Very rapid reduction of FeNO after biologic treatment

Optimizing treatment monitoring with biologics based on regular FeNO home measurement

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Summary

This is the clinical case of a severe asthmatic patient with associated severe and uncontrolled nasal polyposis, undergoing therapy with dupilumab, and for whom regular home measurement of FeNO made it possible to identify, from the very first days of therapy, a significant inflammation reduction effect. **Regular home measurement of FeNO can be a useful tool to readily identify patients responding to dupilumab.**

Case history

A 58-year-old man with a history of asthma since the age of 39, with sensitization to house dust mites and grass pollens, and progressive worsening of the clinical respiratory picture up to a diagnosis of severe asthma in the last two years. The patient has chronic rhinosinusitis with nasal polyps (CRSwNP) as the most relevant comorbidity; for this disease he underwent two surgical interventions, however with recurrence of the nasal polyposis after about 6 months from each surgery. At the time of enrollment, he had severe uncontrolled CRSwNP: NPS=6 (Nasal Polyp Score) and SNOT-22=69 (Sino-Nasal Outcome Test 22). The patient is also affected by central serous chorioretinopathy and therefore has a contraindication to the use of both topical and systemic corticosteroids[1]. He is on chronic therapy for severe asthma with Montelukast 10 mg/day, Tiotropium bromide Respimat 2.5 mcg two inhalations/day, and Salmeterol 25 mcg two inhalations/day. Spirometry showed moderate airflow limitation (FEV=61% of predicted, FEV1/FVC=66%). Blood eosinophils were between 700 and 930 cells/mcl, total serum IgE was 242 kU/ml, and the Fractional exhaled Nitric Oxide (FeNO) measured in the clinic was 362 ppb. The patient had poor asthma control according to the Asthma Control Test (ACT score 7) and at least 1-2 exacerbations requiring systemic OCS (oral corticosteroids) per year. The patient was deemed eligible for therapy with dupilumab, an anti-IL4 receptor alpha monoclonal antibody, with a dual indication: severe asthma with evidence of Type 2 inflammation and severe, uncontrolled CRSwNP[2,3].

Problem statement

The patient undertook treatment with dupilumab and enrolled in the FeNO@home protocol for daily measurement of FeNO, with the intention of closely monitoring the progress of the biomarker and correlating it to the clinical efficacy of the biologic drug.

Investigation

The patient was included in the FeNO@home study[4] outside grass 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

FeNO values were reduced by 23% in a single day of dupilumab therapy: from a baseline value of more than 300 ppb to 231 ppb; further reduction occurred in the following 4 days down to 80 ppb on the fifth day of therapy, corresponding to a reduction of 73.3% compared to the baseline value (see figure). Dupilumab therapy was associated with rapid improvement in asthma symptoms and control, rhinosinusitis outcomes (SNOT-22: 69 to 6 at 3 months, and up to 4 after 6 months of therapy; NPS 6 to 2 after 3 months, down to 0 after 6 months of therapy), and respiratory function which normalized at 6 months (FEV1 61% to 111% of predicted).

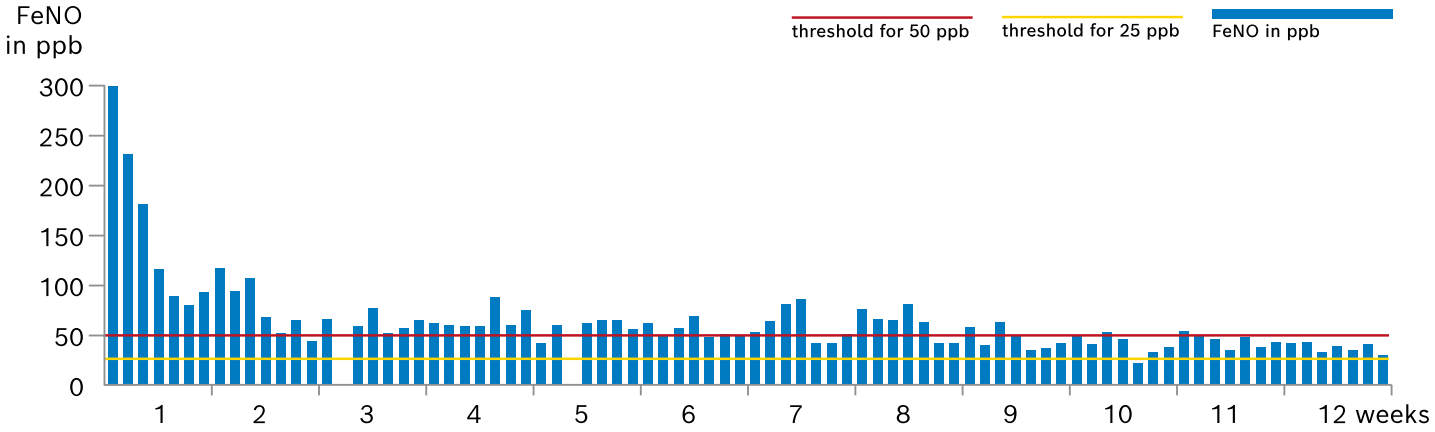

Figure: Course of the FeNO values based on regular home measurements by patients, thresholds according to ATS guideline[5]

Discussion

In severe asthma it is important to choose biologic therapy according to the predominant endotype. However, identifying the most appropriate biologic is often complex, especially in patients who fall into multiple phenotypic classifications (as in the case of the patient described here who is allergic and therefore potentially eligible for omalizumab, eosinophilic and therefore eligible for anti-IL5 drugs, and with evidence of high levels of FeNO and therefore eligible for dupilumab). It is therefore important to have a biomarker available that changes with rapid kinetics, after the start of treatment, if the immunological target of the biologic drug is correct; in fact, this allows for the rapid identification of patients who will have a high probability of a clinical response and therefore feel confident in continuing the therapy. Both in clinical trials and in real life studies[6-8], dupilumab has proven effective in improving clinical and inflammatory outcomes (precisely FeNO[8]) very quickly. This case report confirms and extends the rapid action of dupilumab in reducing FeNO in a patient who is clinically particularly responsive for both asthma and CRSwNP.
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 reinforce the beneficial effects of FeNO home measurement for physicians and asthma patients.

Conclusion

In conclusion, the case described here highlights an extremely rapid effect of dupilumab in terms of FeNO reduction, concomitant with a rapid improvement in clinical outcomes of asthma and nasal polyposis. This finding would not have emerged if FeNO had not been measured regularly at home.

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