Rhinology, 22, 241-246, 1984

Effect of ipratropium bromide on nasal mucociliary transport

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SUMMARY

Ipratropium bromide is a parasympatholytic drug. After application to the nose, the nasal mucociliary transport time was measured using the method of the saccharin test. This compound did not cause any changes in the nasal mucociliary transport function.

Topical use of many kinds of drugs has recently been developed. Ipratropium bromide is a parasympatholytic drug and an anticholinergic agent. It has an inhibitory effect on methacholine-induced hypersecretion 5 minutes after intranasal application (Borum, 1978; Borum et al., 1979a). Because of this reason, ipratropium bromide was used topically to non-allergic perennial rhinitis (Borum et al., 1979b).

The purpose of this paper is to clarify the effect of the use of ipratropium bromide on the nasal mucociliary transport system.

MATERIAL AND METHOD

Subjects

Twelve normal volunteers, who had no significant nasal complaints and no rhinoscopical abnormalities at the time of this study, were selected. Their ages varied from 24 to 33 years old, the mean age was 27.2 ± 2.4 years old. Of the twelve volunteers 7 were male and 5 female. Only one of them was a smoker and the others were non-smokers. During this study, all other kinds of medication were avoided.

Methods

All experiments were performed from April to June, 1983, and from 2 p.m. to 5 p.m.

1. Application of ipratropium bromide.

Ipratropium bromide was administered by a pressurized hand nebulizer which was equipped with a nasal adaptor. The placebo, an aerosol solution, contained no ipratropium bromide. With one puff 40 µg of ipratropium bromide was freed from the active spray bottles and no ipratropium bromide was freed in case of the

placebo. Two puffs were applied to each nostril. Two active spray bottles and two placebos were numbered at random. The spray bottles could not be distinguished from each other. The key to this numbering was kept secret until the experiments were finished.

2. Saccharin test (Andersen et al., 1974 a and b; Sakakura et al., 1983).

The saccharin test was performed according to the method as used by Sakakura et al. (1983). A small granule of saccharin of approximately 2.5 × 0.5 mm diameter which contained 20% saccharin, and weighed about 5 mg, was placed on the nasal septum at almost the same site in all experiments. The site at which the granule was placed was about 1 cm behind the nostril. The subjects were sitting quietly on chairs. The time required to experience a sweet taste was measured from the moment of administration of the drug. The test (ST) was terminated if nothing was tasted within 45 minutes.

3. Experiments.

On the first day, the baseline ST was measured. At least 24 hours later, two puffs of the test aerosol were applied to the nostril. Fifteen minutes later, ST was measured again. ST measurements were done for each spray bottle (No. 1, 2, 3 and 4) at intervals of at least 48 hours.

4. Statistical analysis.

ST analysis was performed using the two-tailed paired t-test between baseline and each measurement. Student t-test was also used between the active and placebo aerosol solutions.

RESULTS

The mean baseline ST, which indicated normal mucociliary transport time of healthy persons, was 13.3 ± 1.1 minutes (mean $\pm$ SEM). The ST's were respectively, 13.2 ± 0.9 minutes for the first spray bottle, 12.3 ± 1.0 minutes for the second, 12.8 ± 1.8 minutes for the third and 10.1 ± 1.1 minutes for the fourth bottle.

Figure 1 shows the baseline ST and the changes which occur after application of the active and placebo aerosol. There was no significant difference in ST of the baseline, active and placebo groups.

Mean ST of the active aerosol was 13.0 ± 1.0 minutes and the means of the placebo aerosol was 11.6 ± 0.8 minutes. Among the baseline, the active and placebo groups, there was no significant difference in ST (Figure 2).

None of the subjects has had any symptoms of a dry mouth, headache, occasional blurring of vision and palpitation.

DISCUSSION

The airway plays a role in the modification of the physical condition of inspired air, namely by cleaning the air of impurities, and protecting their delicate alveo-

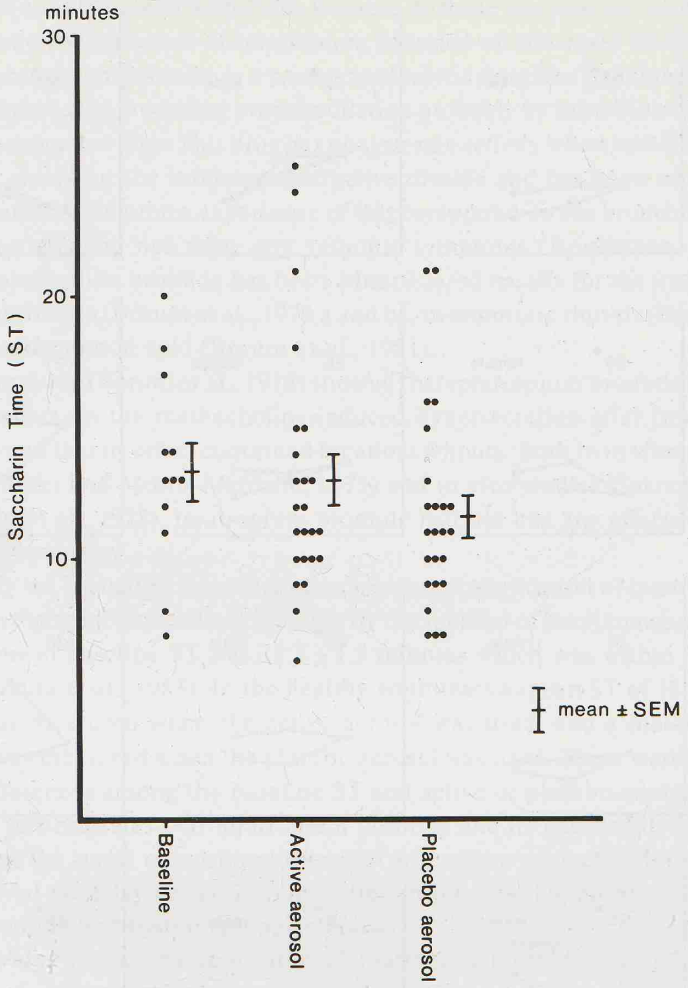

Figure 1. The comparison of saccharin time among baseline ST, active and placebo aerosol solutions.
* indicates age in years

lar terminates against noxious materials and by cleaning their surface continuously. For these purposes the mucociliary function is essential. Therefore, for topically used drugs, it is extremely important to avoid any impairment to the mucociliary function. To measure this mucociliary function, particle transport time (PTR) and/or saccharin transport time (ST) were used by many authors (Andersen et al., 1974 a and b; Proctor et al., 1978; Sakakura et al., 1983). The former reflects the transport rate of the outer mucous layer and the latter reflects the transport rate by periciliary fluids as well as by the outer mucous layer. ST is far

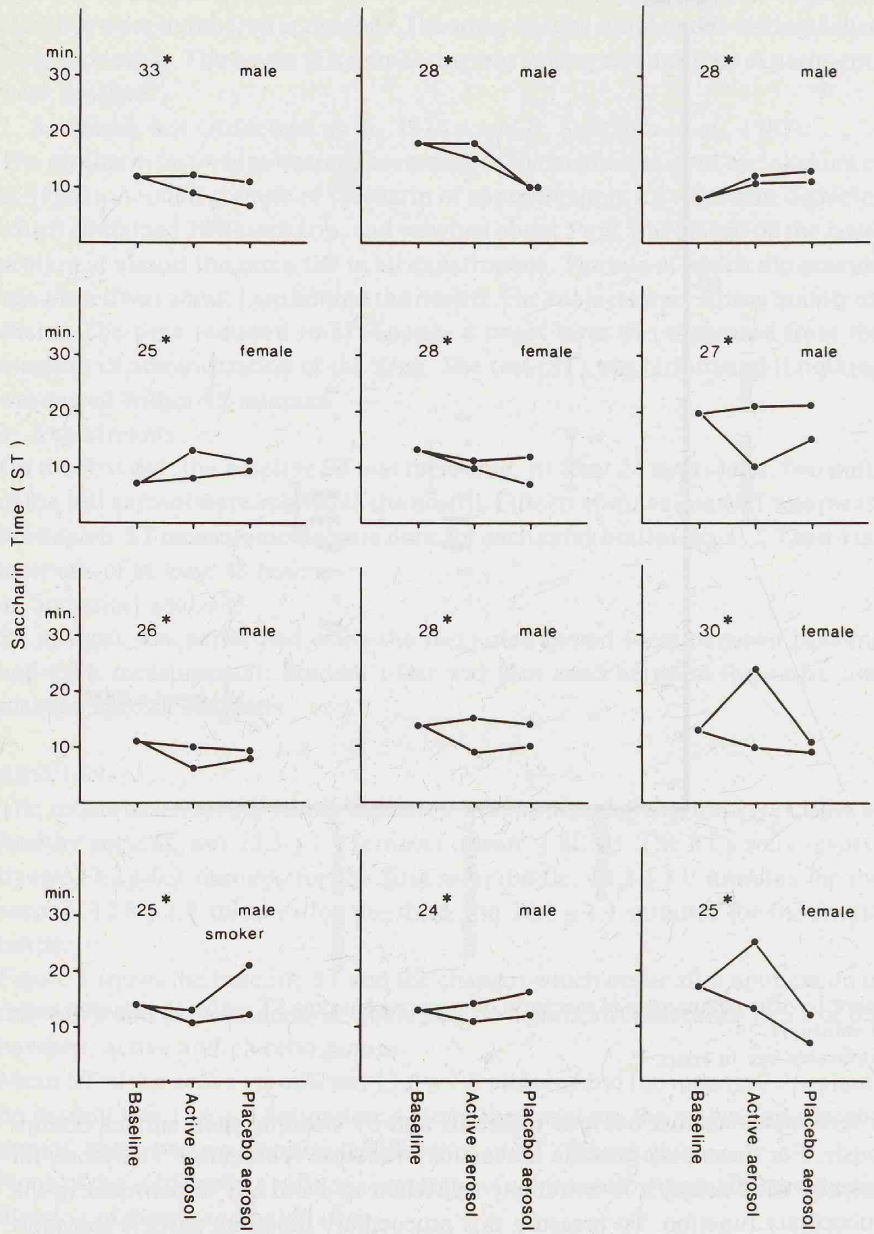

Figure 2. The comparison of saccharin time in each subject.

simpler and correlates well with PTR. Because of these reasons, we used ST in order to study the influence of ipratropium bromide on the nasal mucociliary function. Ipratropium bromide is a parasympatholytic drug like atropine. It is an anticholinergic agent producing bronchodilation probably by inhibition of cholinergic bronchomotor tone. This drug has no systemic activity when inhaled in the therapeutic doses for the bronchoconstructive disease and has been used as a bronchodilator. A long-term experience of this compound on the bronchitis and bronchial asthma did not show any systemic symptoms (Brinkmann, 1975). Recently, ipratropium bromide has been administered nasally for the treatment of perennial rhinitis (Borum et al., 1979 a and b), vasomotoric rhinitis (Borum et al., 1978) and common cold (Borum et al., 1981).

A laboratory study (Borum et al., 1978) showed that ipratropium bromide had an inhibitory effect on the methacholine-induced hypersecretion after intranasal application and that its effect continued for about 4 hours. Both in in vitro (Iravani, 1972; Iravani and Morris-Mebville, 1975) and in vivo studies (Sakner et al., 1976; Ruffin et al., 1978), ipratropium bromide had not had any effects on the ciliary beat frequency.

In this study we evaluated the effect of an intranasal application of ipratropium bromide on the nasal mucociliary function by the method of nasal transport time (ST). The mean baseline ST was 13.3 ± 1.1 minutes which was within normal range (Sakakura et al., 1983). In the healthy volunteers a mean ST of 13.0 ± 1.0 minutes was measured when the active aerosol was used, and a mean ST of 11.6 ± 0.8 was measured when the placebo aerosol was used. There were no significant differences among the baseline ST and active or placebo aerosol solutions. This fact indicates that ipratropium bromide and its additionals have no influence on the nasal mucociliary transport of healthy subjects. Murai et al. (1983) showed no delay on ST 24 hours after an intranasal application of ipratropium bromide and hydroxypropylcellulose.

The effect which a long-term application of ipratropium bromide has on the nasal mucociliary function remains to be studied.

In future, ipratropium bromide will be of value in the continuous treatment of perennial rhinitis patients who do not react to glucocorticosteroid therapy (Borum et al.,1979b; Mygind, 1979).

Also occasional use of ipratropium bromide will be of value in patients with infrequent attacks of watery rhinorrhoea and in patients with the beginning of symptoms of common cold (Borum et al., 1981).

RÉSUMÉ

Le bromure d'ipratropium est une drogue parasympatolytique. Son action sur le drainage mucociliaire a été évaluée à l'aide du test à la saccharine. 80 µg d'ipratropium ou un placebo ont été appliqués sur la muqueuse nasale chez 12 volon-

taires. La durée du transport transnasal a été de 13.3 ± 1.1 minutes pour le produit actif et 11.6 ± 0.6 minutes pour le placebo. Il n'y a pas de différence significative entre les deux valeurs et l'ipratropium n'entraîne donc aucune altération du drainage mucociliaire.

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