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Mucociliary transport in the human nose. Effect of topical glucocorticoid treatment

Kenneth Holmberg and Ulf Pipkorn, Göteborg, Sweden

SUMMARY

The effect of topical budesonide on the human mucociliary transport in the nose was investigated utilizing the saccharin-dye test in 10 healthy volunteers. Measurements were made before treatment, after a single dose and after one week continuous treatment with either placebo or active substance. The design of the study was double blind, randomized and cross-over. A single dose of placebo or budesonide did not alter the mucociliary transport as compared to pretreatment values. A trend towards decrease of mucociliary transport was noted after one week treatment with the active drug, a trend that reached statistical significance in the comparison between the 1 h value and the 1 week value.

INTRODUCTION

The mucociliary activity in the nose contributes to the defence mechanism of both the upper and lower respiratory tracts. Different diseases such as viral infections, chronic bronchitis, asthma are associated with impairment of the mucociliary transport. The chronic sinusitis and bronchiectasis in Kartagener's syndrome is secondary to the immotile cilia and subsequent decrease in mucus transport (Eliasson et al., 1977). Mucociliary transport may also be altered by different medications intended to treat diseases, especially when applied topically in the nose.

It has been shown in animal models that preservatives in topical decongestants will affect the mucociliary transport in an adverse way (Håkansson and Toremalm, 1982). However, not only decongestants are used topically in the nose. During the last decade topically applied glucocorticoids have become a frequent treatment for allergic and vasomotor rhinitis (Mygind, 1982). To our knowledge investigations of their effect on the mucociliary activity are lacking despite demonstration of their therapeutic efficacy. The aim of the present investigation was to study possible effects of a topically applied glucocorticoid (budesonide) on the mucociliary activity in the nose in humans.

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MATERIAL AND METHOD

Study design

The study was designed as a double blind, randomized, cross-over study in healthy subjects. Placebo or active treatment was given for one week with a two week wash out period between the treatment alternatives.

Subjects

Ten healthy volunteers (7 females and 3 males) aged between 16 and 60 years (mean age 37.0 years) participated in the study. The subjects had no history of chronic upper respiratory infection or chronic or recurrent nasal diseases such as allergic or vasomotor rhinitis or nasal polyposis. On physical examination they did not have any structural abnormalities of their nose such as septal deviations. All subjects were also free from any acute disease or condition that might interfere with the function of the nose or with the treatment given. All subjects gave their informed consent to participate in the study and the trial was approved by the Ethics Committee of the University of Göteborg.

Determination of mucociliary transport

The mucociliary transport was determined by the saccharine-dye test (Andersen et al., 1974). Each subject was tested at the same time of day everytime in a supine position. Before the first measurement the length of the nose from the nasal tip to the pharyngeal wall was determined with the help of a cotton swab. A particle of saccharine (⌀ 0.5–1.0 mm) with blue colour included was then placed on the anteriomedial portion of the inferior turbinate at a distance of 4 cm from the nasal tip. The time between application of saccharine and sweet taste defined the transport time which was confirmed by the arrival of the blue dye in the pharynx. The subjects were told not to sniff during the procedure and efforts were made to use the same nostril in each subjects at all determinations. Before entering the drug part of the trial at least two baseline measurements were made at least 24 h apart. Measurements were then made 1 h after the first dose and after one week treatment.

Treatment

The patients received either placebo aerosol or budesonide aerosol (Thalén and Brattsand, 1979) for 1 week. The dosage was 2 puffs into each nostril morning and afternoon resulting in a total daily dose of 400 μg of budesonide/day, which is the recommended clinical daily dose for the treatment of allergic and vasomotor rhinitis. After one week of treatment with either budesonide or placebo a two week wash out period was instituted and then the second treatment was given for one week (Figure 1).

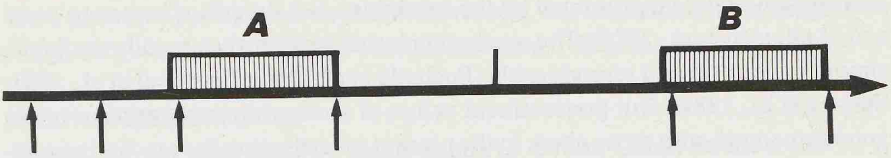

Figure 1. Schematical presentation of the trial. A and B are treatment weeks. A two weeks wash-out period is inserted between the treatment periods.

Statistics

Students t-test was used for evaluation of changes in mucociliary transport.

RESULTS

The initial mucociliary velocity for the patients varied from 4.6 to 12.3 mm/min. The double determinations in each subject revealed a variation of 18%. The values after 1 h and 1 week treatment are given in Figure 2. The change from baseline to 1 h and 1 week was not significant in any of the groups. In comparison to the value after 1 h the value after 1 week treatment was reduced after active treatment ($p < 0.05$). None of the subjects experienced any effects or side-effects of the treatment given.

DISCUSSION

The mucociliary system of the upper and lower airways forms a unique apparatus for transport of fluid and particles. The clearance of particles from the nasal

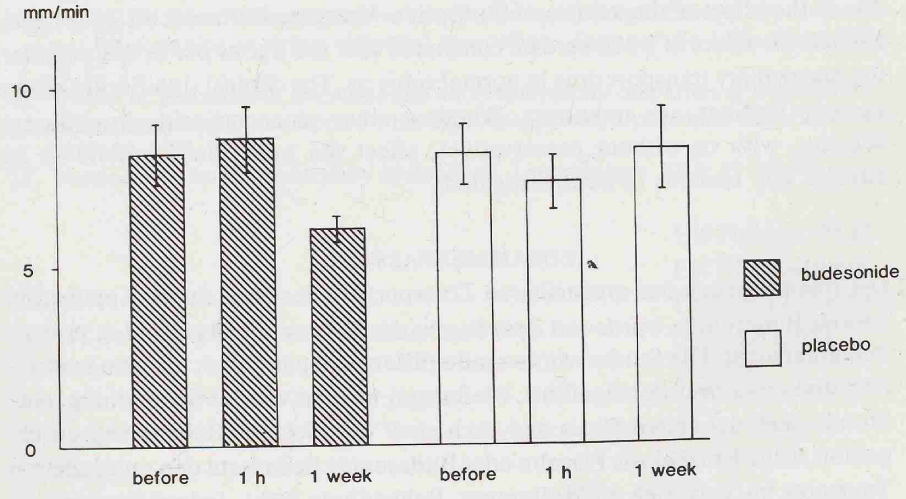

Figure 2. Results. Mean ± SEM. Velocity in mm/min.

mucosa can easily be examined by the saccharine test described some ten years ago (Andersen et al., 1974). The saccharine test is inexpensive, readily available, simple to perform and reproducable (Puchelle et al., 1981; Brondeel et al., 1983; Stanley et al., 1984). Our pretreatment values of saccharine transport time are in good agreement with those cited. In the present investigation the saccharine crystals were coloured blue which make them possible to be detected in the nose as well as in the pharynx. The mucociliary activity can be studied in vitro as well as in vivo in animal models. However, as many of the effects of steroids are time dependent, also in the nose (Pipkorn, 1982), and may be shown only after days or weeks treatment, most in vitro models are unsuitable for the study of prolonged treatment effects.

This is demonstrated in the present study. Since the number of patients in the study is limited also trends is of interest. One dosage of the glucocorticoid did not alter the mucociliary activity but one week of treatment did actually impair the mucociliary transport time by 30% as compared to the 1 h value. Whether this effect of the topical glucocorticoid was a change of ciliary beat frequency, ciliary shape, pattern or an alteration of the viscosity of the mucus or a combination of these can not be determined from the present study. The clinical relevance of the present finding as regards to patients with allergic and vasomotor rhinitis must be evaluated further as it has been suggested that nasal antigen challenge per se might alter the nasal mucociliary transport (Wanner, 1983). The results from the present study differ slightly from a recent report by Connell (1984) who studied patients with grass pollen allergy during season. He found that beclomethasone dipropionate aerosol did not alter the mucociliary transport after one week treatment while flunisolide nasal pump spray impaired the transport by 50%, probably due to the effect of the vehicle of flunisolide. However Borum et al. (1979) who studied the effect of freon aerosol concluded that the freons per se did not alter the mucociliary transport time in normal subjects. The clinical significance of the present findings are unknown. Whether other glucocorticoids in different vehicles, with or without preservatives, affect the mucociliary system in an adverse way remains to be investigated.

ZUSAMMENFASSUNG

Die Beeinflussung des mucociliaren Transports in der Nase durch Applikation lokaler Budesonide wurde mit dem Saccharin-Farbtest an 10 gesunden Probanden untersucht. Die Studie wurde randomisiert, doppelt blind, placebo kontrolliert und cross-over durchgeführt. Meßungen wurden vor der Behandlung, eine Stunde nach der ersten Dosis und nach einer einwöchigen Behandlung durchgeführt. Eine Einzeldosis Placebo oder Budesonide beänderte den mucociliaren Transport im Vergleich zu Werten vor Behandlung nicht. Jedoch konnte eine Abnahme des mucociliaren Transports nach einer einwöchigen Behandlung mit

dem aktiven Medikament beobachtet werden, mit statistichem Signifikanz bei Vergleich von dem 1-Stunden-Werten mit dem 1-Wochen-Werten.

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Ulf Pipkorn, M.D.
ENT-Department
University Hospital
S-22185 Lund
Sweden