

# Respiratory Infections Tied to PPIs

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MONTREAL — The association of proton pump inhibitors with an increased risk of severe respiratory infections is dramatically pronounced in the first 2 weeks of drug therapy, according to a new study.

However, the reasons for this particularly high risk are not clear, Dr. Laura Targownik said at Canadian Digestive Diseases Week. "I reported the data because they are very dramatic, but the question remains, is it a protopathic effect?" she said in an interview, describing the possibility that patients' early symptoms of pneumonia might mimic gastroesophageal reflux and prompt a prescription for a proton pump inhibitor (PPI). "Then they go on to develop obvious pneumonia, but the PPI actually played no

**The use of PPIs was associated with an increased risk of severe respiratory infection or pneumonia, especially in the first 2 weeks of therapy.**

role in it," said Dr. Targownik of the University of Manitoba, Winnipeg.

Recent studies have described the increased risk of infections such as community-acquired pneumonia and *Clostridium difficile* associated with PPI use, she explained. While the mechanism for this association is not known, the most common hypothesis suggests that PPIs' reduction of gastric acid allows gastric pathogens to flourish and, via reflux, infect either the gastrointestinal tract or the lungs.

Dr. Targownik's study analyzed 1,276 cases of severe community-acquired infections identified in the Manitoba Health Database between 1996 and 2004. All cases were matched to up to 10 controls with no history of serious infections on the index date.

For 296 cases of urinary tract infection and 289 cases of gastrointestinal infection, Dr. Targownik found no increased risk associated with PPI therapy. However, PPI use was associated with an increased risk of severe respiratory infection or pneumonia (adjusted odds ratio [AOR] 1.35), she reported. And a subanalysis of 62 patients with respiratory infection and PPI use found that the risk of respiratory infection was most pronounced within 14 days of PPI initiation, compared with cases in which PPIs were started earlier (AOR 24.5 vs. 1.12).

The findings suggest that "you may be inducing some bacterial changes that [initially] increase the risk," Dr. Targownik explained, before the body subsequently adjusts. She described her findings as "hypothesis generating," adding that further research is being done to disentangle the effect of gastroesophageal reflux in the data.

The meeting was sponsored by the Canadian Association of Gastroenterology. ■

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