Peripheral airway/alveolar nitric oxide concentration in asthma

We read with great interest the paper by Gelb and colleagues who suggest that peripheral airway/alveolar nitric oxide (NO) concentration after correction for axial NO back-diffusion (CalvNO\textsubscript{corrected}) is normal during asthma exacerbation (with a hypothesis of an incidence of >30% of its increase). If one admits that an exacerbation constitutes the ultimate expression of loss of asthma control, their results are in line with ours demonstrating that CalvNO\textsubscript{corrected} is not a marker of asthma control. Nevertheless, some of their patients with an exacerbation had an increase in CalvNO\textsubscript{corrected} since one can see in their figure 5 that almost 20% of their patients are above the 95th percentile of healthy subjects (~7 ppb). The small size of their cohort (n=15) is an obvious limitation that is acknowledged by the authors.

We therefore reanalysed the results of our multicentre trial\textsuperscript{1} to evaluate the prevalence of increased CalvNO\textsubscript{corrected}. When using an upper normal limit of 7 ppb for CalvNO\textsubscript{corrected} (that corresponds approximately to their upper normal value\textsuperscript{1}), the prevalence of its increase is 23% (41/175) in our population of adults and children with asthma. In our study we further demonstrated a negative relationship between CalvNO\textsubscript{corrected} and mid forced expiratory flow (FEF\textsubscript{25–75}%), which may suggest that peripheral NO could be associated with airway remodelling\textsuperscript{2}. This latter result was in line with the demonstration that peripheral airway/alveolar NO concentration (without correction for axial NO back-diffusion) correlated with FEF\textsubscript{25–75} in children with refractory asthma.\textsuperscript{3} Puckett and colleagues recently suggested that children with asthma with increased CalvNO\textsubscript{corrected} (46/179, 26%) had significantly worse asthma control and morbidity.\textsuperscript{4} Overall, all these results emphasise that peripheral airway/alveolar NO concentration, after correction for axial NO back-diffusion, can be increased in some patients with asthma (~25%). Whether peripheral NO helps to identify a specific ‘phenotype’ of asthma which may be more closely linked to severity than to control warrants further studies.

Gelb and colleagues also show that 2/15 subjects with an exacerbation had normal exhaled NO values.\textsuperscript{1} Similarly, we have previously shown in a multicentre trial that patients with acute asthma admitted to the emergency department can have normal peripheral NO fraction (2/65 patients in our study).\textsuperscript{5}

In conclusion, the clinical usefulness of techniques to discriminate NO gas exchange between large central airways and peripheral smaller airways/alveolar compartments in patients with asthma remains to be established, and the factors governing the increase in exhaled NO remain partly determined.

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