GIG CYMRU NHS WALES

Respiratory Health Implementation Group

Y Grŵp Gweithredu ar Iechyd Anadlol

Consensus statement for FeNO testing in adults in Wales

Supporting notes

THE ALL WALES ASTHMA DIAGNOSIS GUIDELINE

icst.info/the-all-wales-asthma-diagnosis-guideline

THE ALL WALES ASTHMA MANAGEMENT & PRESCRIBING GUIDELINE

icst.info/the-all-wales-asthma-management-and-prescribing-guideline

BACKGROUND

The fraction of exhaled nitric oxide (FeNO) can be a useful test to identify eosinophilic airway inflammation and hence may be useful in the diagnosis and monitoring of asthma. A raised FeNO level can predict steroid responsiveness however the interpretation of FeNO depends closely on the clinical context. As with any test, it can produce false positive and false negative results (for example in neutrophilic asthma phenotypes) and its accuracy depends on the pre-test probability, and the competence of the user. Interpretation will depend on the current therapy a patient is receiving. In a steroid naive patient with a low FeNO, it is unlikely their symptoms will respond to inhaled corticosteroids (ICS). However, in a confirmed asthmatic patient fully concordant with an appropriate dose of ICS (which is successfully suppressing airway inflammation), the FeNO will also be low.

Currently in Wales the uptake and use of FeNO is variable and it is of concern that there are no agreed standards of quality control, systematic training or audit. The test is non-invasive but can be costly to buy and maintain.

This group was formed to review the use of FeNO within Wales and designed to represent views from community, primary and secondary care teams. Members include a pharmacist, GP, respiratory consultants, a specialist nurse and respiratory physiologist.

We considered current NICE, British Thoracic Society (BTS) and GINA (Global Initiative for Asthma) guidelines in order to recommend a safe, practical and prudent approach to applying FeNO in everyday clinical management for adult respiratory patients. We make no comments on its use in paediatric patients.

We hope our consensus statement will be considered and endorsed by the Respiratory Health Implementation Group, Welsh Thoracic Society and Welsh Difficult Asthma Group.

WHERE AND BY WHOM SHOULD FENO BE PERFORMED?

- There is currently insufficient evidence to support the high cost of adopting a roll-out of FeNO as a standard, first line asthma test in all centres.
- FeNO should not be used in isolation, but, in a targeted manner, in conjunction with an appropriate history and detailed examination, alongside other evidence of variable airflow obstruction.
- FeNO could be used in Community Pharmacies and Primary Care by those with an interest and experience in managing asthma.
- It is now more widely used in secondary care respiratory clinics and is a useful tool in specialist asthma clinics (below).
- Use of FeNO should be an opt-in with the caveats that all users have appropriate training (below), competency assessments and ongoing audits.
- We do not recommend any specific make nor type of FeNO monitor but advise each prospective user to trial various models before purchase.

FENO AS A DIAGNOSTIC TOOL

- Asthma – when there is a clear diagnosis of asthma (history, examination, variable airflow obstruction, and evidence of atopy and/or response to treatment) a FeNO test adds nothing to the diagnosis and is a waste of resource.
- In borderline cases with some features of asthma then a FeNO >40 ppb will influence the probability of an asthma diagnosis and is suggestive of airway inflammation that would respond to ICS.
- Raised FeNO is suggestive of eosinophilic inflammation. However, rhinitis, atopy, rhinovirus infection, nitrate medications and nitrate rich foods (including spinach and beetroot) can raise FeNO (leading to false positives).
- However, a normal result does not exclude asthma and a normal FeNO level often occurs neutrophilic asthma phenotypes who respond less well to ICS. Smoking can also reduce FeNO (leading to false negatives) eg in smoking asthmatics.
- There is insufficient evidence to support the use of FeNO to diagnose any other respiratory condition other than asthma, including ACOS (asthma COPD overlap syndrome).
- The All Wales Asthma diagnosis guideline highlights the role of FeNO as supportive, but not conclusive, evidence for an asthma diagnosis

FENO TO CHECK MEDICATION CONCORDANCE

- Persistently raised FeNO can be a useful marker of poor concordance with prescribed ICS. However, this should be as an adjunct to the conventional markers of concordance: inhaler pick-up rate should be documented to be above 80% over the previous 12 months, good inhaler technique should be demonstrated and adherence with asthma management plans corroborated.
- A raised FeNO can be used as an educational tool when discussing poor concordance. A drop in FeNO with improved concordance can reinforce the need for regular therapy.
- A FeNO suppression protocol is currently not feasible outside a difficult asthma service.

FENO TO GUIDE TREATMENT DECISIONS

- A persistently raised FeNO after checking inhaler pick-ups, technique and asthma plan adherence, may indicate ongoing airways inflammation. In these circumstances, it can guide:
    - Increases in ICS dose
    - Referral to or advice from secondary care
    - Consideration of co-existent allergic rhinitis
    - The need for additional caution when considering a reduction in ICS dose in the context of clinical stability
- There is insufficient evidence to use persistently raised FeNO to influence the prescribing of systemic steroids or biologic treatments.

TRAINING AND SURVEY

We ask that RHIG incorporate training in the use and interpretation of FeNO as part of the asthma National Welsh Standards accessible to everyone across Wales. We have also penned 4 cases based on real-life experiences relating to these potential uses.

We also suggest a baseline email survey of FeNO usage across primary and secondary care in Wales using the following 2 simple questions:

a. How many times do you use FeNO in your clinical practice?
    i. Never
    ii. 1-5 times per month
    iii. 6-10 times per month
    iv. >10 times per month

b. Do you have any comments on FENO in your workplace?
    i. (Usefulness, expense etc)

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REFERENCES

https://www.nice.org.uk/Guidance/DG12

https://www.brit-thoracic.org.uk/document-library/clinical-information/asthma/btssign-asthma-guideline-2016/

Korevaar, D. (2015). Diagnostic accuracy of minimally invasive markers for detection of airway eosinophilia in asthma: a systematic review and meta-analysis. The Lancet 2015; 3(4), 290-300

CASE STUDIES

CASE 1: FENO assisting in a difficult asthma diagnosis

Overweight, 52-year-old male estate agent, with long standing history of hay fever. Complains of intermittent shortness of breath on exertion, dry cough and occasional wheeze. Patient attributes this to significant weight gain, age and being an ex-smoker with a 12-pack year history. Baseline spirometry and physical examination normal. PEF monitoring identified 10-12% variation, however technique in clinic questionable. Patient had previously been prescribed a SABA and reported he found it helpful. FENO identified to be high (above 50ppb). Low dose ICS prescribed and FENO repeated 6 weeks later. On review FENO 15ppb. Patient reports significant symptom relief with minimal variation now in PEFR, supporting asthma diagnosis.

CASE 2: FENO assisting asthma concordance

25 year old male, non-smoker, asthma since childhood, current prescription of high dose ICS/LABA plus SABA. On checking repeat history appeared concordant with preventer but having SABA monthly indicating overuse. Seen January 2018 for annual asthma review and noted to have regular daytime symptoms particularly on exercise and using SABA daily for a 'tight chest' on waking. PEFR 510L/min (68% best ever), FENO 38 ppb. On questioning he admitted to often missing doses of his ICS/LABA and his girlfriend had recently bought two kittens. Inhaler technique assessed as good, asthma management plan provided, educated on correct use of preventer (advised to take daily even when well) and antihistamine added for allergy. At follow up 8 weeks later large improvement in PEFR, now 720L/min and a large reduction in FENO now 15ppb. Asthma currently being monitored and if remains stable, for at least a three month period, the plan is to reduce ICS dose. Will then need ongoing review to monitor control and concordance.

CASE 3: FENO stopping ICS reduction

45 year old male patient initiated on high dose ICS/LABA BD via Aerochamber and mask following admission to hospital for exacerbation of asthma. Attended asthma clinic review one month later feeling much better with no nocturnal symptoms, improved exercise tolerance and minimal SABA use. Asked to return to clinic in three months at which stage remained symptomatically well however FENO found to be 55ppb. Prescription pick up rate confirmed to be high and inhaler technique confirmed as good. Dose of ICS/LABA not stepped down, despite good apparent symptom control, as evidence of on-going inflammation and high dose ICS still justified to reduce further exacerbation risk.

CASE 4: FENO leading to doubling ICS and secondary care opinion

38y old female, with a history of asthma and rhinitis, on regular treatment with low dose ICS/LABA (2 puffs BD) and regular nasal steroid. Non-smoker. Increase in asthma symptoms with two recent exacerbations despite apparent good control between attacks. Prescription pick up rate confirmed to be 100% and inhaler technique excellent. Trial of montelukast initiated and advised to use ICS/LABA as per MART regime (maintenance and reliever therapy) in place of SABA. On review minimal daily symptoms with PRN use of ICS/LABA approximately twice a week however one 'out of hours' GP attendance requiring oral steroids for an exacerbation. FENO checked and found to be elevated at 62ppb. ICS/LABA changed to regular high dose regime (2 puffs BD with PRN SABA) and referral for secondary care opinion given recurrent exacerbations. Awaiting repeat FENO on high dose inhaled therapy.

This Consensus statement was based on a round-table discussion on 24th April 2018 and subsequently endorsed by all members.

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