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CME/CE Information

CME/CE Released: 12/21/2010; Valid for credit through 12/21/2011

Target Audience

This article is intended for primary care clinicians, gastroenterologists, and other specialists who care for patients using acid-suppression drugs.

Goal

The goal of this activity is to provide medical news to primary care clinicians and other healthcare professionals in order to enhance patient care.

Learning Objectives

Upon completion of this activity, participants will be able to:

1. Describe the association between the use of acid-suppression drugs and community-acquired pneumonia.
2. Describe the association between the use of acid-suppression drugs and hospital-acquired pneumonia.

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Developed and funded by

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From Medscape Education Clinical Briefs **Acid-Suppressive Drugs Linked to Increased Risk for Pneumonia** CME/CE

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CME/CE Released: 12/21/2010; Valid for credit through 12/21/2011

December 21, 2010 — Use of acid-suppressive drugs is linked to increased risk for pneumonia, according to the results of a systematic review and meta-analysis reported online December 20 in the *Canadian Medical Association Journal*.

"Several previous studies have shown that treatment with acid-suppressive drugs might be associated with an increased risk of respiratory tract infections and community-acquired pneumonia in adults and children," write Chun-Sick Eom, MD, from Seoul National University Hospital in Korea, and colleagues.

"However, the association between use of acid-suppressive drugs and risk of pneumonia has been inconsistent. Given the widespread use of proton pump inhibitors and histamine₂-receptor antagonists, clarifying the potential impact of acid-suppressive therapy on the risk of pneumonia is of great importance to public health."

Two evaluators independently extracted data from studies identified through a search of MEDLINE (PubMed), Embase, and the Cochrane Library from inception to August 28, 2009. Pooled estimates of effect were calculated through random effects meta-analysis to account for heterogeneity. Of 31 studies identified, 5 were case-control studies, 3 were cohort studies, and 23 were randomized controlled trials.

Overall risk for pneumonia was higher in persons taking proton pump inhibitors (adjusted odds ratio, 1.27; 95% confidence interval [CI], 1.11 - 1.46; Higgins I^2 value, 90.5%) and in those taking histamine-2 receptor antagonists (adjusted odds ratio, 1.22; 95% CI, 1.09 - 1.36; Higgins I^2 value, 0.0%), based on a meta-analysis of the 8 observational studies. Use of histamine-2 receptor antagonists was also associated with an increased risk for hospital-acquired pneumonia (relative risk, 1.22; 95% CI, 1.01 - 1.48; Higgins I^2 value, 30.6%), based on a meta-analysis of the randomized controlled trials.

"Use of a proton pump inhibitor or histamine-2 receptor antagonist may be associated with an increased risk of both community- and hospital-acquired pneumonia," the study authors write. "Given these potential adverse effects, clinicians should use caution in prescribing acid-suppressive drugs for patients at risk."

Limitations of this study include selection of only English-language publication observational studies, possible confounding by the presence of gastroesophageal reflux disease, and heterogeneity in study characteristics.

These findings suggest that 1 of every 200 inpatients treated with acid-suppressive drugs will develop pneumonia, which is even more clinically meaningful given that 40% to 70% of hospitalized patients receive these medications.

"Clinicians should carefully consider any decision to prescribe acid-suppressive drugs, especially for patients who are already at risk for pneumonia," the study authors conclude. "Since it is unnecessary to achieve an achlorhydric state in order to resolve symptoms, we recommend using the optimal effective dose of the drug necessary to achieve desired therapeutic goals."

The Basic Science Research Program of the National Research Foundation of Korea, which is funded by the Ministry of Education, Science, and Technology of the Korean government, supported this study. The study authors have disclosed no relevant financial relationships.

CMAJ. Published online December 20, 2010.

The American College of Gastroenterology's [Guidelines for the Diagnosis and Treatment of Gastroesophageal Reflux Disorder](#) are available online.

Clinical Context

Potent acid-suppression drugs, including proton pump inhibitors and histamine-2 receptor antagonists, can increase gastric pH and allow bacteria colonization. Treatment may increase the risk for respiratory tract infections, but no studies have examined pneumonia as a primary outcome of acid-suppression treatment.

This is a meta-analysis and systematic review of the literature to examine the association between use of acid-suppression drugs and risk for pneumonia.

Study Highlights

- Included were observational studies and randomized controlled trials on acid-suppression drug use that included pneumonia as an outcome.
- The databases that were searched included MEDLINE, Embase, and the Cochrane Central Register for Controlled Trials.
- Studies that were included were case-control, observational, and randomized controlled studies that reported on proton pump inhibitors and histamine-2 receptor antagonists separately.
- The Jadad score was used to assess the quality of studies, with a maximum score of 5 and high quality defined as a score of 3 or higher.
- A total of 23 articles met criteria; these included 5 case-control studies, 3 cohort studies, and 23 randomized controlled trials.
- The mean quality scores were 8.4 for the observational studies and 3.1 for the randomized controlled trials.
- 26 articles, including the 23 randomized controlled trials, reported hospital-based studies.
- Of the observational studies, 5 evaluated the association between use of acid-suppression drugs and risk for community-acquired pneumonia, and 3 evaluated the use of these drugs and hospital-acquired pneumonia.
- There were significant positive associations between use of proton pump inhibitors and risk for pneumonia overall (adjusted odds ratio, 1.27).
- There was also a significant association between use of histamine-2 receptor antagonists and risk for pneumonia (adjusted odds ratio, 1.22).
- Meta-analysis of the randomized trials examining risk for hospital-acquired pneumonia in association with use of histamine-2 receptor antagonists confirmed the findings of the observational studies (relative risk, 1.22).
- There was a significant positive association between use of proton pump inhibitors and community-acquired pneumonia (adjusted odds ratio, 1.34), and a significant positive association between use of histamine-2 receptor antagonists and hospital-acquired pneumonia (adjusted odds ratio, 1.24).
- Subgroup analysis indicated a dose-response relationship.
- A higher dose of proton pump inhibitors was more strongly associated with risk for pneumonia (adjusted odds ratio, 1.52) than the usual dose (adjusted odds ratio, 1.37).
- Subgroup analyses by duration of exposure showed that the strength of the association between proton pump inhibitors and pneumonia decreased with longer duration of therapy before the index date.
- There were positive associations between proton pump inhibitor use and risk for pneumonia within 7 days (adjusted odds ratio, 3.95) and from 30 to 180 days before the index date (adjusted odds ratio, 1.36).

- The risk for pneumonia was greater with the use of histamine-2 receptor antagonists within 7 days before the index date (adjusted odds ratio, 5.21).
- The risk also was greater with use of these drugs within 30 days of the index date (adjusted odds ratio, 1.49) and from 30 to 180 days (adjusted odds ratio, 1.21).
- Subgroup analysis of the randomized controlled trials by comparators showed a significant positive association between use of histamine-2 receptor antagonists and risk for pneumonia in studies that used sucralfate as a control (relative risk, 1.33).
- 24 to 25 cases of pneumonia can be expected for every 1000 recipients of acid-suppression drugs.
- This translates to 1 case of pneumonia for every 200 inpatients treated with acid-suppressive drugs.
- The authors concluded that use of acid-suppression drugs was associated with both community-acquired and hospital-acquired pneumonia, and that the risk was highest within the first week of use.

Clinical Implications

- Use of proton pump inhibitors is associated with increased risk for community-acquired pneumonia.
- One case of pneumonia can occur for every 200 patients treated with acid-suppressive drugs.

CME Test

A community-based patient was prescribed a proton pump inhibitor for acid suppression. Which of the following *best* describes his risk for community-acquired pneumonia?

- Not increased
- Increased by 10%
- Increased by 23%
- Increased by 34%

Which of the following *best* describes the number of cases of pneumonia expected for every 1000 recipients of acid-suppression drugs?

- 15
- 25
- 50
- 100

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