

The effect of oral drugs on the cytologic picture of nasal mucosa in hay fever

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The aim of the present study was to assess the influence of H_1 -antihistamine and sympathomimetic drugs given orally on cytologic smears of the nasal mucosa. Thirty-five patients with hay fever evaluated cytologic smears of the nasal mucosa before and after a 2-week treatment. Fourteen patients received chlorpheniramine with phenylephrine, 10 patients dexchlorpheniramine, and 11 patients pseudoephedrine. The investigated drugs significantly changed nasal cytograms. The number of eosinophils increased after chlorpheniramine with phenylephrine and after pseudoephedrine but decreased after dexchlorpheniramine. Thus, the sympathetic nervous system stimulation seems to produce local eosinophilia on the nasal mucosa. In view of such a significant correlation between hay fever symptoms and the number of eosinophils in the cytograms, it can be concluded that the combination of antihistamine and sympathomimetic drugs may adversely affect the course of the disease. Although, at the initial stage of the treatment, sympathomimetics reduce swelling and improve the patency of the nose through decongestion of the blood vessels, their negative effect can influence the immunologic mechanisms.

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The normal structure of the nasal mucosa epithelium determines the correct functioning of the nose. The cytologic picture of smears from the nasal mucosa exhibits cells of the multicolumnar as well as the stratified squamous epithelium and migratory cells (7, 8, 10). In allergic rhinitis these smears show the prevalence of neutrophilic and eosinophilic granulocytes (9, 11, 13, 16).

The application of nasal drops and ointments may damage the epithelium. Nasal drops paralyse the cilia and, through blood vessel decongestion, induce ischaemia of the mucosa (1). Thus, their prolonged application results in the destruction of the nasal mucosa (3, 5). The shrinking of the glands and the change of the normal into squamous epithelium take place at the expense of the goblet and columnar cells. This undesirable effect of sympathomimetics restricts their topical application since, when administered orally, they adversely affect the cardiovascular system (14). However, their action on the nasal mucosa may reduce the nasal blockage.

Our study has explored the effect on the cytologic picture of the nasal mucosa of antihistamines and sympathomimetics, the drugs most frequently used in the treatment of allergic rhinitis.

Material and methods

The cytologic examination of 35 patients (20 males, 15 females; aged 13-45 years) with hay fever corroborated by positive skin tests performed with grass antigens was conducted during the peak pollen period May-June (1990, antihistamines; 1991, sympathomimetics). The treatment involved neither specific immunotherapy nor topical nasal drug application. Fourteen patients were treated with two daily doses of the compound preparation "Dristan 12 h" (0.004 chlorpheniramine combined with 0.02 phenylephrine). Ten patients were treated daily with four doses 0.002 dexchlorpheniramine, preparation "Polaramine". The above study, which revealed different effects of antihistamine depending on whether it is administered singly or combined with sympathomimetics, was complemented during the 1991 season by an investigation of the pseudoephedrine effect on the cytologic picture of the nasal mucosa in patients with hay fever. Eleven patients received daily two doses 0.12 pseudoephedrine, preparation "Sudafed 12 h".

The cytologic examination performed both before drug administration (initial cytology) and 2 weeks

after the treatment involved the quantitative evaluation of cells in the nasal smears. Samples taken by the scrape technique from the inferior nasal turbinates were stained with hematoxylin/eosin and examined under a light microscope in a double-blind study, allowing us to determine the amount (profuse, average, scant) as well as the ratio of epithelial to migratory cells, first in the whole smears and then in a sample of 200–500 cells (7). The nonparametric chi-square test was employed in the statistical analysis.

Results

The smears from the 14 hay fever patients treated with the combination of chlorpheniramine and phenylephrine revealed a percentage of the cytologic pictures with profuse cells significantly higher after than before the therapy (Table 1), while the pictures in the 10 patients on dexchlorpheniramine failed to exhibit any statistically significant differences. Simultaneously, smears from the 11 patients on pseudoephedrine revealed cytologic pictures with scant cellular material more often after than before the therapy.

Characteristically, the original smears in all three groups exhibited cytologic pictures with prevalent epithelial cells (64.3%, 60%, and 63.6%, respectively). But after the treatment, smears from the patients on combined drugs revealed an increased number of the migratory cells, their percentage approximating

the number of the epithelial cells (Table 2). At the same time, the cytologic pictures of smears from the patients on dexchlorpheniramine revealed the epithelial cells to be even more numerous after than before the treatment, the difference being statistically significant ($P < 0.05$).

After the combined treatment with chlorpheniramine and phenylephrine, the cytograms demonstrated an increased number of migratory cells, i.e. eosinophils, neutrophils, and lymphocytes (from 17%, 17.8%, and 0.04% to 22.6%, 23.6%, and 2.2%, respectively), as well as squamous cells (from 8.4% to 15.6%), while the numbers of the columnar and basal cells decreased (from 10.7%, 18.7% to 4.9%, 10.1%, respectively; Table 3).

The 2-week-long treatment of hay fever with dexchlorpheniramine produced effects on cytologic pictures different from those caused by the combined antihistamine and sympathomimetic therapy. A detailed analysis of the cytograms of patients treated with antihistamine administered alone revealed an increase in the columnar cell number from 11.9% before to 20.2% after the therapy. It also showed that the percentage of the goblet cells increased from 28.9% to 31%, that the basal cells decreased from 14.8% to 6.0%, and that the number of the squamous cells remained unchanged (Table 4). Changes in the migratory cell contents showed a reduced percentage of eosinophils in the cytograms from the original 26.7% to 12.8% after the therapy and an increased percentage of neutrophils from 7.8% to 19.2% following dexchlorpheniramine administration. A global comparison of the cytograms before

Table 1. Cytologic pictures of profuse, average, and scanty numbers of cells in nasal smears from patients with hay fever before and after 2-week treatment with chlorpheniramine combined with phenylephrine, dexchlorpheniramine, and pseudoephedrine

Cell numbers	Chlorpheniramine and phenylephrine	
	Before treatment	After treatment
Profuse	8/14 (57.14%)	8/14 (57.14%)
Average	2/14 (14.29%)	5/14 (35.71%)
Scanty	4/14 (28.57%)	1/14 (7.14%)
	$(\chi^2 = 23.124; P < 0.05)$	
Cell numbers	Dexchlorpheniramine	
	Before treatment	After treatment
Profuse	6/10 (60%)	7/10 (70%)
Average	3/10 (30%)	2/10 (20%)
Scanty	1/10 (10%)	1/10 (10%)
	$(\chi^2 = 2.768; P < 0.2)$	
Cell numbers	Pseudoephedrine	
	Before treatment	After treatment
Profuse	3/11 (27.27%)	3/11 (27.27%)
Average	6/11 (54.54%)	2/11 (18.18%)
Scanty	2/11 (18.18%)	6/11 (54.54%)
	$(\chi^2 = 37.506; P < 0.001)$	

Table 2. Epithelial and migratory cell incidence in nasal smears from patients with hay fever before and after 2-week treatment with chlorpheniramine combined with phenylephrine, dexchlorpheniramine, and pseudoephedrine

Cell types	Chlorpheniramine and phenylephrine	
	Before treatment	After treatment
Epithelial	9/14 (64.29%)	7/14 (50%)
Migratory	5/14 (35.71%)	7/14 (50%)
	$(\chi^2 = 3.447; P < 0.06)$	
Cell types	Dexchlorpheniramine	
	Before treatment	After treatment
Epithelial	6/10 (60%)	9/10 (90%)
Migratory	4/10 (40%)	1/10 (10%)
	$(\chi^2 = 22.426; P < 0.05)$	
Cell types	Pseudoephedrine	
	Before treatment	After treatment
Epithelial	7/11 (63.64%)	7/11 (63.64%)
Migratory	4/11 (36.36%)	4/11 (36.36%)

Table 3. Initial cytograms and cytograms obtained after 2-week combined treatment with chlorpheniramine and phenylephrine in 14 patients with hay fever

Cell types	Cell medium percentage	
	Before treatment	After treatment
Columnar	10.7	4.9
Goblet	26.9	25.2
Basal	18.7	10.1
Squamous	8.4	15.6
Neutrophils	17.8	23.6
Eosinophils	17.0	22.7
Lymphocytes	0.04	2.2
$(\chi^2 = 12.471; P = 0.08)$		

Table 4. Initial cytograms and cytograms obtained after 2-week treatment with dexamethasone in 10 patients with hay fever

Cell types	Cell medium percentage	
	Before treatment	After treatment
Columnar	11.9	20.9
Goblet	28.9	31.0
Basal	14.8	6.0
Squamous	8.6	8.6
Neutrophils	7.8	19.2
Eosinophils	26.7	12.8
Lymphocytes	0.9	1.2
$(\chi^2 = 17.304; P = 0.01)$		

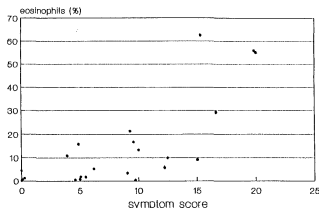
and after the treatment revealed statistically significant differences ($P = 0.01$).

The control cytograms in both groups of patients on antihistamine (a parallel study) failed to reveal statistically significant differences ($\chi^2 = 6.762$; $P = 0.2$). Simultaneously, the difference between cytograms after the combined treatment (antihistamine and sympathomimetic) and after the antihistamine administered alone proved statistically significant ($\chi^2 = 16.203$; $P = 0.01$).

Two weeks after pseudoephedrine administration, the global picture of the mucosa showed a statistically significant change, as compared with the initial examination ($P < 0.05$; Table 5). A detailed analysis

Table 5. Initial cytograms and cytograms obtained after 2-week treatment with pseudoephedrine in 11 patients with hay fever

Cell types	Cell medium percentage	
	Before treatment	After treatment
Columnar	14.0	2.5
Goblet	33.6	27.9
Basal	0	2.2
Squamous	20.3	30.2
Neutrophils	10.1	8.0
Eosinophils	19.7	29.2
$(\chi^2 = 13.554; P = 0.05)$		

Fig. 1. Relationship between symptom intensity and incidence of eosinophils in nasal cytograms ($r = 0.526$, $t = 2.837$, $P < 0.01$).

revealed an increased number of eosinophils (from 19.7% to 29.2%) and a reduced number of neutrophils (from 10.1% to 7.9%). After 2 weeks on pseudoephedrine, the percentage of the epithelial cells was as follows: columnar cells decreased from the original 14% to 2.5%, the number of goblet cells remained practically unaffected (from 33.7% to 27.9%), squamous cells increased from 20.2% to 30.2%, and basal cells, absent in the initial examination, showed an incidence of 2.2%.

A study of the correlation between symptom intensity and the incidence of particular cells in the cytologic pictures of the nasal smears from 23 hay fever patients involved the use of diary cards filled in by the patients during the 2-week treatment (Fig. 1). The nasal cytologic pictures of patients with seasonal allergic rhinitis revealed a substantial correlation between the increased intensity of the disease symptoms and the presence of the migratory cells, as well as a statistically significant correlation between the incidence of eosinophils and fits of sneezing ($r = 0.526$; $P < 0.01$). There was no correlation between the number of epithelial cells in the nasal smears from hay fever patients and the intensity of the disease symptoms.

Discussion

The effect of the orally administered antihistamine on the cytologic picture of the nasal mucosa was the subject of our investigation. The study involved two drugs: a combination of chlorpheniramine (antihistamine) with phenylephrine (sympathomimetic), and dexamethasone (antihistamine), an isomer of the former. The investigation revealed the effect of these two drugs on the cytologic picture of the nasal mucosa epithelium, particularly the migratory cells. The essential difference between these drugs was their contrary effects on the number of eosinophils in the cytologic smears (Table 6). After treatment

Table 6. Effect of dexchlorpheniramine, chlorpheniramine combined with phenylephrine, and pseudoephedrine on cytologic picture of nasal mucosa in hay fever

Cell types	Dexchlor-pheniramine	Chlorpheniramine and phenylephrine	Pseudoephedrine
Columnar	↑	↓	↓↓ *
Goblet	0	0	0
Basal	↓	↓	0
Squamous	0	↑	↑ *
Neutrophils	↑	↑	↑
Eosinophils	↓	↑	↑ *
Lymphocytes	↓	↓	0

↑ increase, ↓ decrease of cells in smears as compared with initial cytograms, * changed direction dependent on stimulation of sympathetic nervous system.

with dexchlorpheniramine, the percentage of migratory cells became lower than before the therapy, while after the combined (antihistamine and sympathomimetic) drug administration the percentage of eosinophils was higher than during the initial examination. This increase may have been caused by the action of phenylephrine, a drug which stimulates the sympathetic nervous system. An analogous increase in the number of eosinophils was observed after administration of pseudoephedrine, a sympathomimetic drug, singly (Table 6).

Phenylephrine and pseudoephedrine stimulate the sympathetic nervous system in different ways. While phenylephrine directly affects the adrenergic receptors, an indirect action of pseudoephedrine liberates catecholamines from the presynaptic fibres. Thus, one may hypothesize that stimulation of the sympathetic nervous system produces local eosinophilia on the nasal mucosa surface. In view of such a significant correlation between hay fever symptoms and the number of eosinophils in the cytograms, it can be concluded that the combination of antihistamine and sympathomimetics may adversely affect the course of the disease. Although, at the initial stage of the treatment, sympathomimetics reduce swelling and improve the patency of the nose through decongestion of the blood vessels, their negative action can change the immunologic mechanisms. Since an increase in the number of eosinophils characteristic of the late phase of the allergic reaction is also correlated with intensive allergic diseases of the upper and lower airways (2, 4, 6, 12, 15), one must assume that sympathomimetics should be used only in emergencies.

The combined drug action on the epithelial cells (antihistamine and sympathomimetic) exhibited an effect on the epithelial cells stronger than that of antihistamine administered alone. A comparison with the results of the initial examination has shown that the cytologic pictures in patients on combined drugs contain an increased number of squamous cells and a reduced number of columnar cells, an

effect not observed after dexchlorpheniramine action. Since analogous changes are produced after pseudoephedrine administration, changes affecting the cytologic picture of the nasal mucosa epithelium after combined drug therapy may also be provoked by a component which stimulates the sympathetic nervous system (Table 6). An increased number of squamous cells at the expense of columnar cells reflects the action of the offending medications which damage the multicolumnar epithelium. Such a cytologic picture is characteristic of the prolonged use of nasal drops and some corticosteroids (5, 17). The use of sympathomimetics, both topical and systemic (for 2 weeks in our study), also adversely affected the mucous membrane of the nose. For this reason drugs containing sympathomimetics should not be employed in prolonged treatment.

References

1. ANGGARD A, EDWALL L. The effects of sympathetic nerve stimulation on the tracer disappearance rate and local blood content in the nasal mucosa of the cat. *Acta Otolaryngol* 1974; 77: 131-7.
2. BOUSQUET J, CHANEZ P, LACOSTE JY, BARNEON G. Eosinophilic inflammation in asthma. *N Engl J Med* 1990; 323: 1033-9.
3. CAPEL LH, SWANSTON AR. Congesting nasal decongestants. *Br Med J* 1986; 233: 1258-9.
4. CAPRON M. Eosinophils: receptors and mediators in hypersensitivity. *Clin Exp Allergy* 1989; 19 (Suppl. 1): 1-8.
5. CONNELL JT. Nasal disease: mechanisms and classification. *Ann Allergy* 1983; 50: 227-35.
6. KAY AB. Eosinophils and asthma. *Allergy Today* 1989; 1: 13-14.
7. KRAUSE HF. Nasal cytology in clinical allergy. In: KRAUSE HF, ed. *Otolaryngic allergy and immunology*. Philadelphia: WB Saunders, 1989: 112-21.
8. MAKOWSKA W, ZAWISZA E. Cytologic evaluation of the nasal epithelium in patients with hay fever. *Acta Cytol* 1975; 19: 564-7.
9. MULLARKEY MF. Eosinophilic nonallergic rhinitis. *J Allergy Clin Immunol* 1988; 82: 941-9.
10. NAIK ZM. Cytology of upper respiratory tract - trachea, larynx, nasopharynx. In: NAIK ZM, ed. *Exfoliative cytology*. Boston: Little, Brown, 1970: 189-92.
11. PELIKAN Z, PELIKAN-FILIPK M. Cytologic changes in the nasal secretions during the immediate nasal response. *J Allergy Clin Immunol* 1988; 82: 1103-12.
12. PIPKORN U. Late phase allergic reactions in the nose. *Allergy Today* 1988; 2: 10-11.
13. PIPKORN U. Involvement of different cell types in allergic rhinitis. In: MYGIND N, NACLERIO RM, eds. *Rhinoconjunctivitis*. Toronto: Hogrefe & Huber, 1989: 19-26.
14. REYNOLDS JEF. Adrenaline and some other sympathomimetics. In: REYNOLDS JEF, ed. *Martindale: the extra pharmacopoeia*. 39th ed. London: Pharmaceutical Press, 1982: 1-34.
15. SHURLOCK B. Early diagnosis of allergic rhinitis could avoid later complications. *Allergy Today* 1990; 3: 4-5.
16. WATANABE K, WATANABE I. Changes of nasal epithelial cells and mucus layer after challenge of allergen. *Ann Otolaryngol* 1981; 90: 204-9.
17. ZAWISZA E, MAKOWSKA W. Cytologic picture of the nasal mucosa following corticosteroid therapy in hay fever. *Ann Allergy* 1977; 39: 355.

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