How to use FENO-guided asthma control in routine clinical practice

Asthma is a chronic inflammatory disease of the airways. This has implications for the diagnosis, management and potential prevention of the disease.

While the role of the underlying inflammation is critical, there is considerable variability in the pattern of inflammation, indicating phenotypic differences in asthma that influence correct diagnosis and treatment responses.

The primary drivers of asthma morbidity and mortality are incorrect diagnosis and inadequate treatment. In addition, poor adherence to medication, improper inhaler technique and persistent allergen exposure prevent disease control.

FENO, Fractional exhaled Nitric Oxide, measures airway inflammation responsive to inhaled corticosteroid (ICS) therapy. This point-of-care test is simple, non-invasive and provides an objective measure within minutes.

Nitric Oxide (NO) – a marker of inflammation

Monitoring asthma symptoms is important, but correct interpretation of the underlying inflammation determines the therapy. Measuring exhaled NO provides an immediate answer to three critical questions:

- Which patients with non-specific respiratory symptoms have allergic airway inflammation?
- Is the patient compliant and responding to the prescribed therapy?
- Has there been a change in allergen exposure?
Asthma has until now been defined by characteristic symptoms, impaired lung function and airway reversibility or hyper-responsiveness. The reason why this inflammatory disease has not been defined by its underlying pathophysiology is that we until recently have been missing a simple and reliable tool to measure airway inflammation.

A standard clinical assessment that relies on structured or non-structured recordings of symptoms and lung-function tests, gives very little useful information about potentially corticosteroid-responsive disease.
When it has been confirmed that a patient’s symptoms are caused by airway inflammation responsive to ICS therapy, the primary goal is to control the underlying inflammation. FENO provides a rapid and objective measure of inflammation control following anti-inflammatory therapy.

For patients who remain symptomatic after having achieved a normalized FENO, indicating inflammation control, appropriate additional intervention should be considered.

Inflammation monitoring using FENO also allows the identification of patients who do not attain inflammation control despite ICS therapy. These patients are typically helped by addressing therapy adherence and inhaler technique, as well as considering allergen exposure reduction regimens.
Use FENO measurement to determine whether there is allergic inflammation in the airways or not

A normal FENO value in a symptomatic patient indicates a diagnosis other than allergic asthma (airway inflammation). Starting ICS therapy is therefore not indicated.

An elevated FENO value confirms ongoing allergic inflammation of the airways that is highly likely to be reduced by ICS therapy. As a consequence, the patient is likely to respond clinically irrespective of symptoms and lung function at baseline.

Anti-inflammatory therapy is the cornerstone of asthma management. However, several disorders other than allergic asthma are manifested by similar symptoms. Untreated allergic inflammation will lead to increased risk of exacerbations and increasingly impaired lung function (airway remodeling).
Patient with chronic cough or symptoms suggestive of asthma

History, symptoms, FENO measurement

Normal FENO*

Consider:
Diagnosis other than (allergic) asthma

Elevated FENO**

Strong predictor of allergic asthma (or eosinophilic bronchitis)
ICS responsiveness likely

Management and control

INITIAL ASSESSMENT

* 5–25 ppb for adults
5–20 ppb for children < 12yrs
** above 25 (20) ppb

Based on group consensus cut-offs given in:
**SABA¹ + ICS dose adjustment FENO follow-up**

- **FENO normalized**
  - Inflammation controlled and patient symptom-free
    - **Continue therapy**
  - Inflammation controlled, but patient symptomatic
    - **Consider:**
      - Co-morbidities
      - LTRA³ or LABA² add-on therapy
  - Inflammation not controlled
    - **Address:**
      - Adherence and inhaler technique
      - Persistent allergen exposure
    - **Consider:**
      - Oral corticosteroid treatment
      - Anti-IgE treatment

- **FENO not normalized**

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¹ Short-acting bronchodilator
² Long-acting bronchodilator
³ Leukotrine antagonist
Monitor airway inflammation to achieve asthma control

For a patient who is symptom-free and has obtained a normal FENO value, the therapy should continue. If the ICS is tapered, FENO should be followed closely.

For patients who remain symptomatic after having achieved inflammation control and normalized FENO, appropriate additional intervention should be considered.

If FENO is not normalized, the inflammation is not under control. Investigate the patient’s therapy adherence, inhaler technique and the presence of persistent allergen exposure.

Symptoms and lung function tests alone cannot clearly determine inflammation control following medication. To properly manage and control asthma, inflammation control is a fundamental prerequisite. FENO is an objective and direct marker of inflammation control.

For some patients, ICS therapy and dose escalation is not the sole remedy to achieve control.
“After all, does anyone seriously advocate treating hypertension without measuring the blood pressure, or kidney disease without knowing the glomerular filtration rate? Neither seems to me to be any dafter than using anti-inflammatory medications without measuring inflammation.”
Andrew Bush, Royal Brompton Hospital, United Kingdom.

“Measurement of exhaled nitric oxide is better than many of our more conventional methods in determining steroid-responsive disease.”

“We conclude that exhaled NO signals allergen-triggered Th2-driven inflammatory mechanisms within the bronchial mucosa, primarily those induced by IL-4 and IL-13. Thus, exhaled NO signals the activity of mechanisms of central importance in asthma.”

“The goal of asthma care is to achieve and maintain control of the clinical manifestations of the disease for prolonged periods. When asthma is controlled, patients can prevent most attacks, avoid troublesome symptoms day and night and keep physically active.”
Global Initiative for Asthma (GINA) guidelines 2009.