Exhaled nitric oxide monitoring as a guide to treatment decisions in chronic asthma

BlueCross BlueShield Association

Record Status
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Citation

Authors' objectives
This assessment aims to review the available evidence on whether health outcomes in patients with asthma are improved by using exhaled nitric oxide (ENO) levels to monitor disease activity and assist in management decisions.

Authors' conclusions
The 7 studies that evaluated the predictive ability of ENO, and the potential of ENO to provide prognostic information that could influence management decisions, had considerable methodologic limitations. Differences in the ENO cutoff levels, predictor variables, and definition of outcomes preclude the ability to determine the true value(s) for these parameters. While these studies suggest that ENO may have some predictive ability, they are not definitive in this regard. Also, the lack of a standardized protocol for monitoring ENO creates difficulties for clinicians who may wish to use ENO levels for monitoring.

The 2 RCTs were of fair methodologic quality and suggest possible benefits from ENO monitoring, but substantial uncertainty remains. In one study, comparable outcomes were achieved with a lower overall dose of ICS in the ENO group. This was a single-blinded study, and the main limitation was that clinicians who made treatment decisions were aware of group assignment. Whether the benefit reported in this trial will translate to clinical practice depends on how well the monitoring strategy in the control group reflects actual clinical practice. The monitoring strategy in the control group led to an increased dose of ICS prescribed. This goes against evidence from other clinical trials reporting that the ICS dose can generally be reduced in patients with stable asthma. Thus, the management strategy used in the control group may have led to overtreatment with ICS.

The other study reported that the final dose of ICS was similar in both groups, and that there was an improvement on one of the outcome measures, i.e., bronchial hyper-reactivity. However, bronchial hyper-reactivity is an intermediate outcome that is not well benchmarked to true health outcomes. Also, confidence in the validity of this reported difference is limited by several factors. There was evidence of baseline imbalances on this measure. A substantial number of patients (35%) did not have this measure completed at the end of the study, and these patients were excluded from analysis. The p value of 0.04 did reach statistical significance, but it is unknown whether this significance would have been maintained if intent-to-treat analysis was performed.

Based on the available evidence, the Blue Cross and Blue Shield Medical Advisory Panel made the following judgments about whether monitoring ENO levels in patients with chronic asthma as a guide to treatment decisions meets the Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) criteria.

1. The technology must have final approval from the appropriate governmental regulatory bodies.

Devices intended to measure ENO levels in expired air are subject to 510(k) FDA marketing clearance. The NIOX Nitric Oxide Test System (Aerocrine AB, Sweden) received 510(k) clearance to market on May 1, 2003.
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.

The available evidence does not permit the conclusion that use of ENO monitoring to guide treatment decisions in asthma leads to improved outcomes. The 7 studies that evaluated the predictive ability of ENO, and its potential to provide prognostic information that could influence management decisions, had considerable methodologic limitations and variability in study methodology that precluded synthesis of their results and definitive conclusions.

The two randomized, controlled trials included in the Assessment suggest possible benefits for ENO monitoring, but are not sufficient to conclude that outcomes are improved. Each study reported different benefits that have not been reproduced. Differences in the control management strategy raise questions about the optimal management strategy to which ENO monitoring should be compared.

3. The technology must improve the net health outcome; and 4. The technology must be as beneficial as any established alternatives.

The evidence does not permit conclusions as to whether monitoring of ENO levels improves health outcomes or is as beneficial as established alternatives.

5. The improvement must be attainable outside the investigational settings.

Whether monitoring of ENO levels improves the net health outcome has not been established in the investigational settings.

Based on the above, the use of ENO levels for monitoring patients with chronic asthma does not meet the TEC criteria.