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Effect of nasal air temperature on lung function

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Date:
Accepted for publication 13 August 1998

To cite this article:
Millqvist E. Effect of nasal air temperature on lung function.
Allergy 1999, **54**, Suppl 57, 106–111.

ISSN 0105-4538

Introduction

Inhalation of cold air is known to induce intrapulmonary airway obstruction in sensitive asthmatic patients and this is a condition often ascribed to heat and water losses from the airway mucosa (1–6). However, the pathophysiological mechanism explaining why airway cooling and exercise cause broncho-obstruction is not yet clear. The fact that anticholinergic drugs suppress exercise-induced asthma may indicate a reflex through the vagal nerve, although blockade of this nerve does not completely prevent broncho-obstruction induced by exercise in asthmatic patients (7–11). The fact that sodium cromoglycate prevents the development of exercise-induced asthma (9, 12–15) and that elevated levels of histamine are present in exercise-induced asthma (11, 16–18) indicate that mediators may be involved. The importance of the latter is uncertain, since antihistamines have a poor preventive effect in exercise-induced asthma (19). Changes in osmolarity of the airway lining may also be an important factor (20–22). Furthermore, asthmatic patients react with broncho-obstruction when challenged with hypo- and hyperosmolar solutions (23, 24) (Fig. 1).

Relation between upper and lower airways

Some evidence of a nasobronchial reflex between the upper and lower airways has been reported but its existence has not been established. In animal experiments, mechanical stimuli or insufflation of irritating chemical agents into the nose induces bronchodilation (25, 26) or broncho-obstruction (27, 28), or it may have no bronchial effect at all (29). In humans, mechanical or chemical stimuli in the nose and nasopharyngeal area induce increased resistance in

the intrapulmonary airways in healthy subjects (30). In the older German literature, a reflex from the nose to the lung via the trigeminus nerve was proposed – the "Wetter und Windreflex" (31).

According to the patients, obstruction is often rapidly induced by exposure to cold air. It seems unlikely that the degrees of heat and water losses from the airway mucosa provide the only explanation of these symptoms. Berger et al. noticed that cold stimulation in the nose of asthmatic patients increased the resistance of the lower airways (32). The effect could be blocked by first inhaling an anticholinergic drug. The authors believed that a reflex from the upper airways hastened the onset of obstruction. However, they did not prove that the cold air administered via the nose had failed to reach the intrapulmonary airways, nor did they use any controls. More recently, Fontanari et al. studied the consequences of nasal breathing of cold air in normal and asthmatic subjects and found an increase in interruption resistance that could be prevented by nasal anaesthesia or inhalation of a cholinergic antagonist (33, 34). None of these studies proved that the cold air did not reach the lower airways.

Cold air provocation at the nose and face, respectively, in healthy normals and asthmatic patients induced an increase in airway resistance (35–38). However, in these studies cold air may have reached the pulmonary airways and induced bronchial obstruction by cooling and/or drying of the airway mucosa. Thus, although the existence of a nasobronchial reflex seems likely, at least following mechanical and chemical stimuli, it has not been demonstrated convincingly in connection with cold and warm stimuli.

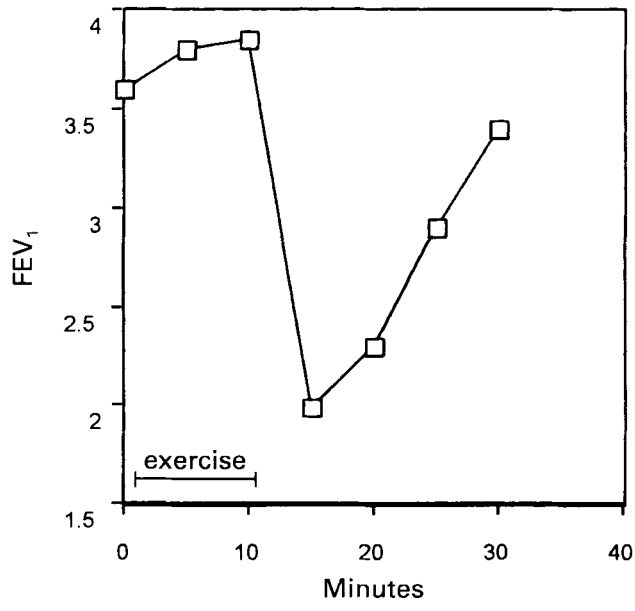

Figure 1. Typical course of exercise-induced asthma. FEV_1 increases during exercise, declines at the end of the exertion, with a maximum a few minutes after cessation, and then gradually returns to the initial level.

The neural control of the human nose and lung is a complex system. The sensory innervation of the nose is derived mainly from the trigeminal nerve. In the human lung, parasympathetic efferent fibres are conducted by the vagus nerves to the parasympathetic ganglions in the bronchial wall. The baseline bronchomotor tone was thought initially to be regulated by a balance between contracting, parasympathetic impulses and dilating, adrenergic impulses having a direct influence on the smooth muscle cell via β-adrenoceptors. A third, efferent, nonadrenergic, noncholinergic pathway remains largely undefined, because no suitable inhibitor for this pathway or its neurotransmitter has yet been described (40–44).

In some individuals, cold air challenge of the nose leads to mast cell inflammatory mediator release (45–48) which could be a possible explanation to our results, described below.

From a clinical point of view, the relationship between asthma and sinusitis has often been discussed (49–51). In patients with allergic rhinitis, bronchial reactivity towards methacholine is increased (52) and in patients with perennial rhinitis, lower airway resistance increases after nasal challenge with histamine (53), but other studies have reported conflicting findings (54, 55). There is a well-known connection between nasal polyps, aspirin intolerance and asthma (56–58). In adults with asthma, intolerance to aspirin occur in 5–10% and in this group about half the patients have nasal polyps (58).

In the study presented below, we investigated whether changes in the nasal air temperature affected lung function in asthmatic patients and healthy subjects, when care was taken to prevent cold air from reaching the lower airways.

Patients and methods

Ten patients, seven women and three men (20–48 years) with a history of cold-sensitive asthma and eight healthy subjects, three women and five men (25–57 years), took part in this study. All patients had regular treatment with inhaled corticosteroids and used intermittent inhaled β_2-stimulants. Two patients had regular treatment with inhaled long-acting β_2-stimulants and one topical nasal corticosteroid. All patients had a history of atopy and had earlier shown an increase in FEV_1 of at least 20% after the

inhalation of a β_2-stimulant. On most days they had no asthmatic symptoms. None of them smoked. No medication was taken for a minimum of 12 h before any test. Long-acting bronchodilators were withheld for at least 24 h.

The provocations were performed on 3 separate days, at approximately the same time each day, in a randomized order with air of various temperatures, i.e. cold air (about −15°C), ambient air (about +22°C) or warm air (about +37°C). At each nasal provocation, an airstream (0.6 l/s) was blown into both nostrils through a nose halter. A provocation consisted of 10 puffs of air of 15 s duration each at 1-min intervals between the puffs. In the halter, just at the edge of the nose, a thermistor recorded the temperature of the air. Cold air was obtained from an air cylinder, stored in a freezer. Ambient air and heated air were obtained from the central hospital system and were led through a temperate water-bath for moistening and regulation of the temperature. The airflow passing from the nose out through the mouth was monitored by a pneumotachograph connected to a mouthpiece. Shortly before each puff of air, the patients made a Valsalva manoeuvre. Positive intrathoracic pressure against the glottis was maintained during the provocation and for a few seconds thereafter. A constant positive pressure excluded any leakage of air from the nose to the lower airways during the nasal provocations. Pressure in the oesophagus was monitored by an oesophageal balloon, which was inserted through the mouth and swallowed without local anaesthesia. The pressure was recorded on a direct writer, together with the provocation air temperature and mouth flow.

Specific airway conductance (SGaw) and 1-s forced expiratory volumes (FEV_1) were determined before and 0, 5, 10 and 15 min after the provocations. SGaw was determined in a body plethysmograph and FEV_1 with a spirometer (Vitalograph, Buckingham, UK). Recordings of SGaw always preceded those of FEV_1 and the recordings were evaluated blindly.

Before each provocation an oesophageal balloon was swallowed. The patients then rested for a quarter of an hour before SGaw and FEV_1 were measured. Thereafter, the nasal provocation took place with the patient seated in an upright position and connected to the nose halter and the mouthpiece, as described above. After the 10 puffs of air lasting 15 s each at 1-min intervals (and therefore 10 Valsalva manoeuvres), the balloon in the oesophagus was removed and again the symptom scores, heart rate and blood pressure were recorded. This was again followed by recording SGaw and FEV_1.

The effects of these provocations were analysed by calculating "the area under the curve" – i.e. an expression of the overall difference from baseline and by analysis of variance (ANOVA) and by the Wilcoxon signed rank test. *P*-values less than 0.05 were considered significant.

Results

Changes in SGaw in percent from baseline after the three provocations are illustrated in Fig. 2. Cold provocation caused a significant fall of SGaw and warm air provocation a significant rise in the asthmatic patients (left panel), whereas there were no significant effects of room air provocations. Furthermore, the differences in SGaw-areas under the curves were significantly different between all three provocations. Ten minutes after the cold air provocation SGaw fell, on average, by 23% ($P<0.005$) and rose directly after the provocation with warm air on average 15% ($P<0.05$). In the normal subjects (right panel) there were no significant differences.

Fig. 3 shows the corresponding results for FEV_1. In the asthmatics (left panel) FEV_1 fell on average by 8% ($P<0.05$) 5 min after the cold air provocation and rose directly after warm air provocation on average by 6% ($P<0.05$). Analysis of the area under the curve revealed that all three provocations differed significantly in the asthmatic patients, in accordance with the SGaw recordings. In the healthy subjects (right panel) the provocations caused no significant differences.

Discussion

The present results confirm the existence of an interplay between the nose and the rest of the airways; the mechanism could be due to a trigeminal reflex or a mediator release.

Cold air stimulation at the nose induced a decrease in airway conductance and FEV_1, and warm air stimulation had the opposite effect. Although it is believed that the nasal mucosa lacks temperature receptors, it has been shown that hyperosmolar stimuli can induce naso–nasal reflexes (47). These sensory nerves could possibly signal to the central nervous system on the basis of the osmolarity of the intraepithelial junction fluid. This continuous impulsing may result in nasal glandular secretion and baseline smooth muscle tone being regulated by the nasal mucosa. When warm, moist air is inhaled the osmolarity is decreased

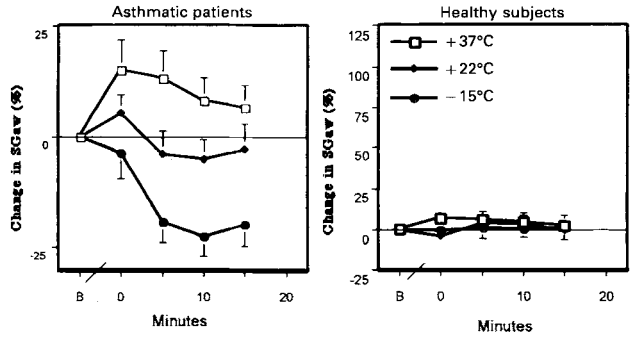

Figure 2. Changes in SGaw after nasal provocations with −15°C, +22°C and +37°C. The results are shown as mean values expressed in percentage of the preprovocation values. Mean values and SE are given. "B" denotes before provocation.

and the impulse rate may drop precipitously. This would result in reduction in airway tone followed by bronchodilation.

We do not know the reason for the discrepancy in the effects of nasal air temperature between asthmatics and normals. Rhinitis is characterized by mucosal hyperreactivity and found in almost all asthmatic patients. Hyperreactivity is, to a great extent, neuronal in nature (subjects with perennial rhinitis respond more intensely to capsaicin and to cold dry air than healthy individuals (60, 61)). It is possible that cold air generate a central spasmogenic reflex by stimulating hyperreactive sensory nerve endings and that this only occurs in a hyperreactive, not healthy nose. Another possibility is that the signal is generated by the nasal mucosa of both groups but leads to bronchial obstruction only in asthmatics. Perhaps the reactions are less pronounced in normal people and therefore remained undetected in the present limited study.

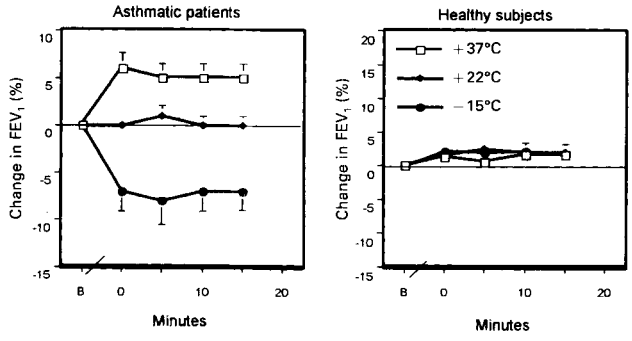

Figure 3. Changes in FEV_1 after nasal provocations with −15°C, +22°C and +37°C. The results are shown as mean values expressed as percentage of the pre-provocation values. Mean values and SE are given. "B" denotes before provocation.

The changes in airway conductance and FEV_1 after cold or warm air provocation may have been due to varying airway muscle tone, to varying degrees of oedema of the airway mucosa, to varying amounts of mucus secretions in the airway lumen or to any combination of these factors. The changes occurred immediately after the provocations, a fact that may indicate a change in muscle tone as the major mechanism. After the provocation with cold air the depression of lung function seemed to occur quicker when measured with SGaw compared to FEV_1. This might be dependent on the SGaw measurements always preceding those of FEV_1 (and thus there was some minutes delay for the FEV_1 measurements) or the possibility that these methods reflected different parts of the lungs, e.g. small and large airways. The results of SGaw and FEV_1 after the provocations are consistent, although there were some individual variations.

During nasal breathing at rest, the inspired air temperature at the carina is about 36°C when breathing room air (about 20°C) and about 33°C when breathing air of −20°C. The inspired air in the trachea is almost saturated with water, irrespective of inspired humidity and temperature. The corresponding air temperatures at the carina during oral breathing are 35°C and 32°C at rest, but there is a fall to about 25°C during maximal hyperventilation with cold air (62, 63). When asthmatic patients hyperventilated cold air, their bronchial obstruction was found to be less severe during nasal than oral breathing (6). If breathing cold air through the nose activates a nasobronchial reflex, its effect is offset by the conditioning capability of the nose. During exercise, however, most people switch to oronasal breathing (64) and bypass much of the heat and moisture exchanging properties of the nose.

Conclusions

This study confirms a relationship between the upper and lower airways. In asthmatic patients, cold air administered in the nose caused broncho-obstruction and warm air resulted in bronchodilation. What may be the importance of a nasobronchial interplay? This appears to be of little or no importance in healthy subjects. In asthmatic patients it may act as a warning signal to prevent the airways from additional exposure to cold air. It is a clinical experience that some asthmatic patients have a very rapid onset of cold-induced asthma symptoms and this could originate from the nose. Further knowledge of the physiology related to the nasobronchial interplay may be of therapeutic value in treating asthma.

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