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TLALELETSO

Managing Dyspepsia

Peptic ulcer disease is a common cause of morbidity in Botswana. Accurate identification of those patients that need endoscopy and those that should be treated for Helicobacter Pylori infection is a high priority!

INTRODUCTION

In this edition of Tlaleletso we review dyspepsia and peptic ulcer disease. Dyspepsia, the presence of chronic or recurrent upper abdominal pain or discomfort, is an incredibly common symptom that clinicians manage regularly in Botswana.

While the exact prevalence of dyspepsia in Botswana is unknown, in the USA approximately 1 in 4 individuals experience dyspeptic symptoms each year.

Peptic ulcer disease is an important and common phenomenon seen regularly in primary care settings. The incidence of peptic ulcer disease is dropping in the US, as the prevalence of H. Pylori drops (more details on page 4). However, it is still an important cause of morbidity in southern Africa, especially in urban settings (Tovey, 2005).

Continued on Page 2

Notes from the Editor….

Tlaleletso is a monthly publication produced by the Botswana UPenn Partnership, in response to your expressed need for accessible, digestible clinical information.

In this issue, we focus on dyspepsia and peptic ulcer disease. We review the role of Helicobacter Pylori infection in the pathogenesis of peptic ulcer disease and the strategies to treat it.

DID YOU KNOW?

The role that Helicobacter Pylori plays in the pathogenesis of peptic ulcer disease was discovered by an Australian doctor, Barry Marshall in 1984, who drank a petri dish of the bacteria and a week later developed terrible gastritis!

DYSPEPSIA

Dyspepsia is a chronic relapsing condition, with up to 80% of patients still reporting symptoms 2 years after diagnosis. Of note, the majority of those seeking medical advice will have no evident abnormality when endoscopy is performed. These individuals are labeled as having 'functional dyspepsia' or non-ulcerative dyspepsia. Even patients who are found to have minor erosions at endoscopy often have functional disease.

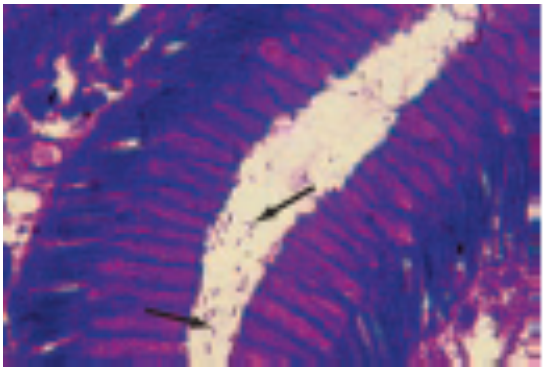
PATHOPHYSIOLOGY

There are many hypotheses as to the pathophysiology of functional dyspepsia. 40% of patients with functional dyspepsia have delayed gastric emptying, but symptoms alone are a poor predictor of which patients will have this dysfunction.

Other factors such as psychological distress and infections have been associated with functional dyspepsia but not confirmed. The role of Helicobacter pylori infection in the pathogenesis of functional dyspepsia is unclear, as the prevalence of infection ranges from 39-87% in this group (Corely, 2006).

CLINICAL APPROACH

Given that diagnostic resources are limited in Botswana, it is important to determine which patients are most likely to benefit from endoscopy (continued on page 3).



Organisms shown on the gastric mucosa (Courtesy of Kumar and Clarke)

ALARM SYMPTOMS

Consider further investigations in any patients with dyspepsia plus any of:

- Unintentional weight loss,
- Hematemesis
- Progressively worsening dysphagia

DIETARY ADVICE FOR PATIENTS

Although certain foods, beverages, and spices cause dyspepsia, there are no convincing data that such specific foods cause, perpetuate, or reactivate peptic ulcers. There are, however, some data that some dietary factors may influence peptic ulcer pathogenesis.

Chili: one study found that lower consumption of chili peppers was associated with increased risk of duodenal ulcers (Kang, 1995), prompting a hypothesis that chili may protect against ulcers!

Coffee: this is a strong stimulant of acid secretion and produces dyspepsia. Caffeine is not the only variable, since decaffeinated coffee is associated with similar symptoms

Milk: milk used to be a treatment for dyspepsia because of its soothing nature. Unfortunately studies have shown that milk actually leads to increased acid production! While it may benefit some patients, it should not be encouraged as part of treatment for most patients.

DYSPEPSIA (continued)

CLINICAL APPROACH

All HIV-infected negative patients that have alarm symptoms, such as **unintentional weight loss, hematemesis, progressively worsening dysphagia** warrant an endoscopy.

Although presence of such symptoms are not reliably predictive of cancer, the absence strongly suggest that the patient does not have cancer (negative predictive value >97%). In those patients that do not have these alarm symptoms, there are two reasonable approaches for managing dyspeptic symptoms:

1. Empiric suppression
2. Helicobacter test and treat

EMPIRIC SUPPRESSION

This is the most appropriate strategy in most settings, producing rapid results. It is also the cheapest option per patient treated!

There are several drugs that can be used– however, proton pump inhibitors, such as omeprazole, are generally more effective than histamine antagonists, such as ranitidine. With both drug options, relapse rates are high. Trials in the US and Europe have not shown significant difference between empiric acid suppression and H. Pylori test and treat approaches when applied to all patients presenting with dyspepsia.

DID YOU KNOW?
Getting a **Barium Swallow** test is a useful alternative test to endoscopy in patients that you are concerned may have peptic ulcer disease. While not as accurate at diagnosing ucerative disease it is much easy to order at PMH!

However, as H. Pylori eradication is more effective than acid suppression in infected individuals, the benefits of test and treat depends on the prevalence of H. Pylori in that population.

HELICOBACTER TEST & TREAT

Evidence from the United States suggests that individuals without alarm symptoms that present with dyspeptic symptoms should be tested for H. Pylori.

In that setting, those patients who test negative for H. Pylori should receive a trial of PPI therapy (e.g. Omeprazole). The test used to diagnose H. Pylori in Botswana is the H. Pylori serology test – (more on page 5 on H. Pylori testing). This test accurately detects those individuals with active infection. However, the test remains positive even after treatment. Therefore even those individuals that do not have active disease, but have previously had H. Pylori will continue to test positive.

PEPTIC ULCER DISEASE

Peptic ulcer disease is the most common structural findings at endoscopy in patients with dyspepsia, occurring in 5 to 15% of cases. Despite many attempts, no useful predictors of underlying pathology have been established based on symptoms alone (Talley, 1993). The percentage of patients with gastric and duodenal ulcers due to Helicobacter pylori is high, 90% and 70% respectively. NSAIDS, such as ibuprofen and aspirin, are the second most common cause (Arents, 2004). Other causes of dyspepsia, such as cancer, biliary pain and pancreatitis are rare.

PEPTIC ULCER DISEASE
(Continued)

HIV-INFECTED PATIENTS

In HIV-infected patients with very low CD4 counts, opportunistic infection with CMV is responsible for a significant amount of dyspeptic morbidity. CMV causes discrete esophageal ulcers, diffuse esophagitis, gastritis, gastric/duodenal ulcers, and enteritis.

Biopsy evidence of intranuclear inclusion bodies can often be detected by histopathology. In such situations the treatment is to initiate valganciclovir, available by specialist order only.

HELICOBACTER PYLORI INFECTION

H. Pylori is a slow-growing spiral Gram negative bacteria which plays a major role in the pathogenesis of peptic ulcer disease. The prevalence of H. Pylori is high in developing countries (80-90%) and much lower (20-50%) in high-income settings.

H. Pylori infection rates are highest in lower income groups. Infection is usually acquired in childhood. Although the exact route is uncertain, it may be feacal-oral or oral-oral, either by kissing or ingestion of contaminated vomit.

Once acquired, the infection persists for life unless treated. The incidence increases with age, probably due to acquisition in childhood when hygiene was poorer and not due to infection in adult life, which is probably far less than 1% in developed countries.

H. PYLORI IN AFRICA

In Africa in general the prevalence of H. Pylori infection is very high, but the incidence of H.Pylori associated morbidities is low, compared to elsewhere in the world (Tanih, 2007).

Scanning electron microscopy, showing spiral-shaped bacterium (Courtesy of Kumar and Clarke)

The prevalence of H. Pylori infection in Africa is estimated at between 61% and 100% (Holcombe, 1992). Studies have also demonstrated that by the age of 10 years >50% of children are infected, with the prevalence rising to >80% in adults (Segal, 2001). In their study of Kenyan school children, Nabwera et al (2000) observed high prevalence among subjects who were only 3-5 years, indicating that most children in the study were infected before they reached their third birthday. There is evidence of family transmission and of poor living conditions increasing the risk of infection (Aguemon, 2005).

The high prevalence of H. Pylori infection in Africa probably reflects that effective public health interventions are necessary. Lack of good drinking water, inadequate basic hygiene, poor diet and overcrowding all seem to place a role in the high prevalence of infection in Africa (Ndip, 2004).

DID YOU KNOW?
Ulcer rates are declining rapidly for younger men and increasing for older individuals in high-income settings. Both duodenal and gastric ulcers are common in the elderly.

H. PYLORI DIAGNOSIS

NON-INVASIVE TESTS

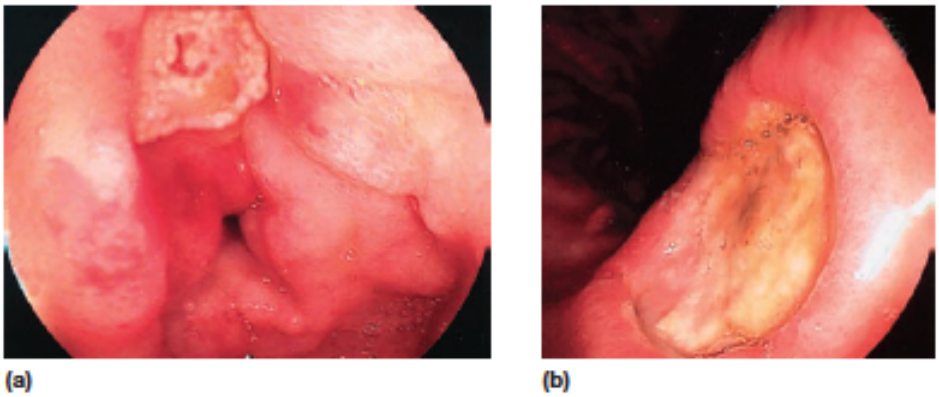
Serological methods: H. Pylori IgG antibodies are quite sensitive (90%). This means that they accurately detect those individuals with H.Pylori infection. They are also reasonably specific (83%). This means they are quite accurate at identifying those individuals that do not have H.Pylori infection. However, levels of antibodies may take up to 1 year to fall by 50% after eradication therapy and therefore are not useful for confirming eradication or the presence of current infection.

C13-Urea breath test: This is a quick and reliable test for H. Pylori. The test is very sensitive (97%) and specific (96%). The test is not currently available in Botswana.

Stool antigen test: A specific immunoassay using monoclonal antibodies for the qualitative detection of H. Pylori is available in many countries. The overall sensitivity is 97% and the specificity is 96%. In the US and the UK, stool antigen levels are used to determine if eradication has worked.

INVASIVE TESTS

There are several techniques employed to confirm H. Pylori infection, in those patients that undergo endoscopy. Culture and histology can both be used to isolate the bacterium. A biopsy urease test can also be performed, although is not routinely done in Botswana.



Endoscopic views. (a) Duodenal ulcer with inflamed duodenal folds, (b) Benign gastric ulcer. (Courtesy of Kumar and Clarke)

Upcoming Lectures

April
Managing Dyspepsia

May
TB infection control

June
Chronic lung disease

July
Updates in PMTC

Got a clinical question about a complicated medical patient or a patient with HIV?

Mike Reid
267 724 78 777
OR
Miriam Haverkamp
267 76516520

H. PYORI ERADICATION

Eradication therapy is recommended for all individuals with peptic ulcer disease and/dyspeptic symptoms with confirmed evidence of H. Pylori infection. Eradication therapy significantly reduces mortality and morbidity related to peptic ulcer disease and reduces the risk of adenocarcinoma and MALT lymphoma, both of which can arise in the setting of chronic H. Pylori infection. Standard eradication therapies are successful in approximately 90% of patients (Kwon, 2001). Single-agent therapy should not be used because of the unacceptably low frequency of eradication.

Reinfection after treatment for H. Pylori is uncommon in developed countries (1%). However, in southern Africa reinfection may be more common, in part because treatment compliance is poor and antibiotic resistance is high (>50%), so failure of eradication is very common.

There are multiple different eradication regimens that have been used to treat H. Pylori infection. In general, these comprise two antibiotics, given with powerful acid suppression in the form of a proton pump inhibitor, all taken for at least 7 days. In adults, the current standard (Maastricht) triple therapy is a combination with a proton pump inhibitor, amoxicillin and clarithromycin.

In Botswana the most commonly used eradication regimen consists of amoxicillin/metronidazole/omeprazole. Given that there are high levels of H. Pylori resistance across southern Africa, a pragmatic approach to those patients who *may* have failed this first line regimen is to repeat treatment with amoxicillin and tetracycline or amoxicillin and erythromycin (Tanih, 2009). Better stewardship of antibiotics more generally (in the treatment of respiratory and gynecological infections, for example), may lead to reductions in H.Pylori antibiotic resistance.

H2 receptor antagonists, such as ranitidine, can be used instead of omeprazole, although they are not as effective. Prolonged therapy with a PPI after a course of PPI-based 7-day triple therapy is not necessary for ulcer healing in most patients.

SUMMARY

Most young patients with dyspepsia have functional or non-ulcerative dyspepsia. However, patients with alarm symptoms and those >55 years of age may warrant endoscopy. Functional dyspepsia is a chronic condition with a high relapse rate.

Testing and treating for H. Pylori is recommended as an initial strategy for most patients with dyspepsia. However, the serology test used in Botswana to detect H. Pylori remains positive after initial infection. Therefore serology is not a useful test of cure or for assessing if a patient has been re-infected after having been treated for H. Pylori in the past.

BOTSWANA-UPENN PARTNERSHIP

NEED CPD?

Botswana's Health Professional Council will soon require all doctors to maintain a minimum number of continuing professional development points/credits.

You will be able to collect these by attending Botswana UPenn Partnership lectures. You can also collect credits by undertaking online courses and lectures. Below are some online CPD resources that you can use towards BHPC requirements:

www.clinicalcareoptions.com

www.medscape.org

http://www.mpconsulting.co.za

http://www.samedical.org/public-lecture.html