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Alterations of neuroreceptors in nasal hyperreactivity

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Cholinergic and adrenergic abnormalities have been observed in nasal allergy and may be due to changes in pharmacological characteristics of neuroreceptors. Radioligand receptor binding studies demonstrated no significant changes in affinities or densities of α-adrenoceptors, a decreased number of β-adrenoceptors and a decreased affinity combined with a decreased number of muscarinic acetylcholine receptors.

Keywords nasal hyperreactivity adrenoceptors muscarinic receptors

Introduction

Nasal hyperreactivity in allergic rhinitis may originate from an imbalance of the autonomic nerve regulation (Mygind, 1982). Systemic adrenergic abnormalities and cholinergic nasal hyperresponsiveness has been observed in allergic patients (Mygind, 1982; Shelhamer *et al.*, 1983). Adrenergic and cholinergic abnormalities have been explained in terms of changes in characteristics of adrenoceptors and muscarinic acetylcholine receptors respectively in the lower airways of asthmatics (Barnes, 1986). In this study radioligand receptor binding studies were performed in order to elucidate the supposed changes in characteristics of adrenoceptors and muscarinic receptors in nasal hyperreactivity.

Methods

Biopsies of human nasal mucosae were obtained from septal and sinus surgeries. Patients were classified into a non-allergic and an allergic group on the basis of the following parameters (Mygind, 1982): nasal symptoms, family history, X-rays of the sinuses, serum IgE, blood and/or nose eosinophils, RAST and skin-tests. The heterogeneous non-allergic group was further subdivided into control individuals, chronic sinusitis and vasomotor rhinitis patients. The control group consisted of patients with traumas, with septum deviations and/or with cosmetic problems.

Nasal mucosae were washed in 0.9% NaCl and stored at −80° C. The tissue was homogenized in buffer with an Ultraturrax for 2 × 10 s, centrifuged (1000 *g*, 5 min) and the resulting supernatant was centrifuged at 100,000 *g* for 1 h. The pellet was resuspended by Potter homogenization. Protein determination was performed according to Bradford. The different incubation conditions of [^{3}H]-prazosin, [^{3}H]-rauwolscine, [^{125}I]-(−)-CYP and [^{3}H]-1-QNB binding to α_1-adrenoceptors, α_2-adrenoceptors, β-adrenoceptors and muscarinic receptors respectively are described elsewhere (Rodrigues de Miranda *et al.*, 1985; van Megen *et al.*, 1989). The agonist binding and the effect of Gpp(NH)p on the agonist binding, which reflects the coupling of the receptor to the effector system via the G-protein, have been investigated for the β-adrenoceptors and the muscarinic receptors in the nasal mucosa.

Results

Specific [^{3}H]-prazosin and [^{3}H]-rauwolscine binding to α_1- and α_2-adrenoceptors was saturable and of high affinity in non-allergic and allergic patients. No significant differences in equilibrium dissociation constants (K_D) or densi-

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Table 1 Binding parameters (mean ± s.e. mean) of [^{3}H]-prazosin, [^{3}H]-rauwolscine and [^{125}I]-(−)-CYP to α_1-, α_2- and β-adrenoceptors and of [^{3}H]-1-QNB to muscarinic receptors in nasal mucosa of non-allergic and allergic patients

	K_D (nM)/(pM)[1]	B_{max} (pmol g^{-1} tissue)	B_{max} (fmol mg^{-1} protein)	n
α_1-adrenoceptors				
Non-allergic	0.4 ± 0.1	0.77 ± 0.14	177 ± 33	5
control	0.4 ± 0.2	0.90 ± 0.17	195 ± 40	3
chronic sinusitis	0.5	0.35	80	1
vasomotor rhinitis	0.2	0.83	218	1
Allergic	0.3 ± 0.1	0.80 ± 0.11	244 ± 50	4
α_2-adrenoceptors				
Non-allergic	2.7 ± 0.5	5.53 ± 1.04	1180 ± 127	14
control	2.7 ± 0.6	4.61 ± 0.87	1070 ± 119	8
chronic sinusitis	3.7 ± 1.4	9.65 ± 3.80	1630 ± 430	3
vasomotor rhinitis	1.6 ± 0.2	3.86 ± 0.59	1020 ± 198	3
Allergic	2.3 ± 0.4	5.21 ± 0.59	1230 ± 96	9
β-adrenoceptors[1]				
Non-allergic	2.7 ± 0.2	0.50 ± 0.06	87 ± 11	18
control	2.8 ± 0.3	0.48 ± 0.06	92 ± 10*	13
chronic sinusitis	2.9 ± 0.2	0.67 ± 0.20	100 ± 46	3
vasomotor rhinitis	2.7/1.6	0.32/0.45	42/30	2
Allergic	3.1 ± 0.4	0.41 ± 0.05	63 ± 6*	14
Muscarinic receptors[1]				
Non-allergic	47.2 ± 4.4*	2.65 ± 0.30*	616 ± 52*	18
control	49.2 ± 5.5°	2.59 ± 0.39°	661 ± 68°	12
chronic sinusitis	39.3 ± 9.4	3.25 ± 0.58#	543 ± 146	3
vasomotor rhinitis	47.0 ± 15.1	2.27 ± 0.87	449 ± 51	3
Allergic	35.0 ± 5.5*°	1.56 ± 0.29*°#	445 ± 57*°	11

[1] K_D in pM for β-adrenoceptors and muscarinic receptors, *°# $P < 0.05$.

ties (B_{max}) could be demonstrated in allergic patients in comparison with non-allergic patients and control individuals (Table 1).

The β-adrenoceptor density, expressed per mg protein, was significantly reduced in allergic patients in comparison with controls (Table 1). The affinities of [^{125}I]-(−)-CYP binding to β-adrenoceptors, however, were not different in allergic patients from controls. No changes in agonist binding or guanine nucleotide coupling of β-adrenoceptors could be observed in allergic patients. Inhibition of the [^{125}I]-(−)-CYP binding with the subtype selective antagonist $LK_{203-030}$ (Milavec-Krizman *et al.*, 1985) demonstrated the presence of a homogeneous population of β_2-adrenoceptors in the nasal mucosa of both allergic and non-allergic patients.

The specific [^{3}H]-1-QNB binding to muscarinic receptors in the nasal mucosa membranes was saturable and of high affinity in all groups of patients. No significant differences could be demonstrated between subgroups of the non-allergic patients. In allergic patients, the K_D- and B_{max}-values were significantly decreased in comparison with non-allergic patients and in comparison with control individuals (Table 1). No differences in agonist binding or coupling to the effector system via the G-protein could be demonstrated in allergic patients.

Discussion

Nasal hyperreactivity in nasal allergy may be due to changes in characteristics of adrenergic and/or muscarinic acetylcholine receptors (Mygind, 1982). No significant changes in affinities or densities of α_1- and α_2-adrenoceptors could be demonstrated in allergic patients in comparison with non-allergic patients and in comparison with controls. As far as the α_1-adrenoceptors, these findings are in agreement with similar reactivity to α_1-adrenoceptor agonists in allergic patients and non-allergic patients (Brooks *et al.*, 1988). The β-adrenoceptor density, expressed per mg protein, was not changed in allergic

patients in comparison with non-allergic patients but was significantly reduced in allergic patients in comparison with controls. These findings emphasize the importance of an accurate characterization of the patients. The changes in receptor density are probably not due to differences in medication, since detailed analysis of the data revealed similar binding parameters from individuals with medication in comparison with individuals without medication in the control or in the allergic rhinitis group. The decreased number of β-adrenoceptors may reflect a β-adrenergic abnormality in nasal allergy but is probably too small to explain the complex allergic reaction (Shelhamer *et al.*, 1983).

The K_D-value and the density of muscarinic receptors were significantly decreased in allergic patients in comparison with non-allergic individuals and in comparison with control individuals. Detailed analysis of the data revealed similar binding parameters from individuals with medication in comparison with individuals without medication in the non-allergic, control or allergic rhinitis group. The increased sensitivity may reflect the cholinergic induced hypersecretion in nasal hyperreactivity (Mygind, 1982). The decreased receptor number may reflect an adaptation of the effector cells to overstimulation or changes in density of inhibitory presynaptic receptors. The small shifts in affinity and receptor density may reflect the cholinergic hyperreactivity in nasal allergy but are probably too small to explain the complex allergic reaction.

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