

# ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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## Is There a Relationship Between GERD and Asthma?



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### G&H How prevalent is gastroesophageal reflux disease in asthma patients?

**JGM** Approximately 25 million Americans have asthma. How many of these individuals have gastroesophageal reflux disease (GERD) depends on how GERD is defined. The prevalence of GERD certainly appears to be higher in asthma patients than in the general population, but studies have used different definitions of GERD, making it difficult to compare their findings and compile data. The prevalence of GERD in asthma patients has ranged from 25% to 80% in studies, many of which use self-reported GERD. In a study conducted by the American Lung Association Asthma Clinical Research Centers (ACRC) Network, 38% of asthma patients had GERD (as defined by a positive pH probe).

### G&H Do all patients with asthma and GERD exhibit classic symptoms of GERD?

**JGM** There is certainly a population of asthma patients who have classic symptoms of GERD, including heartburn. Among these symptomatic GERD patients, pulmonary symptoms, notably cough, may also occur. However, a significant number of asthma patients have silent GERD (ie, GERD only detected by pH probes). In the previously mentioned ACRC study, none of the 38% of patients who had a positive pH probe had classic symptoms of GERD.

### G&H What has been the historical understanding of the relationship between GERD and asthma?

**JGM** It has long been thought that treatment of reflux in asthma patients improves their asthma. This belief

was even reflected in the last set of guidelines from the National Institutes of Health (NIH) for the treatment of asthma. These guidelines recommended that physicians consider administering an empiric trial of antireflux therapy to patients with poorly controlled asthma, even in the absence of GERD symptoms. These guidelines were based on both animal studies, where acid instilled in the esophagus resulted in airway hyperresponsiveness, and previous clinical trials that all had significant limitations such as small sample size, poorly defined asthma, poorly defined GERD, and inadequate treatment time.

### G&H What is the current understanding of the relationship between GERD and asthma?

**JGM** The answer to this question is a bit controversial. Again, it depends on how GERD is defined and if GERD is symptomatic or not. In terms of acid reflux, there appears to be 2 different groups of patients with asthma and GERD, as previously mentioned. One group has asthma and classic GERD symptoms. Some data suggest that GERD treatment in these patients improves their quality of life and may improve asthma exacerbations. In addition, GERD treatment may cause small increases in lung function that are statistically significant but of questionable clinical significance. Thus, at this time, it appears that there may be some relationship between symptomatic GERD and asthma-related quality of life and, possibly, exacerbations in these patients, and treatment of GERD in these patients may have some impact on their asthma.

The second group of patients have asthma and silent GERD. Several large studies, including a recent pediatric study conducted by the American Lung Association ACRC Network that was recently published in *The*

*Journal of the American Medical Association*, have pretty convincingly demonstrated that asthma patients (both adults and children) who have asymptomatic GERD demonstrated by pH probe testing do not have any improvements in their asthma control or lung function when treated with proton pump inhibitors.

These recent, large clinical trials have focused on the treatment of acid reflux. A theory has been put forth that alkali GERD may worsen asthma control; however, to date, this theory has been largely unproven, as only a few small studies have evaluated this type of GERD. A large randomized controlled trial with well-defined asthma patients and objective documentation of alkali GERD is required to answer this important clinical question.

Thus, to date, although GERD treatment may result in nonspecific improvements in quality of life in patients with symptomatic GERD and asthma, by now I think there have been enough studies, including the ACRC study, to conclude that treatment of silent GERD does not improve asthma at all. This conclusion is a significant change from what doctors have believed for a long time. I am not certain that GERD-induced asthma exists. Clearly, some patients with GERD have respiratory symptoms, primarily cough, but the exact mechanism for this relationship is unclear, which, I think, is part of the confusion in this area. However, I do not believe that the presence of these respiratory symptoms is equivalent or sufficient to make the diagnosis of chronic inflammatory asthma. I wonder if there are other effects of GERD, such as worsening of vocal cord dysfunction, that may mimic asthma and have led us in the past to erroneously conclude that GERD was worsening asthma.

### **G&H** Why then is GERD more common in asthma patients than in the general population?

**JGM** It is not entirely clear why GERD is more common in asthma patients. Several theories have been advanced, with the most common one being that pressure swings in the thorax of asthmatics allow more acid to reflux into the esophagus. There are animal studies that suggest that instillation of acid in the esophagus stimulates vagal tone and may increase respiratory resistance and “prime” the airways for bronchoconstriction. These and other animal studies suggest that chronic microaspiration from GERD may trigger bronchoconstriction and also possibly increase inflammation in the airways. However, this hypothesis has not been adequately tested in humans. In addition, some asthma medications, specifically  $\beta$ -agonists and theophylline, may reduce the lower esophageal sphincter tone and, thus, promote acid

reflux in asthmatics; however, again the clinical impact of these changes does not appear to be significant, at least in patients with asymptomatic GERD.

### **G&H** Why does GERD treatment improve (albeit only by a little) quality of life in patients with symptomatic GERD?

**JGM** I am not certain that there is a good answer to this question. It may be that effective treatment of GERD results in an improvement in overall well-being and is, thus, reflected in improved quality of life related to asthma.

### **G&H** Have any studies examined the impact of nonmedical GERD treatment on asthma?

**JGM** Most studies looking at GERD treatment and asthma have evaluated either  $H_2$  blockers or proton pump inhibitors, which, as is known, do not cure reflux. Some researchers have started to wonder whether other GERD treatments, such as Nissen fundoplication, would improve patients' asthma. Thus far, all of the studies evaluating whether Nissen fundoplication (or other surgical procedures that eliminate reflux) improves asthma outcomes have been case reports or very small cohort studies; no randomized trials have yet been conducted on this issue. As the findings have been variable, definitively answering this question would require a large randomized trial of Nissen fundoplication versus sham Nissen fundoplication in well-defined asthma patients with objective evidence of GERD. However, this study would be expensive and challenging to conduct, so I am not certain that we will get a good answer to this question.

### **G&H** Should patients with asthma and symptomatic GERD receive the same treatment as GERD patients without asthma?

**JGM** Yes, an asthma patient with symptomatic GERD should be treated the same as a nonasthmatic patient with symptomatic GERD. GERD treatment should be focused on reducing GERD symptoms and preventing sequelae, as it does not have much of an impact on the patient's asthma, as previously discussed.

Likewise, when determining whether these patients should receive surgical therapy, doctors should follow the standard guidelines for treatment of refractory GERD. Therefore, if an asthma patient who has severe GERD continues to have GERD symptoms despite standard medical treatment, a Nissen fundoplication should be considered, just as if the patient were a nonasthmatic with severe GERD.

**G&H** Has the general community adopted these new treatment guidelines (ie, that asthma patients with silent GERD should no longer receive GERD treatment)? Is there harm in continuing to administer GERD treatment to patients with silent GERD?

**JGM** There are no data available on the impact of these recent data on clinical practice. It will be interesting to see how the NIH asthma guidelines review this issue, as I expect that the NIH may change its previous recommendation for a trial of empiric GERD treatment in poorly controlled asthmatics.

There are growing concerns of side effects of proton pump inhibitor therapy, including a potential increase in upper respiratory infections or pneumonias as well as fractures in children. In addition, these medications are very expensive. However, my major concern is that a proton pump inhibitor trial in asthma patients with asymptomatic GERD will have no impact on their asthma and just delays other therapies focused on their asthma.

**G&H** What are the next steps in research?

**JGM** As mentioned above, the relationship between alkali reflux and asthma should be further investigated. It would also be good to conduct a definitive trial of GERD and asthma comparing surgical treatments (such as Nissen fundoplication or laparoscopic therapies) and medical treatments; however, as mentioned previously, this trial would be expensive, require sham procedures/surgery, and need a very large patient population for

adequate power. At this time, the major need is education regarding the new evidence that asymptomatic GERD does not impact asthma, which will hopefully steer clinicians toward other, more effective therapies for their patients with poorly controlled asthma.

### Suggested Reading

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