Therapy optimization on the basis of regular FeNO measurement

Optimization of therapy based on regular FeNO home measurement by quantifying Type 2 inflammation

Dr. med. Hartmut Timmermann, Pneumologicum Hamburg, Valentinskamp 24, 20354 Hamburg

Summary

The case study refers to a participant of the ongoing FeNO@home study. The patient with asthma known since childhood had reported good asthma control in the last few years. His lung function was normal. He performed FeNO home measurements over a period of 12 weeks under his usual medication. We found unexpectedly high FeNO values confirming an ongoing Type 2 inflammation. He was instructed to double his ICS dose with normalizing of FeNO. **The case illustrates how frequent FeNO home measurements can lead to optimized asthma treatment.**

Case history

The case described in this report relates to a 44-year-old male patient who was diagnosed with asthma in childhood. He is a non-smoker. He has allergies to grass and pollen, house dust mites, and cat epithelium. The patient presents a known comorbidity of allergic rhinitis.

He showed controlled asthma symptoms according to the Asthma Control Test (ACT score 21 units). The lung function was considered as normal (FEV1 of 104%). Measurements of Fractional exhaled Nitric Oxide (FeNO) in medical practice indicated a high FeNO-level (95 ppb).

Investigation

The patient was included in the FeNO@home study¹ outside pollen season. The aim of the study was to investigate whether regular FeNO home measurements had an impact on patient compliance or behavior, variability of FeNO values over a longer period, correlation of FeNO values with symptoms, identification of asthma triggers, and treatment decisions. In this multicenter study, adult patients with diagnosed asthma performed FeNO measurements over a period of 12 weeks using the Vivatmo *me* measurement device for home use. They continued to take their currently prescribed asthma treatment, which could also be adapted. Daily symptoms, use of asthma medication, potential exacerbations, and Peak Expiratory Flow (PEF) were recorded in the device-associated Vivatmo *app*. After 12 weeks, the study ended with a final assessment of asthma control, symptoms, and lung function.

Results and treatment

The medication was adjusted during the study. With normal lung function and a high ACT score, we found unexpectedly high FeNO values confirming an existing Type 2 inflammation. During the first month, the FeNO values were in a very high range (50-80 ppb), leading to an increase of the dose (2x2). After increasing the ICS dose, the majority of FeNO levels were below the 25-ppb-threshold from the ATS guideline². The low FeNO values were accompanied by less coughing and an improvement in general health of the patient. The final assessment in the medical practice indicated normal lung function (FEV1 4,72 I, 103% of expected; FVC 5,49 I; FeNO 18 ppb), and an ACT score of 23 units.

The patient received GINA (Global Initiative of Asthma) treatment step 2-3 consisting of low-dose Symbicort (2x1).

Problem statement

What is the best approach for patients with well controlled asthma and high FeNO values confirming an ongoing Type 2 inflammation?



Figure: Course of the FeNO values based on regular home measurements by patients, thresholds according to ATS guideline²

Discussion

The German Asthma Guideline and GINA recommend the adjustment of the level of asthma therapy in accordance with patient reported control of asthma and lung function tests.^{3,4}

To assess symptom control, the patient should be asked about the following in the past four weeks: frequency of asthma symptoms (days per week), any night waking due to asthma or limitation of activity, and frequency of using a SABA reliever for symptom relief. In our medical practice we use the ACT. It consists of four questions about symptoms and relieving factors and a self-assessment by the patient.

GINA does not recommend FeNO measurement as part of the regular asthma management plan.

One reason for this approach is that in two 12-month studies with mild asthma, severe exacerbations were reduced with as-needed low-dose ICS-formoterol versus as-needed SABA, and versus maintenance ICS, independent of baseline inflammatory characteristics including FeNO.^{5,6}

The 2023 guideline for respiratory specialists published by the German Respiratory Society (DGP) emphasizes the new role of biomarkers, especially blood eosinophils and FeNO, in diagnostic algorithms of asthma and mentions their increased role in monitoring asthma treatment.⁷

With the Vivatmo *me* as the first device approved for home measurement by the patient, an even broader application of FeNO measurement is possible. In this specific case, a therapy improvement could be achieved through regular home measurement with subsequent therapy adjustment.

These are some preliminary results since the study is still ongoing. Thus, only a single patient case is reported. The completion of the study is needed to strengthen the beneficial effects of FeNO home measurement for physicians and asthma patients.

Conclusion

The underlying case illustrates the benefits for therapy optimization based on regular FeNO measurement. The outcome of FeNO monitoring in this patient produced results indicating an ongoing Type 2 inflammation, leading to individualized adjustment of further therapy. Given that, the experience could have significance for other cases. Do we overlook ongoing Type 2 inflammation in patients when we adjust therapy without FeNO measurements and what are potential future consequences? In clinical practice we sometimes see patients who have stable moderate asthma for years and suddenly deteriorate to severe asthma, often after an exacerbation triggered by an infection. Could persistent Type 2 inflammation that goes unnoticed be the cause? Should we move beyond a disease control-based approach to asthma treatment?⁸

References

- 1 This clinical trial was prospectively registered on 01.07.2022 in the German Register of Clinical Trials (DRKS: DRKS00029118); Accessed July 25, 2023 at: https://drks.de/search/de/trial/DRKS00029118
- 2 Dweik RA et al. An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FeNO) for clinical applications. Am J Respir Crit Care Med. 2011;184(5):602-15
- 3 Global strategy for asthma management and prevention (2023 update). Global Initiative for Asthma, 2023 (p.135). Accessed July 30, 2023 at: https://ginasthma.org/reports/

- 4 Guideline for the Diagnosis and Treatment of Asthma Addendum 2020 Guideline of the German Respiratory Society and the German Atemwegsliga in Cooperation with the Paediatric Respiratory Society and the Austrian Society of Pneumology. Pneumologie 2021;75(03):191-200
- 5 Beasley R, Holliday M, Reddel HK, et al. Controlled trial of budesonide-formoterol as needed for mild asthma. N Engl J Med 2019; 380: 2020-2030
- 6 Hardy J, Baggott C, Fingleton J, et al. Budesonide-formoterol reliever therapy versus maintenance budesonideplus terbutaline reliever therapy in adults with mild to moderate asthma (PRACTICAL): a 52-week, open-label,multicentre, superiority, randomised controlled trial. Lancet 2019; 394: 919-928.
- 7 Diagnosis and treatment of asthma: a guideline for respiratory specialists 2023 published by the German Respiratory Society (DGP). Pneumologie 2023. DOI 10.1055/a-2070-2135
- 8 Pavord ID, Beasley R, Agusti A, et al. After asthma: redefining airways diseases. Lancet 2018. DOI: 10.1016/S0140-6736(17)30879-6.