Nasal mucociliary transport in healthy subjects is slower when breathing dry air

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Nasal mucociliary transport in healthy subjects is slower when breathing dry air. B. Salah, A.T. Dinh Xuan, J.L. Fouilladieu, A. Lockhart, J. Regnard.
ABSTRACT: We assessed the effect of dry air (DA) nasal breathing on nasal clearance rate in healthy nonsmoking subjects. We measured saccharin nasal transit time (SNTT), an index of mucociliary clearance rate, in eleven normal subjects (six males, five females) breathing either room air (RA) or DA through the nose in random order on six different study days. On each study day, the trial was conducted at the same time, in the same nostril, using a patent airway. DA was breathed through a light-weight, tight-fitting, nasal mask (SEFAM, France) for 30 min and SNTT was then measured immediately. Saccharin (250 μg) was deposited on the anterior part of the inferior turbinate under visual control and saliva was swallowed every 30 s thereafter. SNTT was the time elapsed between deposition and first perception of saccharin taste. The group-average SNTT on DA was 18.5±8.6 min which was significantly longer than on RA (11.9±5.3 min). Our findings suggest that dry air breathing results in excessive water loss by the nasal mucosa, which may in turn reduce nasal mucociliary clearance rate through changes in the rheological properties or adhesiveness of nasal mucus and/or slowing of ciliary beating.
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Nasal mucociliary clearance is a primary defence mechanism of the upper airways in man [1]. Alteration of the mucociliary function is observed with airway exposure to various ambient pollutant gases [2–4] and/or under various atmospheric conditions [5–7]. Sulphur dioxide reduces nasal [2] and tracheobronchial [3] flow of mucus in man and exposure to ozone alters tracheobronchial mucociliary function in healthy nonsmoking subjects [4]. Results of studies on the effects of atmospheric conditions are less consistent. The noxious effects of extreme temperatures is well established [5], whereas the role of relative humidity remains controversial [6, 7].

Dry air breathing facilitates the incidence of exercise- and hyperventilation-induced asthma in susceptible patients, which suggests that it disturbs the normal structure or function of the airway epithelium through some poorly understood mechanism [8]. Prolonged exposure of the airways to ventilation with dry air causes structural changes of the cilia in dogs [9] and acute inflammation of the mucosa in the trachea of cats [10]. Furthermore, a short exposure of the trachea to dry air also causes marked sloughing and disruption of the tracheal epithelium and local inflammation in guinea-pigs [11].

We wondered whether a short exposure to dry air might alter mucociliary function and reduce mucociliary clearance in man. Whereas nasal mucosa can be exposed to extremely dry air, airway mucosa distal to the pharynx is normally exposed to saturated gas at the prevailing local temperature which is normally about 34–35°C [12, 13]. Therefore, we decided to study the effects of dry air breathing on nasal mucociliary transport.

Subjects

We studied eleven healthy nonsmoking subjects (six males, five females), aged 17–38 yrs (mean±SD, 29±7 yrs), all of whom worked in our laboratory. None had a history of personal or familial atopy, nasal trauma or facial surgery. They had not suffered from an upper or lower airways infection during the two preceding months and had not taken any medication during the month preceding the study. None of them had been submitted to ambient pollutant particles. The study was approved by the Ethical Committee of our Medical School and fully explained to the subjects who gave informed consent.

Methods

Outline of the study

The subjects were studied on six different days and saccharin nasal transit time [14] was measured at the same time on each occasion. They were instructed to abstain from drinking tea or coffee between the

preceding evening and the end of each trial. The subject breathed either ambient room air or dry air for three study days each. The allocation of room or dry air breathing was randomized. Room air breathing could be followed by a consecutive study day whereas there was no further study during the 72 h that followed an exposure to dry air.

Technical details

Compressed air, desiccated (by passing it through silica gel) and filtered, was supplied at a flow rate of 20 $l \cdot min^{-1}$ to a light-weight, tight-fitting nasal mask (SEFAM, France). It was administered for 30 min while the subject breathed through the nose. Temperature and relative humidity (RH) of both dry air and ambient room air were measured on each study day with a capacitance probe (Model Pt 100, SOLOMAT, England). Partial pressure of water vapour (P_{IH_2O}) in ambient air was calculated from ambient temperature, RH and barometric pressure.

In order to consider both circadian and nasal rhythms [15], the most patent nostril to airflow, as determined by inspection with a headlight and nasal speculum was chosen for deposition of saccharin. The same nostril was used throughout the study. Saccharin powder (250 µg) was placed on the anterior part of the inferior turbinate by visual inspection, 2 cm posterior to the nostril aperture. The subject was asked not to breathe through the nose or to sniff. If the subject sneezed, the study was cancelled. After saccharin deposition, saliva was swallowed every 30 s. The saccharin nasal transit time (min) was the time elapsed between the deposition of saccharin and the first perception of a sweet taste by the subject.

Statistical analysis

The entire set of values of saccharin nasal transit time was analysed by a two-way analysis of variance for repeated subject measurements with crossed over experimental conditions, namely ambient and dry air.

Results

Temperature and RH of ambient room air were 22–24°C and 40–43%, respectively. Dry air RH and temperature were below 0.1% and 25–29°C, respectively. Accordingly, P_{IH_2O} was 0.8–1.6 kPa and zero, in room and dry air, respectively.

Triplicate values of saccharin nasal transit time did not differ by more than ±3 min in a given subject studied in the same experimental conditions. Intra-individual coefficients of variation are listed in table 1. Triplicate measurements on room air as well as on dry air did not differ from one another. Individual saccharin nasal transit time averaged over the three days on ambient

room air and dry air are presented in figure 1. Differences between subjects were large (fig. 1) with interindividual coefficients of variation on ambient room air and dry air of 0.44 and 0.46, respectively. Compared to ambient room air, dry air breathing significantly increased the group average saccharin nasal transit time (SNTT) from 11.9±5.3 min to 18.5±8.6 min (mean±SD), respectively (p<0.01). There was no correlation between P_{IH_2O} and SNTT on ambient air breathing.

Table 1. – Intra-individual coefficients of variation of saccharin nasal transit time

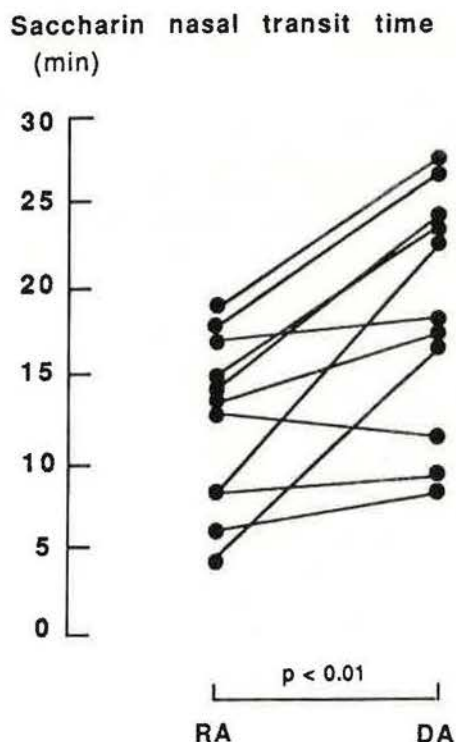| Subject no.	Room air	Dry air
1	0.20	0.25
2	0.19	0.10
3	0.29	0.19
4	0.38	0.19
5	0.09	0.08
6	0.10	0.24
7	0.28	0.14
8	0.12	0.71
9	0.00	0.50
10	0.17	0.33
11	0.08	0.11

Fig. 1. – Means across three study days of individual saccharin nasal transit time on ambient room air (RA) (T=22–24°C, P_{IH_2O}=0.8–1.6 kPa) and after 30 min on dry air (DA) (T=25–29°C, P_{IH_2O}=0), P_{IH_2O}: partial pressure of water vapour; T: temperature.

Discussion

The main finding of our study is that a short exposure of nasal airways to dry air impaired nasal mucociliary clearance, as demonstrated by the consistent

and significant prolongation of saccharin nasal transit time in healthy nonsmoking subjects.

Since we only studied healthy nonsmokers, any potential bias related to the effect of smoking on mucociliary function [16] was eliminated. The saccharin nasal transit time that we used to assess nasal mucociliary clearance was originally described by ANDERSEN and co-workers [14]. This method is both safe and non-invasive and does not involve use of radioactive particles [17], radio-opaque material [18], or sophisticated and expensive equipment. Although some authors found that saccharin mean transit time was poorly correlated with nasal mucus velocity and was therefore unsatisfactory [18, 19], other authors found a good correlation between both tests in normal subjects [14, 20]. Reasons for this discrepancy are not known. In our study, day to day reproducibility of saccharin mean transit time on both room and dry air was on average acceptable, although it varied between individuals (table 1) despite standardized experimental conditions. We also found large inter-individual variations of the saccharin nasal transit time in our subjects, an observation already reported [21, 22], but the reasons for such large differences are still unknown [1].

The study was not double-blind, because the subjects were aware of breathing dry air. Furthermore, saccharin nasal transit time is subjectively determined since it relies on perception by the subject of a sweet taste. However, with the exception of three of the authors, the subjects did not know the potential effect of dry air on nasal mucociliary clearance. Therefore, the study was virtually single-blind.

The visual assessment of nasal patency may not reflect nasal resistance which would have been better assessed by anterior rhinomanometry. However, inspection through a light nasal speculum takes very little time and so disturbs nasal mucociliary clearance rate less than the longer obturation of both nostrils necessary for anterior rhinomanometry. Since each trial started at the same hour of the day, our finding that the same nostril was always the more permeable one is consistent with the concept that the nasal cycle is tied into the circadian system [15].

Results of previous studies [5–7] in climatic chambers are less clear-cut than our results. ANDERSEN and co-workers were unable to detect any change in nasal mucus flow rate with 8 h exposures to 70, 50, 30 and 10% RH [5] and with 78 h exposure to 9% RH [6], at 23°C. PROCTOR et al. found only a slight decrease in nasal mucociliary clearance rate when the temperature of ambient air was reduced to 15°C [7]. The marked slowing of nasal mucociliary clearance rate in our study may be due to technical reasons. We used a nasal mask continuously flushed with dry air and exclusive nasal breathing throughout the exposure to dry air. Conversely, it is likely that subjects exposed to cold and dry air in climatic chambers for various periods of time breathed through both nose and mouth. It is possible, therefore, that we used a stronger, though less physiological stimulus, than was used in the other studies. Alternatively, adaptation may take place during

prolonged exposure to dry air [6] and offset the acute initial effects of the latter.

We can only speculate about the reasons for the significant slowing of nasal mucociliary clearance rate caused by dry air in our subjects. We do not know whether nasal airflow resistance increased after dry air exposure as has been reported after cold air breathing [7]. Since a rise in nasal airflow resistance results from vascular congestion [23] and since increased water evaporation in dry air must have a cooling effect, we can hypothesize that dry air breathing enhanced nasal airflow resistance. However, none of our subjects complained of nasal obstruction and the role of vascular congestion in the slowing down of nasal mucociliary clearance rate has not, to our knowledge, been documented. It is unlikely that our results were biased by a residual effect of an initial exposure on subsequently measured SNTT. Firstly, there was no significant difference between SNTT measured either on two consecutive study days on room air or 72 h apart on dry air. Secondly, SNTT on room air was the same whether it was measured on the initial study day or 72 h after an exposure to dry air.

It is likely that the primary reason for the prolonged nasal mucociliary clearance was the result of excessive water loss due to prolonged dry air breathing [24]. As a result of dehydration dry air breathing may result in a reduced thickness of the sol phase of the periciliary fluid or in changes of the rheological properties of the mucus itself. Such modification of the nasal airway lining fluid may in turn inhibit ciliary movements. Results of studies of the correlation between nasal ciliary beat frequency and mucus transport rate are controversial [22, 25, 26]. Modification of the mucus itself may play a major role in alterations of nasal mucociliary clearance [1]. We can only speculate that the primary factor of the prolonged saccharin nasal transit time after dry air breathing was a change in the rheological properties or in adhesiveness of the mucus. Firstly, there is a positive correlation between the transport capacity of human nasal mucus measured *in vitro* on frog palate [27] and the nasal mucociliary clearance assessed *in vivo* by the saccharin nasal transit time [28]. Secondly, there is circumstantial evidence in favour of changes in the rheology of nasal secretions after breathing dry air. Cholinergic reflexes [15] or local release of neuropeptides [23] may be activated by the irritant effect of dry air and stimulate secretion of watery fluid by nasal glands. In addition studies with human tissue *in vitro* have shown that secretion of airway mucus is controlled by cholinergic mechanisms [29, 30].

Since the correlation between nasal and tracheobronchial clearance is controversial [14, 21] our finding that dry air breathing markedly reduced nasal mucociliary clearance rate cannot be extrapolated to tracheobronchial mucociliary clearance. We do not know whether the slowing of nasal mucociliary clearance rate on dry air breathing has any deleterious effect on the protective role of nasal airways mucosa.

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RÉSUMÉ: Nous avons étudié l'effet de l'inhalation nasale d'air sec sur le transport muco-ciliaire nasal, chez des sujets sains et non fumeurs. A cet effet, nous avons mesuré le temps de transit nasal de la saccharine (TTNS), indicateur du transport muco-ciliaire nasal, chez onze sujets sains (six hommes et cinq femmes) pendant six jours d'étude différents répartis de façon aléatoire entre jours avec inhalation d'air ambiant et d'air sec, les sujets respirant uniquement par le nez. L'étude a débuté chaque jour à la même heure pour un même sujet, et le TTNS a été mesuré pour chaque sujet dans la même narine afin de tenir compte des rythmes circadien et nasal. L'air sec a été inhalé grâce à un masque léger et bien ajusté (SEFAM, France) pendant 30 minutes, et le TTNS a été mesuré immédiatement après. La poudre de saccharine (250 µg) a été déposée à la partie antérieure du cornet inférieur sous contrôle visuel, et l'on a demandé au sujet d'avaler sa salive toutes les 30 secondes jusqu'à perception d'un goût sucré. Pour l'ensemble des sujets, le TTNS est significativement plus long (analyse de variance: p<0,01) sous air sec (18.5±8.6 minutes) que sous air ambiant (11.9±5.3 minutes). Nos résultats suggèrent qu'un air desséché peut entraîner une déperdition hydrique excessive de la muqueuse nasale, ce qui peut réduire le taux de clairance muco-ciliaire nasale par modification des propriétés rhéologiques ou de l'adhésivité du mucus et/ou par ralentissement des battements ciliaires.