Rhinology, XVII, 193–198, 1979

On nasobronchial reflex in asthmatic patients

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SUMMARY

In 27 asthmatic patients a single cold stimulus into the nose resulted in a sudden increase of airway resistance, measured continuously by a new forced-oscillations-technique. The effect could be blocked by previous intrabronchial application of an anti-cholinergic drug.

In laryngectomised patients, who no longer have a connection between the upper and the lower airpathways, cold stimuli into the nose caused a bronchoconstriction just as it did in the asthmatics. So the cold effect must be based on a reflex mechanism.

Patients suffering from obstructive respiratory disease often complain of an increase in discomfort when they inhale cold air. Several investigators have already proven that this is not the result of a direct, local effect of cold, but a vagus reflex (Nolte and Ulmer, 1966; Nolte, 1975; Strauss et al., 1977; Wells et al., 1960). On the other hand, it is a little known fact that cold irritation outside of the sensitive vagus region – e.g. the facial skin and mucous membrane of the nose – can produce reflectory bronchoconstriction (Josenhans et al., 1969). Consequently, the advice often given to asthma patients that they should breathe through the nose when they are out in cold weather is of questionable value. Just how important the reflectory connections between upper and lower airways can be for the asthma patient will be demonstrated by the following experiments.

METHODS

By several investigators the bronchoconstrictory effect of cold air has been demonstrated by the bodyplethysmographic method (Nolte and Ulmer, 1966; Strauss et el. 1977; Wells et al., 1960). Although we have been concerned

Paper presented at the 7th Congress of the European Rhinologic Society. Davos (Switzerland), September, 1978.

with the most accurate method of measurement up to now, bodyplethysmography is not the most optimal for the problem as given because continuous measurement of airway resistance immediately after the application of the cold irritation is possible by very complicated means only. These particular experiments, therefore, were not conducted by the bodyplethysmographic method, but by the forced-oscillations-technique (Smidt et al., 1976) because it allows a continual measurement of airway resistance. Unfortunately the oscillatory resistance (R_{OS}) is influenced not only by the cross section of the airways, but also by the elastic properties of chest wall, lung and airways. Only when these factors remain constant do changes of oscillatory resistance indicate changes of the cross section of the airways.

The oscillation apparatus used was Model Siregnost FD 5 from Siemens, Erlangen, West Germany. The reader is referred to the present literature for details of the method (DuBois et al., 1956; Förster et al., 1978; Smidt et al., 1976).

The cold irritation was generated by a metered aerosol:

A local cold irritation is induced by the spray process when the propellant goes from the liquid to the gaseous state. With the aid of a special experimental design, it was possible to spray the aerosol into the nose without interrupting the measuring procedure (Figure 1). The duration of the single cold stimulus was only about 1 sec.

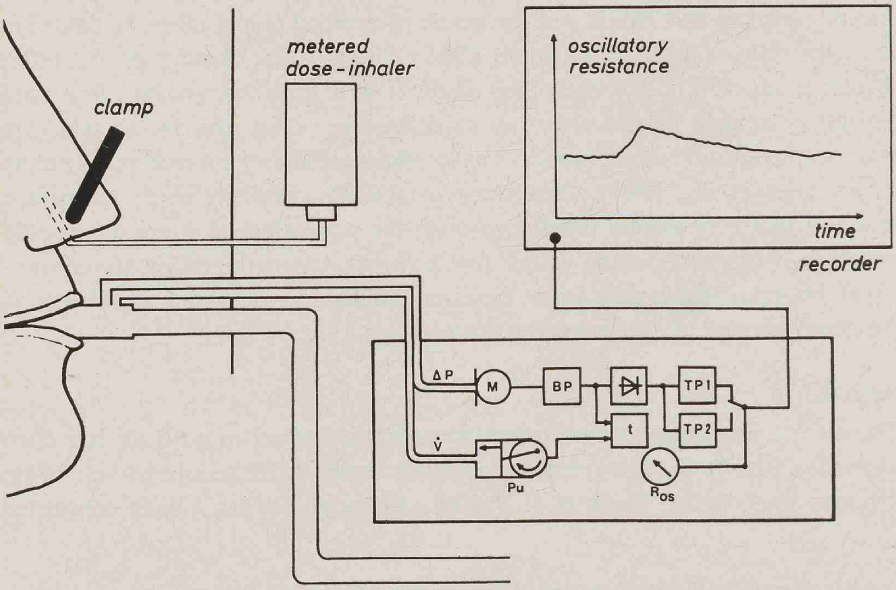

Figure 1. Experimental design.

Test Groups

1. 27 patients with bronchial asthma; criteria for this diagnosis: dyspnoea attacks and spontaneous or pharmacodynamic reversibility of an existing bronchial obstruction.
2. 3 patients who had been laryngectomised because of carcinoma of the larynx and who, in addition, had chronic bronchitis; criteria for this diagnosis were permanent cough and expectoration.
3. 7 healthy control subjects.

Experimental procedure

The seated proband was connected to the oscillation apparatus. After an adaptation time of at least one minute either instantaneous or time-averaged oscillatory resistance could be registered by a recorder. The patient did not know beforehand when the spraying process would be carried out.

RESULTS

Among 7 subjects with healthy lungs not one single case of a bronchoconstrictory effect was evident.

Among the 27 patients, 25 showed a marked increase in oscillatory resistance when the propellant was sprayed into the nose.

The resulting value increased from an average of 4,8 $cmH_2O/1/sec$ to 6,5 cm $H_2O/1/sec$. The difference among the mean values was statistically significant (student t-test, pair comparison, $p < 0{,}001$).

In each case the bronchoconstriction began immediately after application of the cold irritation and reached its peak within 10 seconds.

One can be quite sure that the observed initial increase in resistance is not an artifact of the oscillation method: when oscillatory and bodyplethysmographic measurements of the airway resistance are carried out simultaneously, initial resistance increase is confirmed here as well.

In 5 patients the effect of an anticholinergic drug has been proved. Preinhalation of 0,1 mg Ipratropiumbromide 15 minutes before the cold stimulation led to a markedly decrease of bronchoconstriction in all cases.

DISCUSSION

Clinical physicians have known for a long time how close the functional connections are between the upper and lower airways and furthermore, that manipulations in the nasal and laryngeal regions can easily induce bronchial spasms in asthma patients. In the last century these connections were proven with rather simple methods of measurement (Roy and Brown, 1885); however, it was first possible to explain them in recent times through extensive animal experiment studies (Angell and Daly, 1972; Boushy et al., 1972;

Kaufmann and Whright, 1970; Nadel and Widdicombe, 1962; Ulmer et al., 1971).

It is a question of a nociceptive reflex (Nolte, 1975) which, according to our findings, is of virtually no importance to lung-healthy subjects. On the other hand, this reflex can be pronounced in individual cases of asthma patients, as well as patients with hypersensitive bronchial system. According to experience, the cold irritation can be blocked on the efferent pathway by previous application of an anti-cholinergic substance: Figure 2 shows that there is no initial increase in resistance if the patient inhales the anti-cholinergic substance Ipratropiumbromid beforehand.

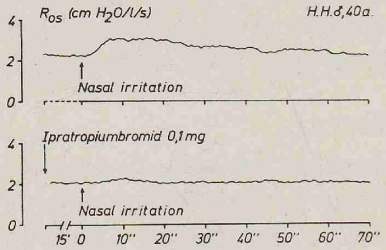

Figure 2. Blockage of the reflectory bronchoconstriction after pre-inhalation of the anti-cholinergic substance Ipratropiumbromide. Continuous registration of the time-averaged oscillatory resistance in an asthma patient during an attack-free phase.

Further proof of the reflectory nature of these effects are our observations of the laryngectomised patients. Although such patients no longer have a connection between the upper and lower airpathways, the propellant sprayed into the nose causes a bronchoconstriction just as it does in the asthma patient (Figure 3).

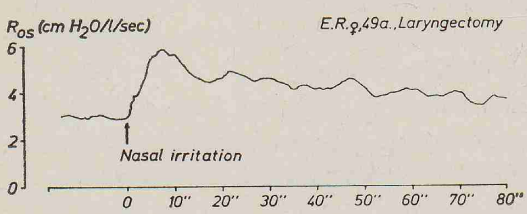

Figure 3. Reflex bronchoconstriction in a laryngectomised patient caused by intranasal cold irritation. Continuous registration of the time-averaged oscillatory resistance.

The reflectory connections between the nose and lower airways originate in the following way:

1. The afferent part is the trigeminal nerve. Bodyplethysmographic investigations carried out by Josenhans et al. (1969) demonstrated an increase in the airway resistance after the application of cold irritation to the facial skin. In patients who had a one-sided resection of the trigeminal nerve because of trigeminal neuralgia, Kaufmann et al. (1970) were able

to provoke an increase in airway resistance only by irritation on the healthy side. According to experience the reaction was also absent when the sensitive nerve endings were numbed by a local anaesthetic.

2. The efferent side is formed by the vagus nerve. Numerous animal experiments have proven that no resistance increase is further observable (Nadel and Widdicombe, 1962; Ulmer et al., 1971) after a dissection of the vagus nerve or after application of atropine. Specific experiments in which the pre-inhalation of the vagolytic substance Ipratropiumbromid could suppress the cold air effect support this as well.

These findings make it clear why asthma patients, who complain about an increase in the severity of their symptoms in cold weather, react with a bronchial spasm even when advised to breathe through the nose, instead of the mouth; the cold irritation in the trigeminal region alone is sufficient to induce the reflex bronchoconstriction.

ZUSAMMENFASSUNG

Intranasale Kältereize führten bei 27 Patienten mit Asthma bronchiale zu einem plötzlichen Anstieg der Atemwegsresistance, welche mit Hilfe einer neuen Oszillationsmethode kontinuierlich aufgezeichnet wurde. Durch vorherige Inhalation eines Anticholinergicums konnte dieser Effekt verhindert werden.

Auch bei Laryngektomierten, bei denen keine Verbindung der oberen und unteren Atemwege mehr besteht, riefen intranasale Kältereize – ebenso wie bei den Asthmatikern – eine Bronchokonstriktion hervor. Die beobachteten Effekte müssen daher auf einem Reflexmechanismus beruhen.

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