 - * ? Nonpharmacological interventions
 - * ? Pharmacological management & monitoring

**NAUSEA & VOMITING
Complications**

- ◆ Complications
 - * metabolic disturbances, dehydration, renal failure, Malory-Weiss tear, wound disruption, aspiration, pneumothorax
- ◆ Assessment
 - * pathophysiology, detailed hx, work-up for unexplained vomiting.

**ANTIEMETICS
Antihistamines & Anticholinergics**

- ◆ Most frequently prescribed:
 - * Dimenhydrinate (Dramamine)
 - * Meclizine (Antivert, Bonine)
 - * Scopolamine (Transderm-Scop)
- ◆ Interrupt visceral afferent pathway
- ◆ Use only for simple pathology
- ◆ Side effects include drowsiness and anticholinergic effects

PHENOTHIAZINES

- ◆ **Uses: general, motion sickness**
- ◆ **Frequently used agents**
 - * Prochlorperazine (Compazine)
 - * Promethazine (Phenergan)
- ◆ **Most commonly prescribed drugs**
- ◆ **Block dopamine in the CTZ**
- ◆ **Most effective if simple pathology**
- ◆ **Side effects: EPSE, sedation, hypotension**

**NAUSEA & VOMITING
Treatment Considerations**

- ◆ **Etiology of symptoms**
- ◆ **Frequency, duration, and severity**
- ◆ **Dosage forms patient can take**
- ◆ **Success & tolerability of previous tx.**

GASTROENTERITIS

- ◆ **Common, very young at highest risk**
- ◆ **Often refractory to antiemetics**
- ◆ **Pediatrics: educate parents**
 - * > 700 deaths annually
 - * Awareness of sx
 - * Must provide energy, water
 - * Seek medical attention if complications

REHYDRATION GUIDELINES

- ◆ Rapid rehydration w/ oral glucose-electrolyte solution over 4-6 hours
- ◆ Restoration of diluted milk after 6 hours
- ◆ Lactose need not be eliminated
- ◆ Solids reintroduced after successful rehydration

DIABETIC GASTROPARESIS

- ◆ Vomiting is a common complication
- ◆ Progressive - no good antiemetic tx
- ◆ Symptomatic improvement with bethanecol or metoclopramide
 - * Stimulate gastric motility
 - * Metoclopramide first line

MOTION SICKNESS

- ◆ Agents w/strong anticholinergic effects work best
- ◆ Act on receptors in the vomiting center
- ◆ Phenothiazines are ineffective
- ◆ Primary agents
 - * Scopolamine patch - convenient & effective, but expensive (supply problems in past)
 - * Dramamine - inexpensive option

PREGNANCY
Nausea & Vomiting

- ◆ Incidence > 50%
- ◆ Hyperemesis gravidarum is a serious, infrequent complication
- ◆ Concern with teratogenicity of meds
- ◆ Drugs of choice:
 - * Cyclizine (Marezine)
 - * Meclizine (Antivert)
- ◆ Ondansetron may be useful

PEDIATRICS
Nausea & Vomiting

- ◆ Unique differences
 - * Reglan: >EPSE
 - * Phenothiazines: >dystonia
 - * cyclizine, scopolamine not for <12 yrs of age
- ◆ Viable options
 - * Dimenhydrinate (Dramamine)
 - * Trimethobenzamide (Tigan)

PATIENT EVALUATION

- ◆ Symptomatic relief may be unobtainable until underlying condition corrected
- ◆ Substitute agent w/different pharmacology if persistent N/V
- ◆ Be mindful of fluid/electrolyte problems, especially in pediatrics
