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## **PEPTIC ULCER TREATMENT AND H. PYLORI**

### **SUMMARY:**

- While the majority of peptic ulcers can be healed with either cimetidine or ranitidine relapse of symptoms is likely within one year.
- Management of peptic ulcer disease is moving towards eliminating H. pylori infection rather than continuous acid suppression as recurrent peptic ulcer disease can be prevented by its eradication (1, 2, 3). The need for continuous acid suppression therapy must now be reviewed.
- "Classic" triple therapy consisting of bismuth, metronidazole and amoxycillin or tetracycline is a widely evaluated regimen for the eradication of H. pylori.
- Newer therapies with proton pump inhibitors in dual and triple regimens look promising.

### **INTRODUCTION:**

Peptic ulcer disease (PUD) is reported to affect 5 to 10% of the population but this is an underestimate as it may be asymptomatic. The association between PUD and H.pylori has provided a new approach to the treatment of peptic ulcer. Guidelines now recommend eradication of H.pylori in the management of ulcer patients with H. pylori infection (4).

### **H. PYLORI AND PEPTIC ULCER DISEASE:**

H. pylori is a Gram negative, spiral, flagellate bacillus found under the mucus layer of the stomach mucosa. Its exact mode of transmission is unclear but is thought to be via the faeco-oral or oral-oral route (5, 6) and infection is common particularly in the elderly and lower socio-economic groups.

Ulcer healing follows H. pylori eradication (7) with a marked reduction in the rate of ulcer relapse compared to conventional therapies (8, 9, 10). Approximately 90% of patients with duodenal ulcer are infected with H. pylori (6) and peptic ulcer is more likely to develop in patients with gastritis who are H. pylori positive (11). H. pylori is diagnosed by endoscopy using histological and biochemical (CLO test) techniques. Non-invasive methods including serological and urea breath tests permit diagnosis without endoscopy but more than one test may be necessary.

## **ACID SUPPRESSION OR H.PYLORI ERADICATION - THE CHOICE**

While the majority of peptic ulcers can be healed with H<sub>2</sub> antagonists or proton pump inhibitors alone, relapse of symptoms occur in up to 80% of patients within one year compared to 8% (9) if treated with H. pylori eradication therapy. The search for the ideal regimen continues and a number of options are available.

- "Classic" triple therapy consisting of bismuth chelate 120mg four times daily, metronidazole 400mg three times daily and amoxycillin or tetracycline 500mg four times daily is one of the most widely studied regimens. Treatment for two weeks has been recommended (12) but shorter regimens have been prescribed (13). This can be taken after healing has been achieved or can be used to heal in which case bismuth should be used for a further two weeks. This eradicates H. pylori in approximately 80% of patients (12, 14). However it may be associated with adverse effects (see next page).
- Dual therapy consists of omeprazole 20mg twice daily and amoxycillin 1g twice daily for two weeks. It is easier to administer than triple therapy but its efficacy is less well established. Variable eradication rates of up to 80% have been found with this regimen but one large study shows an eradication rate of only 54% (15). Clarithromycin 500mg three times daily is a useful alternative in patients known to be allergic to amoxycillin. Clarithromycin has also been combined with omeprazole and metronidazole (16) but more data is awaited on this regimen. Conflicting claims regarding dual (15, 17), triple (7, 18) and quadruple therapy (19) exist. Until well designed clinical trials show a significant superiority in efficacy the "classic" triple therapy or dual therapy is recommended for H. pylori eradication.
- Conventional acid suppression therapy which includes cimetidine (Tagamet) 400mg twice daily, ranitidine (Zantac) 150 mg twice daily, omeprazole (Losec) 20mg daily or lansoprazole (Zoton) 30mg daily for four to eight weeks will heal most peptic ulcers. All four compounds are effective but are usually followed by ulcer relapse. These regimens are most likely to be superseded by H. pylori eradication therapy, except in the treatment of H. pylori-negative peptic ulcer, where non-steroidal anti-inflammatory drugs (NSAID's) are often an associated factor.
- Long term acid suppression therapy is common and a significant number of patients are prescribed continuous medication without a definitive diagnosis (20). The case for continuous acid suppression in PUD is weakened by the key role of H. pylori in its pathogenesis leading to a re-evaluation of this prescribing practice.

## **WHEN TO PRESCRIBE H. PYLORI ERADICATION THERAPY**

- All patients with confirmed peptic ulcer who are H. pylori positive. Failure to respond requires further investigation before an alternative regimen is commenced.
- Eradication therapy is not yet recommended for non-ulcer dyspepsia (4).
- If eradication is not possible the patient should be treated with maintenance H<sub>2</sub> antagonists (21) under supervision.

## **PRACTICAL PROBLEMS WITH H. PYLORI ERADICATION.**

A positive diagnosis of *H. pylori* currently involves referral to a specialist for assessment. Endoscopy with biopsy, urea breath tests and serology tests are available but the need to screen all patients with dyspeptic symptoms is daunting and not all hospitals offer these tests (22). A simple finger prick test may shortly be available for general practice use.

Adverse effects to "classic" triple therapy were found in over 50% of patients (23) which together with the complex dosage regimen may lead to poor compliance and the development of resistance to antibiotics. Bismuth and metronidazole share the common side effects of nausea, vomiting and unpleasant taste. Bismuth can cause darkening of the tongue and stools and should be used with caution in renal disease. In addition to causing gastrointestinal symptoms amoxycillin and tetracycline may rarely precipitate pseudomembranous colitis (24). The absorption of tetracycline may be reduced by bismuth if taken concurrently.

Dual therapy is associated with adverse effects in less than 4% of patients (15) and omeprazole generally presents a spectrum of mild reactions. The prescriber should consult the drug data sheet for a full description of adverse effects.

## **IMPORTANT DRUG INTERACTIONS**

- Cimetidine may reduce the elimination of warfarin, phenytoin and theophylline leading to toxicity. Where H<sub>2</sub> antagonists are prescribed, ranitidine is the preferred choice of therapy in these circumstances.
- Omeprazole and lansoprazole may alter the elimination of phenytoin and warfarin and it is advised to monitor patients on these medications.
- Clarithromycin may lead to an increase in the blood levels of theophylline, warfarin, digoxin, terfenadine and potentiate the effects of carbamazepine.
- The effectiveness of the oral contraceptive pill may be reduced by tetracycline, metronidazole, amoxycillin and lansoprazole.
- Metronidazole when taken with alcohol may induce nausea, vomiting, headaches, flushing and high blood pressure. Care should be taken when prescribing lithium or warfarin.

## **PEPTIC ULCER TREATMENT AND H. PYLORI ERADICATION IN PREGNANCY**

Generally *H. pylori* eradication therapy is not recommended during pregnancy as the bismuth component is contraindicated, while insufficient data on its safety precludes the use of omeprazole. The routine use of cimetidine and ranitidine cannot be recommended.

Non-absorbable antacids like aluminium hydroxide/magnesium hydroxide (Maalox) or magaldrate (Dynese) are quite safe in the second and third trimester but safety in the first trimester is not fully established. The reflux suppressant containing alginate (Gaviscon) is regarded as safe in all stages of pregnancy (24).

## **CONCLUSION**

This topic is rapidly evolving at present and will need to be reviewed in the near future. The role of *H. pylori* eradication in patients with non-ulcer dyspepsia and in the prevention of gastric carcinoma awaits clarification.

## COSTS

- Preparations for treating peptic ulcer disease account for over 10% of the total GMS spend on medicines in 1994.
- Over 700,000 prescriptions were prescribed for this condition at a cost of almost £12 million.

### **COST OF PEPTIC ULCER TREATMENT** **Drug costs are based on data from GMS 1995**



\* "Classic" triple therapy for eradication of *H. pylori* consists of bismuth (De-Nol) for 14 days with metronidazole and amoxicillin/tetracycline for 14 days. De-Nol is prescribed for a further 14 days if ulcer healing is required.

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