COPD Phenotype Tied to More Exacerbations

BY MARY ANN MOON

FROM THE NEW ENGLAND JOURNAL OF MEDICINE

It appears that chronic obstructive pulmonary disease with frequent exacerbations constitutes a distinct phenotype of the disease that can occur at mild, moderate, or severe levels of illness, according to results from a data analysis.

The frequency of COPD exacerbations appears to be relatively stable over time, and a distinct subgroup of patients appears to be prone to frequent (two or more times per year) exacerbations year after year, said Dr. John R. Hurst of University College London Medical School and his associates.

VITALS

Major Finding: A COPD patient's frequency of exacerbations remains stable over time, and the subgroup of patients with frequent exacerbations appears to have a particular phenotype of the disease.

Data Source: A secondary analysis of data collected in the multinational, prospective, observational, 3-year ECLIPSE study of 2,138 patients with mild, moderate, or severe COPD.

Disclosures: The ECLIPSE study was funded by GlaxoSmithKline. Dr. Hurst and his associates reported ties to numerous pharmaceutical companies.

"Despite the importance of exacerbations, we know relatively little about their incidence, their determinants, and their effects in patients with COPD at various levels of severity," the investigators noted. They used data from a large observational study – the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) – to examine exacerbation frequency.

The international ECLIPSE study included 2,138 patients aged 40-75 years with a history of 10 or more pack-years of smoking, a forced expiratory volume in 1 second (FEV_1) of less than 80% of predicted value, and an FEV_1-to-forced vital capacity ratio of 0.7 or less after use of a bronchodilator. The subjects had a wide range of COPD severity, and were evaluated at baseline, 3 months, and 6 months, and at 6-month intervals thereafter for 3 years.

Although exacerbations tended to increase with increasing disease severity, patients also tended to fall into and remain in one of two groups: those with infrequent exacerbations (0 or 1 per year) or those with more frequent exacerbations.

For example, 1,187 patients had infrequent exacerbations in the first year of the study, and 987 (83%) of them also had infrequent exacerbations in the second year. Another 492 patients had frequent exacerbations in year 1, and 296 of them (60%) had frequent exacerbations in year 2 as well. "Thus, exacerbation frequency in the first year had a sensitivity of 60% and a specificity of 83%" for predicting the frequency in the second year, Dr. Hurst and his colleagues said (N. Engl. J. Med. 2010;363:1128-38).

Similarly, 994 (84%) of the 1,187 patients with infrequent exacerbations also had infrequent exacerbations during the third study year, while 276 (56%) of the 496 with frequent exacerbations also had frequent exacerbations in the third year.

And 210 (71%) of those with frequent exacerbations during years 1 and 2 went on to have frequent exacerbations in year 3, while 388 (74%) of those who had no exacerbations during years 1 and 2 also had no exacerbations in year 3.

The easiest and most accurate way of predicting a patient's susceptibility to exacerbations was simply to ask that patient how many exacerbations they had had the preceding year, the researchers said. ■

VIEW ON THE NEWS

What Is the Mechanism?

The finding of a distinct phenotype of chronic obstructive pulmonary disease implies that some underlying genetic, biologic, or behavioral mechanism determines either susceptibility or resistance to recurrent exacerbations, independent of disease severity, according to Dr. Donald P. Tashkin.

"Such a mechanism could include greater or lesser susceptibility to respiratory tract infection (the principal trigger of exacerbations); microaspiration from gastroesophageal reflux; psychological factors such as perception of dyspnea (the major symptom of exacerbation); and medication adherence.

"Understanding the mechanistic basis for frequent exacerbations might lead to more effective preventive therapy," he wrote.

It is important for clinicians to identify which patients fit the phenotype, because effective therapies are already available to curb the frequency of exacerbations.

In addition, "a better understanding of the underlying mechanisms that predispose a patient to exacerbations could lead to the development of more targeted preventive strategies," which in turn would favorably affect the overall course of COPD, he added.

DR. TASHKIN *is at the University of California, Los Angeles. These comments were taken from his editorial accompanying Dr. Hurst's report (N. Engl. J. Med. 2010;363: 1183-4).*

Delivering Asthma Meds at School Improved Outcomes

BY PATRICE WENDLING

FROM THE ANNUAL MEETING OF THE PEDIATRIC ACADEMIC SOCIETIES

VANCOUVER, B.C. – A school-based intervention that focused on medication adherence and reducing exposure to tobacco smoke significantly improved outcomes among inner-city children with asthma in a randomized trial.

Children receiving the intervention had almost 1 additional symptom-free day per 2-week period during the peak winter asthma season of November to February.

The number of symptom-free days increased from an average of 8 days for all children at baseline to 11.9 days per 2-week period with the intervention vs. 11.2 days with usual care. "This difference is larger than what has been seen with more intensive and costly interventions," said Maria Fagnano, M.P.H., of the University of Rochester (N.Y.) Medical Center.

The children receiving the intervention were significantly more likely than controls to have fewer nights with symptoms (mean 1.5 nights vs. 2.0 nights), fewer days with limited activity (1.2 vs. 1.6), and fewer days with rescue medication use (1.59 vs. 2.61), Ms. Fagnano reported at the annual meeting of the Pediatric Academic Societies.

The intervention group also was significantly less likely than controls to have any acute visit for asthma (12% vs. 18%). In addition, the intervention group had fewer days absent from school due to asthma (0.3 days vs. 0.4 days).

Although additional efforts are needed to evaluate costs of the intervention and to develop dissemination strategies, collaborations with schools provide a unique opportunity to reach high-risk children and target those at greatest need for assistance, Ms. Fagnano said.

VITALS

Major Finding: The number of symptom-free days increased from an average of 8 days per 2-week period for all children at baseline to 11.9 days with the intervention vs. 11.2 days with usual care.

Data Source: School-Based Asthma Therapy trial in 530 children with asthma.

Disclosures: SBAT was supported by grants from the National Heart, Lung, and Blood Institute and the Halcyon Hill Foundation. Ms. Fagnano and Dr. Halterman disclosed no financial conflicts.

"This type of intervention is widely applicable for asthma care in the community nationwide, as well as for management of other chronic diseases, and could potentially reduce disparities between poor and nonpoor children," she said.

The School-Based Asthma Therapy (SBAT) trial, led by colleague Dr. Jill Halterman, was implemented in 2006 in 54 schools and preschools in Rochester, N.Y., to reduce morbidity in poor children aged 3-10 years with physician-diagnosed asthma.

The school nurse was given a canister of preventive medication (fluticasone propionate or fluticasone propionate with salmeterol), with a spacer and mask as appropriate, and asked to give one dose to the child each school day. A supply of preventive asthma medications also was delivered to parents, who were instructed to use the medications on days the child did not attend school.

The intervention also used motivational interviewing to counsel the primary caregiver about how to reduce environmental tobacco smoke (ETS) in the home for smoke-exposed children, Ms. Fagnano said. Overall, 54% of children lived with one or more smokers at baseline. A home-based counseling session was delivered by a trained nurse, with two follow-up telephone calls made at 1 and 3 months after the 30-minute session.

In the usual care group, parents and physicians were notified of the child's asthma severity and encouraged to start on appropriate preventive treatments, but no medication was provided, she said.

At baseline, 69% of children were on preventive medications, 73% received Medicaid, 58% were male, 63% were black, and 28% were Hispanic. Their mean age was 7 years. There were 265 children in each arm.

In a regression analysis, the intervention was associated with 0.92 days per 2 weeks more symptom-free days (*P* less than .001), Ms. Fagnano said.

A stratified analysis showed a significant intervention effect on the primary outcome of symptom-free days for children with and without ETS exposure in the home. The mean number of symptom-free days among non-ETS exposed children was 11.6 days in the treatment group vs. 10.9 days in the control group; and was 11.6 days vs. 10.0 days, respectively, in smoke-exposed children, she said.

An audience member remarked on the improvement observed, even among controls. Ms. Fagnano said that monthly follow-up calls could have "clued parents in to what the child was experiencing," and that asthma calendars given to these families may have helped them notice more symptoms. ■