

Nasal airwayb nitric oxide – methodological aspects and influence of inflammation

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ABSTRACT

Nitric oxide (NO) is an endogenously formed free radical gas involved in numerous biological processes. In 1991 NO was discovered to be present in exhaled air of humans. Soon after, it was reported that the largest amounts of NO were found in the upper airways, and that the levels of NO were increased in the lower airways of patients with asthma. The high levels of NO in the nasal region are believed to be involved in functions as various as primary host defence, including killing of microbes and stimulation of ciliary motility, in inflammation and in aiding oxygen uptake in the lower airway. Extremely low values of nasal NO have been found in patients with ciliary dysfunction and cystic fibrosis. Consensus has been reached on how to measure orally exhaled NO, but the methodology for nasal NO measurements is still being discussed.

Besides NO, carbon monoxide (CO) is also found in exhaled air, and, like NO, CO levels are altered in various airway disorders. Furthermore, CO has been found in the upper airways of healthy humans. Thus, CO and NO seem to coexist in the airways, both in health and disease.

We wanted to establish a new method for nasal measurements of NO and CO, and to characterize normal upper and lower airway output of NO and CO in healthy subjects. We also wanted to study airway NO release in humans with systemic or localized inflammation, as in HIV/AIDS, endotoxaemia and allergic rhinitis.

Surprisingly, we found that only NO, but not CO, could be consistently detected in the healthy human upper airway. we also found that a mouthwash procedure, aiming at increasing pH in the oral cavity, did not influence levels of nasally exhaled NO, whereas it reduced both oral contribution to and methodological variation in the measurements of NO in orally exhaled air. Hence, we introduced a new method for nasal NO measurements, based upon a highly standardized single breath technique The method provides information about the contribution of the supravelar space to airway NO release.

Using this method, we found reduced nasal NO levels in patients with HIV/AIDS, and suggested that this reduction may contribute to the decreased resistance to airway infections in these patients.

Orally exhaled NO, but not nasal NO, increased during experimental human endotoxaemia. Further studies will show whether exhaled NO may be valuable as a marker of sepsis-induced lung injury.

Also, a high inter-individual variation in nasal NO levels was found, and orally exhaled NO levels were elevated in patients with allergic rhinitis. Further studies will reveal if the patients with allergic rhinitis and decreased nasal NO are at risk of developing paranasal sinus disease, and if those with increased orally exhaled NO are at risk of developing asthma.

In conclusion: Nasal NO measurements are non-invasive and easy to perform. With improved methodology such measurements may be useful for the screening, diagnosing or monitoring of inflammatory disorders affecting the upper airways.