PEPTIC ULCER DISEASE

Muhammad Sarfraz

Abstract: Gastric and duodenal ulcers usually cannot be differentiated based on history alone, although some findings may be suggestive. Epigastric pain is the most common symptom of both gastric and duodenal ulcers.In uncomplicated peptic ulcer disease (PUD), the clinical findings are few and nonspecific. "Alarm features" that warrant prompt gastroenterology referral[1]include bleeding, anemia, early satiety, unexplained weight loss, progressive dysphagia or odynophagia, recurrent vomiting, and family history of GI cancer. Patients with perforated PUD usually present with a sudden onset of severe, sharp abdominal pain. Documentation of PUD depends on radiographic and endoscopic confirmation. Testing for H pylori infection is essential in all patients with peptic ulcers. A fasting serum gastrin level should be obtained in certain cases to screen for Zollinger-Ellison syndrome.Upper GI endoscopy is the preferred diagnostic test in the evaluation of patients with suspected PUD. Most patients with PUD are treated successfully with cure of H pylori infection and/or avoidance of NSAIDs, along with the appropriate use of antisecretory therapy.the recommended primary therapy for H pylori infection is proton pump inhibitor (PPI)–based triple therapy.[1] These regimens result in a cure of infection and ulcer healing in approximately 85-90% of cases.[2] In patients with NSAID-associated peptic ulcers, discontinuation of NSAIDs is paramount, if it is clinically feasible. For patients who must continue with their NSAIDs, proton pump inhibitor (PPI) maintenance is recommended to prevent recurrences even after eradication of H pylori.[3, 4] The indications for urgent surgery include failure to achieve hemostasis endoscopically, recurrent bleeding despite endoscopic attempts at achieving hemostasis (many advocate surgery after 2 failed endoscopic attempts), and perforation.

Key words: Pepticular disease, NSAID, H.Pylori, PPI, Gastric Cancer.

Epidemiology

Dyspepsia occurs in 40% of the population annually and leads to a primary care consultation in 5% and endoscopy in 1%.
Of those who undergo endoscopy:

- About 40% have functional or non-ulcer dyspepsia.
- 40% have gastro-oesophageal reflux disease (GORD).
- 13% have ulcer disease.
- 2% have gastric cancer.
- 1% have oesophageal cancer.

In the past, duodenal ulcer was 10 times as common in men as in women and gastric ulcer had a male preponderance of 3:2. Now the frequency is much less, largely because of H. pylori eradication and the sex incidence being more even.

Peptic ulcer disease prevalence is decreasing in the West, except in certain populations such as immigrants.[6] A UK population-based cohort study reported an overall incidence of uncomplicated peptic ulcer as being 0.75 cases per 1,000 person-years, declining from 1.1 to 0.52 cases per 1,000 person-years between 1997 and 2005. A reduction in H. pylori-related peptic

Article Citation: Sarfraz M, Peptic Ulcer Disease. Indep Rev Jun-Jul 2018;20(1-6): 48-53.

Date received: 24/09/2017
Date Accepted: 07/12/2017

Dr Muhammad Sarfraz, MBBS, FCPS
Assistant Professor of Medicine
Independent Medical College, Faisalabad.

1. Dr Muhammad Sarfraz, MBBS, FCPS
Assistant Professor of Medicine
Independent Medical College, Faisalabad.

ulcers, changing patterns in non-steroidal anti-inflammatory drug (NSAID) use and increasing proton pump inhibitor (PPI) use may have contributed to this.[7]

Etiology[8,9]

- H. pylori.
- NSAIDs.
- Pepsin.
- Smoking.
- Alcohol.
- Bile acids.
- Steroids.
- Stress.
- Changes in gastric mucin consistency (may be genetically determined).[10]

Defence mechanisms include mucus, bicarbonate, mucosal blood flow and prostaglandins.

Presentation[11]

Symptoms

Symptoms of peptic ulcer disease are sometimes very nonspecific and a diagnosis is unreliable on history alone:

- Epigastric pain, usually 1 to 3 hours postprandial - it may sometimes wake the patient in the night, and be relieved by food.
- Nausea.
- Oral flatulence, bloating, distension and intolerance of fatty food - the last is also associated with gallstones.
- Heartburn sometimes occurs although it is more typically associated with gastro-oesophageal reflux.
- A posterior ulcer may cause pain radiating to the back.
- Symptoms are relieved by antacids (very nonspecific).

In Taiwan, silent peptic ulcer disease is not uncommon but in Western countries this is unusual.[12] One study suggests that silent peptic ulcers are more commonly associated with bleeding and may be a manifestation of reduced visceral sensation.[13]

Signs[11]

In uncomplicated cases there is very little to find on examination:

- There is often epigastric tenderness.
- If gastric emptying is slow, there may be a succussion splash.
- Differential diagnosis
- Abdominal aortic aneurysm.
- GORD.
- Gastric cancer.
- Gallstones.
- Chronic pancreatitis.
- Crohn's disease.
- Diverticular disease.
- Irritable bowel syndrome.
- Drug-induced dyspepsia.
- Hepatitis.
- Acute ulcers (occur at times of severe physiological stress - eg, severe burns/head injury).
- Zollinger-Ellison syndrome (if H. pylori is negative, or has been eradicated and ulceration is refractory/recurrent).
- Coronary heart disease.
- Investigations[14]
- FBC may show evidence of iron-deficiency anaemia.

Testing for H. pylori.[15] Test using a carbon-13 urea breath test or a stool antigen test, or laboratory-based serology where its performance has been locally validated. If re-testing is required, a carbon-13 urea breath test is the chosen test. There is currently insufficient evidence to recommend the stool antigen test as a test of eradication. [5] Office-based serological testing is not currently recommended because of its

inadequate performance.

Endoscopy:

National Institute for Health and Care Excellence (NICE) guidelines state that endoscopy is not required unless the patient is presenting for the first time above the age of 55, or there are warning signs (as below).[5]

Irrespective of age, endoscopy is required if there is:

- Iron-deficiency anaemia.
- Chronic blood loss.
- Weight loss.
- Progressive dysphagia.
- Persistent vomiting.
- An epigastric mass.
- In patients aged over 55 years, referral should also be considered if there is:
- Previous gastric ulcer.
- Previous gastric surgery.
- Pernicious anaemia.
- NSAID use.
- Family history of gastric carcinoma.

Management

Modification of behaviour[16]

If drugs are the cause then they should be stopped or replaced but this may not be possible. Being more meticulous about the instructions for taking alendronate or taking NSAIDs including aspirin after food may be required.

Cessation of smoking should be advised if applicable. Smoking increases the risk of peptic ulcer and delays healing as well as opposing the action of H2-receptor antagonists. It has many effects on other parts of the gut including facilitating gastro-oesophageal reflux.

Healing ulcers - H. pylori-positive[17]

Treatment for H. pylori-associated ulcer disease is mainly directed at eradication of infection.

Healing ulcers - H. pylori-negative, NSAID-induced

The NSAID should be stopped. More than 90% of gastric or duodenal ulcers heal with eight weeks of standard-dose H2-receptor antagonists - eg, ranitidine 150 mg twice a day if the NSAID is discontinued.[18] However, PPI drugs are now the mainstay of treatment rather than H2-receptor antagonists.

A large randomised trial has not shown any difference in gastric ulcer healing between groups receiving esomeprazole 40 mg, esomeprazole 20 mg and ranitidine.[19] NICE recommends full-dose PPI for two months.[5]

PPIs are better than standard-dose H2-receptor antagonists and misoprostol for prevention of duodenal ulcers.[18] Patients with high cardiovascular risk should continue to receive prophylactic low-dose aspirin and full-dose naproxen is the preferred NSAID. Co-therapy with a PPI or misoprostol is recommended for these groups. If patients are unable to tolerate PPI treatment, a systematic review of randomised trials found that double-dose H2-receptor antagonists reduce risk of both gastric and duodenal ulcers.

H. pylori-negative NSAID-negative ulcer[20]

Ulceration of the gastric or duodenal mucosa in the absence of H. pylori infection and NSAID or aspirin usage is rare. A careful history of the use of NSAIDs and aspirin is very important in any patient presenting with gastroduodenal ulceration in the absence

of H. pylori infection. The patient might be unaware that several drugs obtainable over the counter as well as some herbal medications contain NSAIDs or aspirin.

To exclude the rare conditions that may cause this, such as Zollinger-Ellison syndrome, samples should be taken from the ulcer and surrounding mucosa.

Bleeding ulcers[21]

Early endoscopic intervention with ablative or mechanical treatment to the bleeding vessels is the treatment of choice.
Management of recurrence and its prevention[5]

For gastric ulcer with H. pylori infection, NICE recommends eradication therapy followed by proof of eradication and repeat endoscopy. This is a consensus statement. If eradication is successful but the ulcer unhealed then malignancy needs to be considered.

Serology tests are applicable only for initial diagnosis, as they remain positive for a long while.

If patients are to be given long-term NSAIDs, a review from Hong Kong suggested that stratification of risk should be used to decide the plan for prevention, and that any patient who has had a peptic ulcer bleed (PUB) or who is put on long-term NSAIDs should be checked for H. pylori infection.[22]

For patients who have relapses, intermittent therapy and annual review are recommended.

Monitoring

Patients should be reviewed at the end of a course of treatment, especially H. pylorieradication, to confirm a satisfactory outcome.

Repeat endoscopy may be required for:[5]
Failure to eradicate symptoms in a duodenal ulcer.

Failure to have eradicated H. pylori.

Follow-up of a gastric ulcer - this requires repeat endoscopy to confirm healing at 6 to 8 weeks along with confirmation of eradication of H. pylori.

NSAID-induced ulcers - these should be treated according to whether they are gastric or duodenal.

If a gastric ulcer persists, referral to secondary care is required. If it is healed but symptoms persist, a course of acid suppression for a limited duration may be in order but, if symptoms persist, referral is necessary.

Effectiveness of interventions[5]

The NICE guidelines give the following data on the effectiveness of interventions based on a number of sources:

In duodenal ulcer, acid suppression for 4 to 8 weeks produces healing of the ulcer in 69%. This rises by an extra 5.4% with eradication therapy too. Number needed to treat (NNT) = 18.

In duodenal ulcer, relapse at 3 to 12 months after treatment is 39% after short-term acid suppression alone but eradication increases this by 52% to 91%. NNT = 2.

In gastric ulcer, supplementation of acid suppression with eradication therapy does not improve healing rates but it does reduce

relapse so that 3 to 12 months later 45% are free of ulcers after just acid suppression but eradication raises this by 32% to 77%. NNT = 3.

In patients taking NSAIDs, eradication did not improve the ulcer healing rate but it did halve the number of endoscopically proven ulcers six months later from 18% to 9%.

Complications[23]

Haematemesis or melaena are associated with erosion of a large blood vessel and significant haemorrhage. Urgent admission to hospital is required. In patients whose ulcers have bled, eradication of H pylori is more effective than even long-term acid suppression without eradication.[24]

Perforation of a peptic ulcer causes an acute abdomen with epigastric pain that may progress to generalised rigidity. In the presence of steroids the symptoms of perforation may be suppressed or absent.

Scarring of the duodenum may lead to pyloric stenosis with vomiting and weight loss but this is rare these days with effective treatment. The classical feature is that the vomit shows food such as tomato skins that were eaten 12 to 24 hours ago.

Adverse reactions to PPIs and H2-receptor antagonists are usually rare and mild but severe problems can arise. Rare but not serious problems may include taste disturbance, peripheral oedema, photosensitivity, fever, arthralgia, myalgia and sweating. Serious problems include liver dysfunction, hypersensitivity reactions (including urticaria, angio-oedema, bronchospasm, anaphylaxis), depression, interstitial nephritis, blood disorders (including leukopenia, leukocytosis, pancytopenia, thrombocytopenia) and skin reactions (including Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous eruption).

Misoprostol often causes diarrhoea and abdominal pain, especially at higher doses.

Prognosis[13]

Prognosis is excellent if the underlying cause such as H. pylori infection or drugs can be addressed.

Eradication of H. pylori decreases the ulcer recurrence rate from 60-90% to 10-20%. This is still higher than previously reported and this is thought to be due to an increase in NSAID-related ulcers. The mortality rate is 1 in 100,000, a figure which has decreased modestly in the last few decades.

References

1. Chey WD, Wong BC. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. Am J Gastroenterol. Aug 2007;102(8):1808-25. [Medline].

2. Javid G, Zargar SA, U-Saif R, Khan BA, Yatoo GN, Shah AH, et al. Comparison of p.o. or i.v. proton pump inhibitors on 72-h intragastric pH in bleeding peptic ulcer. J Gastroenterol Hepatol. Jul 2009;24(7):1236-43.[Medline].

3. Lai KC, Lam SK, Chu KM, Wong BC, Hui WM, Hu WH, et al. Lansoprazole for the prevention of recurrences of ulcer complications from long-term low-dose aspirin use. N Engl J Med. Jun 27 2002;346(26):2033-8. [Medline].

4. After eradication of Helicobacter pylori in nonsteroidal anti-inflammatory drug users--a randomized trial. Aliment Pharmacol Ther. Oct 15 2003;18(8):829-36.

5. Dyspepsia and gastro oesophageal reflux disease: Investigation and management of dyspepsia - symptoms suggestive of gastro oesophageal

reflux disease - or both; NICE Clinical Lai KC, Lam SK, Chu KM, Hui WM, Kwok KF, Wong BC, et al. Lansoprazole reduces ulcer relapse Guideline (Sept 2014)

6. Vakil N; Dyspepsia, peptic ulcer, and H. pylori: a remembrance of things past. Am J Gastroenterol. 2010 Mar;105(3):572-4.

7. Cai S, Garcia Rodriguez LA, Masso-Gonzalez EL, et al; Uncomplicated peptic ulcer in the UK: trends from 1997 to 2005. Aliment Pharmacol Ther. 2009 Nov 15;30(10):1039-48. Epub 2009 Aug 26.

8. Mynatt RP, Davis GA, Romanelli F; Peptic ulcer disease: clinically relevant causes and treatments. Orthopedics. 2009 Feb;32(2):104.

9. Prabhu V, Shivani A; An overview of history, pathogenesis and treatment of perforated peptic ulcer disease with evaluation of prognostic scoring in adults. Ann Med Health Sci Res. 2014 Jan;4(1):22-9. doi: 10.4103/2141-9248.126604.

10. Niv Y; H. pylori/NSAID--negative peptic ulcer--the mucin theory. Med Hypotheses. 2010 Nov;75(5):433-5. Epub 2010 May 4.

11. Najm WI; Peptic ulcer disease. Prim Care. 2011 Sep;38(3):383-94, vii. doi: 10.1016/j.pop.2011.05.001.

12. Lu CL, Chang SS, Wang SS, et al; Silent peptic ulcer disease: frequency, factors leading to "silence," and implications regarding the pathogenesis of visceral symptoms.; Gastrointest Endosc. 2004 Jul;60(1):34-8.

13. Gururatsakul M, Holloway RH, Talley NJ, et al; Association between clinical manifestations of complicated and uncomplicated J Gastroenterol Hepatol. 2010 Jun;25(6):1162-9.

14. Peptic ulcer disease; Surgical-tutor.org.uk

15. Ricci C, Holton J, Vaira D; Diagnosis of Helicobacter pylori: invasive and non-invasive tests. Best Pract Res Clin Gastroenterol. 2007;21(2):299-313.

16. Dyspepsia - proven peptic ulcer; NICE CKS, December 2012 (UK access only)

17. Test and treat for Helicobacter pylori (HP) in Dyspepsia - Quick Reference Guide for Primary Care; Public Health England

18. Malfertheiner P, Chan FK, McColl KE; Peptic ulcer disease. Lancet. 2009 Oct 24;374(9699):1449-61. Epub 2009 Aug 13.

19. Goldstein JL, Johanson JF, Hawkey CJ, et al; Clinical trial: healing of NSAID-associated gastric ulcers in patients continuing Aliment Pharmacol Ther. 2007 Oct 15;26(8):1101-11.

20. McColl KE; Helicobacter pylori-negative nonsteroidal anti-inflammatory drug-negative ulcer. Gastroenterol Clin North Am. 2009 Jun;38(2):353-61.

21. Holster IL, Kuipers EJ; Update on the endoscopic management of peptic ulcer bleeding. Curr Gastroenterol Rep. 2011 Dec;13(6):525-31.

22. Chan FK, Graham DY; Review article: prevention of non-steroidal anti-inflammatory drug gastrointestinal complications--review and recommendations based on risk assessment. Aliment Pharmacol Ther. 2004 May 15;19(10):1051-61.

23. Hermansson M, Ekedahl A, Ranstam J, et al; Decreasing incidence of peptic ulcer complications after the introduction of the BMC Gastroenterol. 2009 Apr 20;9:25.

24. Gisbert JP, Khorrami S, Carballo F, et al; H. pylori eradication therapy vs. antisecretory non-eradication therapy (with or without long-term maintenance antisecretory therapy) for the prevention of recurrent bleeding from peptic ulcer. Cochrane Database Syst Rev. 2004;(2):CD004062.