

NO help: Nitric oxide monitoring does not help most children with asthma

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The level of nitric oxide (NO) in an asthmatic's exhaled breath can portend worsening asthma symptoms, and may even signify an imminent attack linked to underlying airway inflammation. This has made the monitoring of NO levels, particularly in children, of significant interest as a potential way to help clinicians fine-tune medications and improve treatment outcomes. However, a recent multi-center prospective study found that calibrating medications based on daily monitoring of the fractional exhaled nitric oxide (FENO) and symptoms in asthmatic children showed no significant improvement over medicating based on daily symptom monitoring alone.

The results were reported in the second issue for January of the *American Journal of Respiratory and Critical Care Medicine*, a publication of the American Thoracic Society.

Johan C. de Jongste, M.D., Ph.D., at the Erasmus University Medical Center-Sophia Children's Hospital in the Netherlands, and colleagues randomized 151 children from 15 academic centers and hospitals with mild to moderate asthma to a 30-week monitoring course. Families were called every three weeks and reported on the daily symptoms in the prior three weeks. The child's medication was adjusted accordingly.

The researchers compared the rates of exacerbation, symptoms, use of medications and other endpoints between the last 12 weeks in the two groups. There were no significant differences whether or not FENO had been part of the daily monitoring. However, both groups enjoyed an



impressive overall improvement in symptoms, despite a reduction of about 50 percent in inhaled steroid dose, suggesting considerable benefit of frequent monitoring.

"We speculate that daily supervision and frequent phone contacts have produced an improvement that could not be beaten by additional monitoring of FENO, most likely because of a ceiling effect on compliance," wrote Dr. de Jongste.

The FENO group did, however, have nearly twice as many dosage changes as the symptom-only group, which supports the idea that the lack of difference may be a reflection on the limits of compliance, rather than an inherent limitation in the technique. Still, the added cost and apparent lack of benefit of daily FENO monitoring found in this study suggests that applying the technique in this way is not of benefit to the asthmatic population at large, when compared to daily symptom monitoring.

Another possible explanation for the lack of improvement is that FENO monitoring is most likely to prompt a medication change that symptom-only monitoring would not suggest in patients whose symptoms and underlying inflammation are in discord, but the current study was not designed to assess these patients independently.

Still, in light of these findings, it is clear that FENO monitoring should only be applied to those who stand to gain the most. "There can be no doubt that adding frequent assessments of FENO to management plans of most children and adults with asthma will add unjustifiable costs without providing clinical benefit. Whether there is a role for monitoring FENO to aid management of severe asthma is untested," wrote Stephen Stick, Ph.D., of the Princess Margaret Hospital for Children in Perth, Australia and Peter Franklin, Ph.D., of the Centre for Asthma, Allergy and Respiratory Research at the University of Western Australia in Perth



in an editorial that accompanied the article.

"We did not address other possible applications of frequent FENO monitoring, such as prediction of steroid effect. Loss of control, prediction and prevention of exacerbations, and tapering of steroids in symptom-free children who wheezed in the past," noted Dr. de Jongste. "We think there is good reason to study these potential applications."

Furthermore, as D. Robin Taylor, M.D., of the Dunedin School of Medicine at the University of Otago, in New Zealand, pointed out in separate editorial, "FENO measurements shed complementary light on the underlying inflammatory phenotype and, more importantly, on the potential response to anti-inflammatory treatment. Historically, this has been assessed either by empiric "trials of steroid" or, even more imperfectly. With reference to before/after changes in spirometry, serial or repeated FENO measurements in individual patients may provide additional diagnostic as well as prognostic insights."

Source: American Thoracic Society

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