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Treatment of non-allergic nasal hypersecretion with ipratropium and beclomethasone

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SUMMARY

The effect of ipratropium and beclomethasone administered as nasal aerosols was compared in a double-blind, double-dummy, randomized, cross-over designed study. Twenty-four patients with non-allergic, watery hypersecretion participated in the trial. According to the patients' daily registration of nasal symptoms, no significant difference could be found between the two drugs. It was not possible to characterize patients who would benefit from treatment with either ipratropium or beclomethasone.

INTRODUCTION

Patients with non-allergic, perennial rhinitis whose main symptom is watery rhinorrhoea are treated traditionally with systemic antihistamines or with topical steroids, such as beclomethasone (Malm and Wihl, 1976; Löfqvist and Svensson, 1976). Borum et al. (1979) introduced the topical, anticholinergic drug, ipratropium, which they had found beneficial in the treatment of these patients with troublesome watery rhinorrhoea. Their findings were confirmed by various workers (Von Haacke et al., 1983; Malmberg et al., 1983; Jokinen and Sipilä, 1983).

A comparison between the effect of ipratropium and that of a topical steroid on the cholinergic watery nasal hypersecretion has so far we know not been published. In an open, not randomized study, Bende and Rundcrantz (1985) compared the effects of ipratropium with those of the topical steroid budesonide in patients with watery nasal hypersecretion of unknown etiology. They found budesonide to be superior to ipratropium regarding all nasal symptoms including watery rhinorrhoea.

Therefore we decided to compare the effects of the most common used steroid, beclomethasone, and ipratropium in a double-blind, randomized study in patients with cholinergic non-allergic rhinitis.

Budesonide and beclomethasone are topical corticosteroids with comparable effects (Pipkorn, 1983).

Our study was approved by The National Swedish Social Welfare Board, Stockholm, Sweden, and by the Ethical Committee of the University of Lund, Sweden.

MATERIAL

The material consisted of 31 patients. None of them suffered from chronic asthma, or had nasal polyps. There was no indication of allergy from skin prick testing. None of the women were pregnant.

The patients tested ipratropium to see if it had a beneficial effect on their excessive watery secretion. If ipratropium had an effect on the nasal secretion according to the patients the secretion was considered cholinergic, or vice versa. Of the 31 patients, five (4 women and 1 man) felt no benefit from ipratropium and two (1 woman and 1 man) found the trial regime too time-consuming.

The age and duration of the disease in these seven patients were approximately the same as in the 24 who took part in the trial. Hence their non-participation was not considered to be of importance for any possible difference when comparing the effects of ipratropium and beclomethasone.

The patients participating in the trial included 14 women and 10 men (mean age 49 years, range 20–77 years). The patients had had excessive nasal secretion for a half to 30 years, the mean duration being 5.4 years. Twenty-one of them had excessive nasal secretion each day and three of them on several occasions per week.

The duration of the nasal discharge in 16 patients was more than one hour at a time and less than one hour in eight patients.

In order to see if there was any eosinophilia in these 24 patients, a nasal smear was examined on three occasions: before treatment with the drugs, in the wash-out period between treatments, and when the trial was terminated.

Rhinomanometry was normal in 19 of the patients. Five patients with a high Nasal Airway Resistance (NAR) were treated with 0.1% xylometazoline for decongestion of the nasal mucosa and after treatment one still had a high NAR.

On occasions, long previous to the commencement of the trial, six of the patients had used beclomethasone with beneficial effects but none of the patients had used ipratropium before.

None of the patients had upper airway infection in the two weeks prior to the trial. Other medication was not administered for two weeks preceding or during the trial.

METHOD

The trial was double-blind, double-dummy and cross-over designed. The patients were randomized into two groups. They administered to each nostril, morning and evening, two puffs from one aerosol containing either ipratropium

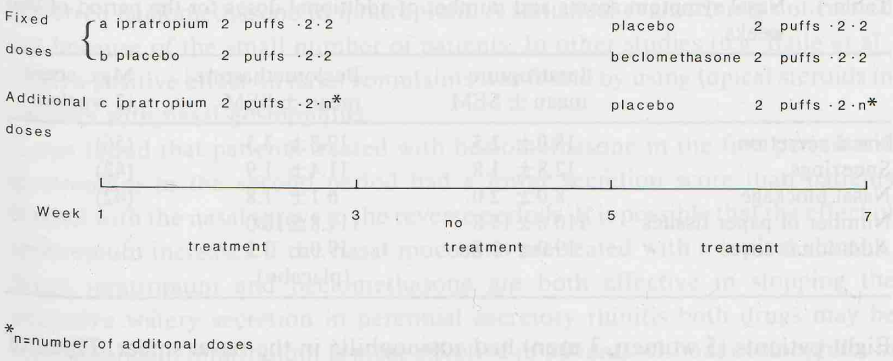

Figure 1. Experimental design. In the first period of treatment the patients could begin either with ipratropium or with beclomethasone and vice versa in the second period.

(a in Figure 1) or beclomethasone and two puffs from another aerosol containing corresponding placebo according to the double-dummy technique (b in Figure 1). The daily dose of ipratropium was 160 μg and of beclomethasone, 400 μg. According to their individual needs, the patients were allowed to take additional treatment every second hour using a third aerosol containing either ipratropium during the ipratropium period (c in Figure 1) or placebo during the beclomethasone period.

After treatment for two weeks followed by a wash-out period lasting two weeks, the patients received treatment for two further weeks (Figure 1).

Nasal symptom scores for secretion, sneezing, blocking and adverse effects were registered daily by the patients using a scale from 0 for no symptoms to 3 or 4 for severe symptoms.

The daily additive use of the third nasal aerosol and the daily number of paper tissues used to absorb the secretion were registered.

Statistical analysis was performed with paired t-test and the Chi^2-test.

RESULTS

Twenty-four patients completed the study. Table 1 presents the comparison of symptom scores for secretion, sneezing, blockage, the number of tissues used and the additional doses of ipratropium or placebo.

Significant differences were not found regarding the number of paper tissues in the two periods of treatment nor were differences in the number of scores for secretion, sneezing, blockage and additive use of ipratropium or placebo. Even if only the last two weeks in the two periods of treatment were compared, there was no difference in effect of the two drugs.

Of the 24 patients, 14 preferred ipratropium treatment and 9 beclomethasone treatment. One patient had no preference. The difference in preference was not significant.

Table 1. Nasal symptom scores and number of additional doses for the period of two weeks.

	Ipratropium mean ± SEM	Beclomethasone mean ± SEM	Max. score (2 weeks)
Nasal secretion	18.0± 2.5	19.8± 3.3	(56)
Sneezings	12.8± 1.8	11.4± 1.9	(42)
Nasal blockage	8.0± 2.0	6.1± 1.8	(42)
Number of paper tissues	110.6±15.8	111.8±16.0	
Additional doses	19.0± 2.8	19.0± 3.2 (placebo)	

Eight patients (5 women, 3 men) had eosinophilia in the nasal smear. Three of them preferred ipratropium and five beclomethasone. In the 16 patients without nasal eosinophilia 11 patients preferred ipratropium and 4 beclomethasone (Chi^2: 2.812).

Of the 12 oldest patients (range 45–77 years) six preferred ipratropium and six beclomethasone. Four of these patients had eosinophilia in their nasal smear. Eight of the younger patients (range 20–44 years) preferred ipratropium and three beclomethasone.

Patients treated with beclomethasone in the first period and with ipratropium in the second period had a lower total secretion score than patients treated with ipratropium in the first period and with beclomethasone in the second period ($p<0.05$).

Side effects of the treatment were negligible.

DISCUSSION

Nasal hypersecretion is often supposed to be caused by cholinergic stimulation. However, nasal hypersecretion may have other causes viz. substance P and vasoactive intestinal polypeptide (VIP) (Änggård et al., 1983; Malm, 1983). Kirkegaard et al. (1987) reported that of 36 patients treated with ipratropium for perennial, non-allergic, secretory rhinitis, four did not respond. Bende and Rundcrantz (1985) found that budesonide was superior to ipratropium regarding all nasal symptoms. The conclusion drawn from these studies is, that the etiology of nasal hypersecretion is not cholinergic in some patients. Therefore, as ipratropium is a selective, anticholinergic drug we found it of no value in testing the effects of ipratropium on patients with non-cholinergic secretion.

This investigation did not show any significant difference of nasal symptoms between the treatment with ipratropium or beclomethasone. Nasal secretion tended to be more reduced by ipratropium than by beclomethasone, which on the contrary seemed more effective against nasal blockage and sneezing.

However, 70% of the patients without eosinophilia in the nasal secretion preferred ipratropium. On the contrary, 5 patients of 8 with nasal eosinophilia,

preferred beclomethasone to ipratropium. A statistical evaluation is not carried out because of the small number of patients. In other studies (e.g. Balle et al., 1980) a positive effect on nasal complaints was found by using topical steroids in patients with nasal eosinophilia.

It was found that patients treated with beclomethasone in the first period and ipratropium in the second period had a lower secretion score than patients treated with the nasal sprays in the reverse periods. It is possible that the effect of ipratropium increases if the nasal mucosa is pretreated with a topical steroid.

Since ipratropium and beclomethasone are both effective in stopping the excessive watery secretion in perennial secretory rhinitis both drugs may be recommended. Ipratropium is most effective in patients without eosinophilia in the nasal secretion and beclomethasone in patients with eosinophilia in the nasal secretion. However, it must be remembered that ipratropium is a specific anticholinergic drug while the action of beclomethasone is more unspecific.

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