Treatment for Nocturnal Reflux Often Falls Short

ARTICLES BY
KATE JOHNSON
Montreal Bureau

MONTREAL — Gastroesophageal reflux symptoms are poorly controlled across North America and Europe, and people with nocturnal symptoms represent the largest treatment gap, according to two different industry-sponsored studies that were presented in a series of posters at the 13th World Congress of Gastroenterology.

"There's a huge unmet prescribing need," said Farah Husein-Bhabha, from Janssen-Ortho Inc. in Toronto, which sponsored one of the studies. "We found that the use of over-the-counter drugs is much higher than prescription drug use, and yet these patients continue to experience symptoms," she told this publication.

The Canadian study randomly polled 2,001 individuals by telephone to assess the prevalence and impact of gastroesophageal reflux disease (GERD) in the general population.

Just over 40% of the respondents (820) reported at least one upper gastrointestinal symptom in the last month, with the most common complaint being GERD (367). Among GERD sufferers, 54% had sought medical help for their problem, while 46% had not.

The U.S./European study (sponsored by AstraZeneca) which randomly polled a much larger sample of about 212,000 households, identified 1,908 respondents who were either formally diagnosed (52%) or undiagnosed but with symptoms suggestive of GERD (48%). Both studies identified a high percentage (64% and 50%, respectively) of patients who reported nocturnal GERD symptoms either alone or together with daytime symptoms.

Despite treatment with either prescriptions or OTC products, 81% of the self-diagnosed group and 68% under a physician's care still had reflux symptoms.

In the Canadian study, 47% of those with nocturnal symptoms reported disturbed sleep, and 43% of these people reported a negative impact on their daytime functioning and productivity as a result.

The U.S./European study found that, when woken up with GERD symptoms, people stayed awake an average of 70 minutes and missed an average of 30 minutes of work per week as a result. This compared with only 6 minutes of lost work time per week in GERD patients without disturbed sleep. GERD-related sleep disturbance was estimated to be responsible for a 15% reduction in work productivity and a 14% reduction in leisure time, compared with an 8% and 10% reduction in GERD patients without disturbed sleep.

Nocturnal GERD symptoms are of particular concern, not only for quality of life reasons but also because of their long-term implications, said Ms. Husein-Bhabha. "If a patient has nocturnal symptoms, it generally means a more severe type of GERD, and there may also be an association with more erosive disease. There is a certain percentage of the population that may progress to esophageal cancer if they are untreated. But for many patients who do not have erosive disease, that risk is small and probably less than we had originally thought." Both studies found that GERD symptoms are undertreated.

In the Canadian population, 57% of GERD patients were taking over-the-counter (OTC) medications, while 25% used prescription medications.

In the U.S./European study, 74% of the diagnosed group were taking prescription medications (55% of which were proton pump inhibitors), while 85% of the undiagnosed group were taking OTC medications.

Despite some improvement resulting from these treatments, the majority of patients in the U.S./European study reported unresolved symptoms (81% of the self-treated group and 68% of those taking prescription medications).

In the Canadian study, only 54% of patients using proton pump inhibitors (PPIs) for nocturnal relief felt satisfied with the treatment.

"[U]se of medication for management of GERD can be improved," concluded the authors. "Symptoms were more likely to improve when GERD was formally diagnosed by a physician and PPIs prescribed. . . . Individuals with persistent GERD symptoms should consult a physician." ■

Testing Feasible for Polymorphism Linked to Esophageal Cancer Risk

MONTREAL — Genetic testing of patients with Barrett's esophagus to determine their risk for progression to esophageal adenocarcinoma might be a reasonable consideration in the near future, according to Alan G. Casson, M.B., professor of surgery at Dalhousie University in Halifax, N.S.

In a recently published paper that he presented at the annual meeting of the Canadian Association of Thoracic Surgeons, Dr. Casson showed that the *CCND1* G870A polymorphism is found with increasing frequency through the chronic inflammation spectrum, from gastroesophageal reflux disease (GERD) through Barrett's esophagus (BE) and on to esophageal adenocarcinoma (EACA).

The *CCND1* G870A polymorphism can be identified easily by blood testing.

"The contribution of this polymorphism to susceptibility of defined stages of progression to esophageal adenocarcinoma suggests [that] the incorporation of *CCND1* genotype analysis in endoscopic Barrett surveillance programs may allow better stratification of individuals at increased risk for malignant progression," he wrote (Cancer 2005;104:730-9).

"If you are a member of a population with this polymorphism, your chance of getting cancer is relatively higher. This now needs to be tested in larger prospective studies, but it looks promising," he said in an interview.

The analysis included 307 patients enrolled in a prospective case-control study designed to evaluate lifestyle risk factors and molecular alterations in GERD (126 patients), BE (125), and EACA (56).

Compared with healthy, asymptomatic controls (95), all patients had elevated levels of the *CCND1* A/A genotype, after adjustment for age and gender, Dr. Casson said. And the prevalence of this abnormality increased from GERD (odds ratio 2.8) through BE (OR 3.7) and EACA (OR 5.9).

"If an individual has this polymorphism, closer screening or surveillance would be warranted to detect early cancer," he explained.

In the second part of the study, which was presented as an award-winning poster at the 13th World Congress of Gastroenterology, Dr. Casson's team identified obesity, smoking, and increased alcohol consumption as significant predictors of risk for progression of GERD and BE to EACA.

Obesity was identified as the main lifestyle risk factor for EACA (OR 4.67), followed by smoking (OR 3.86), whereas increased alcohol consumption was a risk factor for GERD (OR 2.69) and BE (OR 3.86).

"There has been a lot of controversy about the role of alcohol in esophageal cancer," Dr. Casson said. "Although it is a well-documented risk factor for squamous esophageal cancer, its role has been less clear for adenocarcinomas. But we have shown that it is a significant risk factor."

The study found that a diet high in vitamin C can decrease the risk of GERD (OR 0.4), BE (OR 0.44), and EACA (OR 0.2), and that multivitamin supplementation further reduced the risk of EACA (OR 0.17).

In another study, investigators found a progressive increase in levels of nitrotyrosine, a marker for nitric oxide–induced cellular damage, in esophageal tissue samples from patients with GERD (4%), BE (20%), and EACA (35%). ■

Consider Heller Myotomy In Patients With Achalasia

MONTREAL — Surgery should be first-line treatment for achalasia, and those patients with normal or hypotensive lower esophageal sphincter pressure have the strongest indication for this approach, according to Lorenzo E. Ferri, M.D.

"In general, I think everyone should have a laparoscopic Heller myotomy if they have achalasia, but we know that's not the treatment paradigm for most referring physicians in North America," said Dr. Ferri of McGill University, Montreal.

Although absence of peristalsis is the defining characteristic of achalasia, increased lower esophageal sphincter (LES) pressure and incomplete LES relaxation can compound the problem, he explained in an interview.

The goal in treating achalasia is disruption of this LES mechanism, and Heller myotomy has been demonstrated to be the most effective and longest-lasting method to achieve this goal.

However, a trial with endoscopic pneumatic dilatation is often suggested before surgical treatment, Dr. Ferri said. And although this might temporarily improve symptoms in those patients who have hypertensive LES pressure, those with normal/hypotensive LES pressure will likely gain limited benefit from this approach.

"If significantly symptomatic, these patients [normal/hypotensive LES pressure] should go straight to surgery because we know their margin for clinical improvement is decreased, therefore they should have the procedure that has the greatest chance of improving their symptoms," he said.

Patients with normal/hypotensive LES pressure have a decreased margin for symptom improvement because they experience fewer and less severe symptoms, compared with patients with hypertensive LES pressure, according to Dr. Ferri's study.

He presented his research at the annual meeting of the Canadian Association of Thoracic Surgeons.

The prospective study compared symptoms in 38 newly diagnosed achalasia patients, 22 with hypertensive LES pressure (defined as greater than 26 mm Hg) and 16 with normal/hypotensive LES pressure (defined as less than or equal to 26 mm Hg).

Patients with hypertensive LES pressure (group A) had higher esophageal tone (43 versus 19 mm Hg) and less relaxation of the sphincter (50% versus 67%) than did patients with normal/hypotensive LES pressure (group B).

The study data showed that group B had less dysphagia to liquids and soft foods, but not to solid foods, compared with group A. The latter group also scored higher (43 versus 30, with 0 being the best score and 67 being the worst) on the Achalasia Symptom Questionnaire, a structured 12-question survey of achalasia symptoms. ■