

Exhaled Nitric Oxide Promising for Asthma Testing

BY ROXANNE NELSON
Contributing Writer

LYNNWOOD, WASH. — Use of exhaled nitric oxide as an adjunct for diagnosis and management of asthma is now available in some centers, but may be more widely available in the near future, Dr. Jason S. Debley said at a conference sponsored by the North Pacific Pediatric Society.

A special noninvasive analyzer is used to measure exhaled nitric oxide (eNO); how-

ever, a significant drawback is that the analyzers are very expensive. "What may break this field open is a portable device that is used in Europe," one that the Food and Drug Administration is reviewing now, said Dr. Debley of the University of Washington, Seattle.

Asthma, the most common chronic disease of childhood, is an inflammatory condition. Nitric oxide is important in coordinating the immune response but in asthma patients, the concentration of ni-

tric oxide in exhaled air is increased. Measurement of eNO concentration in the breath can be used to monitor asthma airway inflammation.

The combination of bronchial hyperactivity and inflammation leads to symptoms in patients with asthma. Because asthma is an inflammatory disease, national guidelines recommend that children with persistent asthma be treated with daily inhaled steroids. Treatment decisions usually are based on assessments of symp-

toms and traditional measures of lung function, which do not directly or objectively measure underlying eosinophilic airway inflammation, explained Dr. Debley.

The traditional approach to asthma diagnosis consists of evaluating symptoms, a physical examination that is often normal, and pulmonary function testing. "Spirometry is a useful test, but it can typically only be performed in children over age 6 years, and many children with mild to moderate asthma have normal spirometry readings at their baseline," Dr. Debley said. "So it has significant limitations."

Traditional methods of assessing airway inflammation, namely bronchoalveolar lavage, bronchial biopsy, or sputum analysis, are invasive, may require anesthesia, and/or are impossible to perform in children, Dr. Debley pointed out. In contrast, eNO is a noninvasive biomarker of lower airway eosinophilic airway inflammation.

Nitric oxide is a simple molecule, which was once thought of as a pollutant. "It is now known to be one of the most important molecules in human physiology," Dr. Debley said.

Levels of eNO are higher in asthma patients, compared with nonasthmatic patients, and levels decrease after corticosteroid treatment in patients with asthma. The excess nitric oxide seen in asthma patients is primarily caused by an increase in the expression of the enzyme inducible nitric oxide synthase by airway epithelial cells.

In addition to helping diagnose asthma, eNO can be useful in predicting steroid responsiveness, said Dr. Debley. "It can also be used as a marker of compliance, to determine who is taking their medications."

eNO does have its limitations, as eNO levels do not always correlate with National Institutes of Health classifications of asthma severity, and eNO is not always associated with measures of airflow obstruction. Therefore, eNO should not be used by itself to assess asthma severity, but rather as a complementary tool to spirometry.

Dr. Debley pointed out that eNO is used at his institution, and most children aged 6 years and older can perform the procedure. "Many 4- and 5-year-olds are also able to complete the test," he said. "It is easier and more fun to perform than spirometry, and the kids don't seem to mind it."

Another promising future tool is the measurement of biomarkers in exhaled breath condensate (EBC), which is collected by cooling or freezing exhaled breath. It is then analyzed for the presence of inflammatory mediators, cytokines, and other proteins, which have been detected in EBC.

EBC is another area of interest, although the field is still in its infancy, compared with eNO, Dr. Debley said. In patients with asthma, leukotriene and interleukin-4 levels in EBC are reported to be higher, compared with those in healthy individuals.

However, published literature has been inconsistent with regard to levels of leukotriene and other mediators in EBC between asthma and healthy patients, and in some cases, attempts to detect leukotrienes in EBC using commercially available assays have been unsuccessful. ■



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