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# Long-term antibiotics reduce COPD exacerbations, raise questions

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Long-term use of a macrolide antibiotic may reduce the frequency of exacerbations in patients with moderate to severe chronic obstructive pulmonary disease (COPD) by as much as 35 percent, according to a London-based study.

"Our results show a significant effect of low-dose macrolide therapy, reducing exacerbation frequency and severity with moderate to severe COPD," wrote lead author of the paper, Terence A. R. Seemungal, Ph.D., and Jadwiga Wedzicha, M.D., principle investigator.

The encouraging news comes on the heels of World COPD Day 2008 and a new report from the Centers for Disease Control and Prevention (CDC) that detailed the rising number of deaths related to COPD. More women than men now die of COPD, and while death rates for men have leveled, the rate is still increasing for women, according to the CDC.

The latest study is the first ever year-long randomized, double-blind, placebo-controlled study of the effects of erythromycin in COPD. The results were published in the first issue for December of the *American Journal of Respiratory and Critical Care Medicine*, which is published by the American Thoracic Society.

The researchers assessed and followed 109 patients with moderate to severe COPD for a year, after randomly assigning them to receive either a placebo or a twice daily 250 mg dose of erythromycin. The patients recorded their exacerbations and hospitalizations in a daily diary card,

and they were assessed using spirometry, sputum testing and blood testing for lung function, bacterial infection and markers of inflammation.

The researchers found that not only did the patients randomized to receive erythromycin have fewer exacerbations, but among the patients studied, 60 percent of the exacerbations that occurred were within the placebo group. While the number of exacerbation-related hospitalizations was small, more than twice as many occurred among the placebo group—14 versus 6. The median duration of exacerbations from onset to resolution of symptoms was 9 days in the erythromycin group and 13 days in the placebo group.

"Our results did not allow us to determine a mechanism for these findings. However based on in-vitro studies we suspect that the mechanism is likely to involve the anti-inflammatory properties of erythromycin," noted Dr. Seemungal.

While their findings are encouraging, Dr. Seemungal points out that they must be put in context with future findings. Furthermore, the threat of growing antibiotic resistance resulting from widespread prophylactic use of erythromycin is not a trivial concern. "In this scenario, substantial, widespread emergence of macrolide bacterial resistance is virtually foreordained, with attendant reduction in the antimicrobial usefulness of this drug class," wrote Ken M. Kunisaki, M.D. and Denise E. Niewoehner, M.D., of the Veterans Affairs Medical Center in Minneapolis, in the accompanying editorial. "Balancing benefit against harm could pose a dilemma for which there might be no clear answers."

Moreover, not all of the study patients were treated with guideline-recommended therapy, such as inhaled corticosteroids or inhaled long-acting bronchodilators, which have been shown to decrease exacerbation frequency. The degree of added benefit of erythromycin over and above

standard therapy will require further study.

"Observations that any intervention might decrease the frequency and severity of acute exacerbations in COPD present considerable public health implications," observed John Heffner, M.D., past president of the ATS. "Exacerbations occur about once a year among patients with moderate to severe COPD and account for more than $30 billion dollars in direct and indirect costs annually in the United States alone."

"Many patients with advanced COPD receive highly potent, extended spectrum antibiotics during acute exacerbations," commented Dr. Heffner. "The relative risks of breeding resistance with a long-term preventative use of erythromycin versus more frequent short-term dosing of highly potent antibiotics for acute exacerbations require careful analysis. If future studies demonstrate similar efficacy of prolonged erythromycin therapy, especially if patients are already receiving inhaled steroids and long-acting bronchodilators, the benefits likely will outweigh the risks."

Source: American Thoracic Society