PHARM 362 - Advanced Patient Self-Care Winter 2012

Evidence-Based Self-Care Resource (EBSCR) Assignment

Magnesium-Aluminum Antacid – Extended Abstract

I) Graham DY & Patterson DJ. Double-blind comparison of liquid antacid and placebo in the treatment of symptomatic reflux esophagitis. Dig Dis Sci. 1983 Jun;28(6):559-63.

• Study Objectives

To determine the effectiveness of antacids in relieving symptoms of gastroesophageal reflux disease, compared to placebo.

• Methods

- **Design**

Double blind, placebo-controlled trial lasting 5 weeks. Patients recorded symptoms, antacid consumption, frequency and severity of heartburn exacerbations in personal diaries.

- **Allocation**

Patients stratified according to severity of heartburn and severity of endoscopic findings.

- **Blinding**

Double-blinded.

- **Follow-up period**

5 week study with patients seen weekly for symptomatic evaluation.

- **Setting**

Gastrointestinal clinics in Houston

- **Participants**

32 patients with chronic heartburn who were referred to GI clinics. Symptomatic gastroesophageal reflux was confirmed with both a Bernstein (acid perfusion) test and an intraesophageal pH probe. Those with peptic ulcer disease were excluded.

- **Intervention**

15 mL of Maalox Therapeutic Concentration (magnesium hydroxide and aluminum hydroxide with 5.33 mEq neutralizing capacity per mL) taken 7 times daily (1 and 3 hours post prandial as well as at bedtime). This intervention was compared with identical placebo, taken at the same frequency. Additional doses of each could be taken on an as-needed basis for breakthrough heartburn symptoms.

- **Outcomes**

Heartburn frequency and severity score (each ranging from 0 to 4) based on self-reported data.

- **Patient follow-up**

Patient kept ongoing progress notes with the personal diaries. Researchers followed-up weekly.

- **Main results**

Both treatment arms showed decreased heartburn frequency and reduced heartburn severity scores. There was no significant difference between the two groups.

- **Conclusions**

There is no compelling evidence that antacids are any more effective than placebo at decreasing the frequency of heartburn events or reducing the severity of heartburn symptoms.

- **Comments/critical appraisal (including assessment of internal and external validity)**

Trial was published in 1983 and is quite dated by today's standards of randomized controlled trials. Unfortunately, in terms of aluminum/magnesium antacid, finding any quality of trial is difficult.

The authors used an approach by where an initial placebo treatment containing a very small amount of antacid product was given to all patients. Any responders that achieved a remission of heartburn symptoms by the first week were promptly removed from the trial. The authors claim this was to done to more accurately display the differences between the two groups, however, with a trial of only 32 people, when approximately one third of the participants are removed it is difficult not to imagine the results becoming skewed in some way.

II) **Weberg R & Berstad A. Symptomatic Effect of a Low-Dose Antacid Regimen in Reflux Oesophagitis. Scand J Gastroenterol. 1989 May;24(4):401-6.**

• **Study objectives**

To examine the symptomatic effect of antacids in reflux esophagitis.

• **Methods**

- **Design**

Randomized, crossover, double-blind trial.

- **Allocation**

Patients randomly allocated to each treatment arm. After 2 weeks of treatment, arms were switched therapies.

- **Blinding**

Double-blinded.

- **Follow-up period**

Symptomatic assessments, side effects and compliance were evaluated at the beginning of the study as well as after 2 and 4 weeks.

- **Setting**

Outpatient GI clinic in a hospital in Norway.

- **Participants**

Men and women over 18 with endoscopically verified esophagitis grade 1-3. All had chronic or recurrent symptoms of reflux esophagitis for at least 1 month (heartburn, acid regurgitation and/or dysphagia. Patients with malignancy, peptic ulcer disease, previous GI surgery or those receiving regular treatment with heartburn medications (H2-receptor antagonists, antacids) or GI irritating medications (aspirin, NSAIDs). Pregnant and lactating women were excluded. 50 patients were included in the study and all but three were used.

- **Intervention**

Chewable Link antacid tablet (containing aluminum hydroxide and magnesium carbonate, an acid-neutralizing capacity of 30 mmol/tab) compared to identical placebo. Both were given 1 hour after breakfast, lunch and supper, as well as a bedtime dose. After 2 weeks of treatment, patients were switched to alternative treatment for 2 weeks. There was no wash-out interval between therapies. Link antacid tablets were provided for as-needed relief.

- **Outcomes**

Symptom assessment (heartburn, acid regurgitation and dysphagia) were recorded as well as a global symptomatic score.

- **Main results**

Global symptomatic score was reduced by both treatments during period 1. However, during period 2, only the switch from placebo to antacid yielded further improvement in score. Overall, the score was reduced in 78.7% of patients during antacid therapy and 55.3% of patients during placebo therapy.

When disregarding treatment sequence, antacid therapy caused a significant reduction in the acid regurgitation symptom when compared to placebo. Heartburn and dysphagia was not shown to be of significant difference. Upon therapy switch, patients who switched from placebo to antacid had a significantly greater reduction in symptoms of heartburn and acid regurgitation than those switching from antacid to placebo.

- **Conclusions**

Antacids are more effective than placebo at reducing symptoms of gastroesophageal reflux disease, most notably acid regurgitation.

- **Comments/critical appraisal (including assessment of internal and external validity)**

87% of the patients had tried antacids before, meaning technically the patient population selected had already experienced treatment failure with antacids in the past.

Washout period should have been implemented to minimize the effect of initial antacid therapy on the switch to placebo.

Very small study done entirely in Norway. A multi-centered trial would have been more applicable to various populations.

II) <u>Kitchin L & Castell D. Rationale and Efficacy of Conservative Therapy for Gastroesophageal Reflux Disease</u>

- **Study objectives**

To examine the effectiveness of simple interventions such as lifestyle modifications, alginate and antacid in the management of gastroesophageal reflux disease.

- **Scope - describe the scope of included studies (ex. patients, interventions, outcomes, duration, etc.)**

Wide-range of patients because of small size of studies. Interventions involved antacid or alginate or combination for several weeks of treatment.

- **Methods – describe how studies were identified, number and type of trials included, and any other relevant information regarding the methods**

All blinded randomized placebo-controlled trials involving antacids and/or alginate up to the date of publication of the review were included.

- **Main results**

Two trials showed superiority of magnesium/aluminum antacid therapy over placebo while one trial showed no significant difference. Several studies have shown benefit with combination alginate/antacid.

- **Conclusions**

While efficacy data is scarce and any available trials are small and of short duration, the simplicity and low-cost attributes of antacid therapy justifies their use, especially in young, otherwise healthy patients who are disinterested in lifetime acid-suppressive therapy.

- **Comments/critical appraisal (including assessment of internal and external validity)**

Very few, poor quality studies. Many of the studies included combinations with alginate which makes it difficult to draw firm conclusions regarding antacid only usage.

III) DeVault K & Castell D. Updated Guidelines for the Diagnosis and Treatment of Gastroesophageal Reflux Disease. American Journal of Gastroenterology. 2005: 190-200.

• Study objectives

Provide up-to-date guidelines for the management of GERD.

• Scope - describe the scope of included studies (ex. patients, interventions, outcomes, duration, etc.)

Articles reviewed using National Library of Medicine database. When studies were lacking, expert opinion was used from sources including primary literature, author's experience and advice from the Practice Parameters Committee.

• Main results

Antacids are effective for relieving symptoms of heartburn and acid regurgitation. Specifically, antacids are more effective than placebo at treating symptoms induced by a heartburn promoting meal. An estimated 20% of GERD patients experience symptom relief with antacids and other OTC agents.

Limited comparisons between antacids and H2-receptor antagonists. Both have a similar onset of action (less than 30 minutes) but antacids have a significantly shorter duration.

• Conclusions

Antacids are a reasonable first choice in patients with mild GERD symptoms when taken appropriately after meals and before bed. Persistent symptoms may require a change in therapy.

• Comments/critical appraisal (including assessment of internal and external validity)

The trial evidence for antacids is still very weak and recommendations stating definitive benefits of antacids may be unfounded.

The level of evidence for the antacid recommendations was IV (evidence taken mostly from well-designed non-experimental studies and expert opinion).

IV) Armstrong, D., Marshall, J.K., Chiba, N., Enns, R., Fallone, C.A., Fass, R., et al. (2005, January). Canadian consensus conference on the management of gastroesophageal reflux disease in adults: Update 2004. Canadian Journal of Gastroenterology 19(1), 15-35.

• Study objectives

Provide guidelines for the management of GERD from a Canadian perspective.

• Scope - describe the scope of included studies (ex. patients, interventions, outcomes, duration, etc.)

The same studies as used in other guidelines were also considered for the Canadian conference. Limited patient sample, usually a single centre, short duration.

• Methods – describe how studies were identified, how recommendations were graded, and any other relevant information regarding the methods

The Delphi approach was used by a multidisciplinary team of 23 members to develop recommendations. The quality of evidence, strength of recommendation and consensus level was than assessed and the recommendations revised.

• Main results

Over the counter medications such as antacids are appropriate initial therapies for the management of mild GERD symptoms that occur less frequently than 3 times per week.

• Conclusions

Antacids are reasonable as an initial therapy in mild, infrequent GERD symptoms.

• Comments/critical appraisal (including assessment of internal and external validity)

The trials used to establish the efficacy of antacids were of poor quality. Much of the power of the recommendation comes from expert opinion.

V) Gasteroesophageal Reflux Disease. Medscape Reference. Medscape. 2011.

• Source description – describe type of resource, referencing, peer review, date of last update, and any other relevant information regarding the source

Medscape Reference was used to gather information. The authors include many high-ranking physicians specializing in disorders of the GI tract. The article was last updated August 19, 2011. Utilized a wide range of references including RCTs, guideline recommendations, meta-analyses and reviews.

• Summary – describe the author's recommendations for the therapeutic agent

Antacids are effective for the initial treatment of mild GERD symptoms. To maximize symptom control, antacids should be taken after each meal and at bedtime.

• Comments/critical appraisal (including assessment of internal and external validity)

Does not include recommendations of how long is 'initial' therapy and at which point it is appropriate to step up therapy.

Balances out guidelines from several areas of the world to validate antacid use in the general public.