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The effects of autonomotropic drugs on allergic nasal mucosa

Takao Watase and Minoru Okuda, Tokyo, Japan

SUMMARY

The purpose of the present study was to elucidate the effects of different kinds of autonomotropic drugs on the nasal mucosa as well as on the nasal reaction to specific allergens in patients with nasal allergy.

First, phenylephrine (α-agonist), phentolamine (α-antagonist), isoproterenol (β-agonist), propranolol (β-antagonist), methacholine (choline agonist), or ipratropium (choline antagonist) was applied to the nasal mucosa with an atomizer using saline as control. Definitive effects appeared at the spray of α-agonist or choline agonist. Phenylephrine reduced nasal airway resistance, and methacholine increased nasal secretion.

Secondly, after treatment with the drugs, nasal provocations were performed. The statistically significant effects were noted as follows: phenylephrine spray inhibited the increase of nasal airway resistance, while phentolamine or isoproterenol enhanced it. Methacholine enhanced nasal secretion, while ipratropium inhibited it. None of the drugs, however, affected the number of sneezes.

The present results suggest that adreneric receptors are mainly distributed on the walls of vessels and cholinergic receptors mainly on the secretory glands. Pharmacological conditions of the local autonomic nervous system would affect the nasal response in allergy in different ways according to different conditions.

INTRODUCTION

It has been generally accepted that the autonomic nervous system plays an important role in the nasal manifestation of allergy. Many questions, however, remain unsolved concerning the distribution of receptors of the autonomic nerves and the effect of the autonomic nerves on the nasal manifestation of allergy. In order to answer these questions, we examined the direct effect of autonomotropic drugs on the nasal mucosa, as well as the effects of drugs on the nasal reaction to allergen in patients with nasal allergy.

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MATERIALS AND METHODS

First, we examined the effects of drugs on the nasal mucosa using different drugs such as phenylephrine (α-agonist), phentolamine (α-antagonist), isoproterenol (β-agonist), propranolol (β-antagonist), methacholine (choline agonist), ipratropium (choline antagonist) or saline (control) (Table 1).

Table 1. Autonomotropic drugs for study of the effects on the nasal mucosa.

① α-agonist	(phenylephrine	3.2 mg)
② α-antagonist	(phentolamine	1 mg)
③ β-agonist	(isoproterenol	400 μg)
④ β-antagonist	(propranolol	100 ng)
⑤ choline agonist	(methacholine	2 or 6 mg)
⑥ choline antagonist	(ipratropium	140 μg)
⑦ saline (control)	(0.9% Nacl	0.26 ml)

In the experimental procedure, after elimination of excessive nasal secretion, nasal airway resistances (A) were measured using a rhinomanometer, the Mercury NR-1 (England). Immediately after the measurement, 0.26 ml of the drug or saline was sprayed into both sides of the nasal cavity with an atomizer. Then the number of sneezes produced was counted, nasal secretion collected by nose-blowing weighed and the nasal airway resistance (B) measured 15 minutes after the treatment. Changes in the nasal airway resistance before and after treatment were expressed as the ratio of post-treatment to pre-treatment (B/A). Secondly, the effects of the drugs on the nasal provocation reaction were exa-

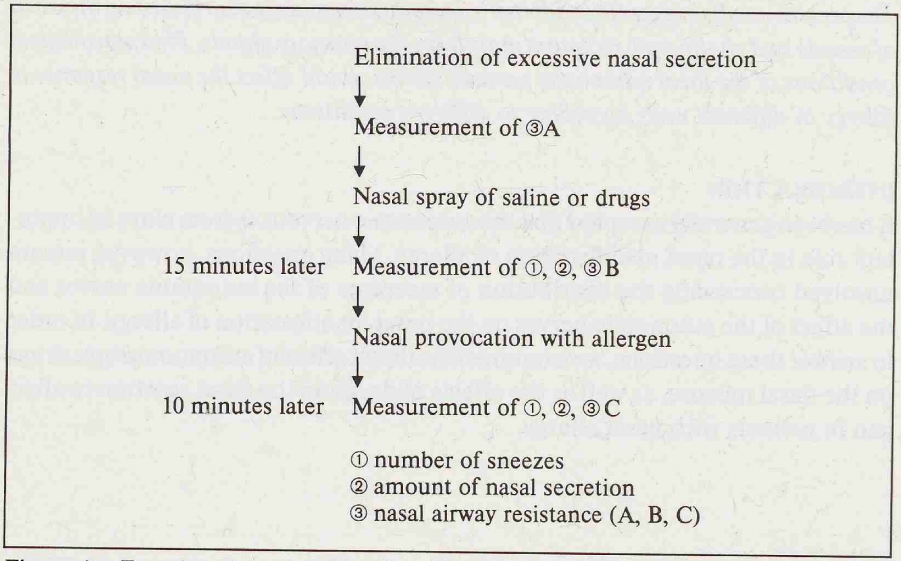

Figure 1. Experimental procedure for effects of autonomotropic drugs on the nasal mucosa.

mined. After the elimination of excessive nasal secretion, nasal airway resistance (A1) was measured by the method mentioned above. Then, 0.26 ml of saline was sprayed into both sides of the nose. Fifteen minutes later, paper discs containing allergen were attached to the bilateral inferior turbinates and the nasal airway resistance (C1), the amount of nasal secretion and the number of sneezes 10 minutes after provocation were examined (Figure 1). Changes in the nasal resistance before and after provocation were expressed as the ratio of post-provocation to pre-provocation (C1/A1). The following day, the same procedure using drugs instead of saline were repeated, and the changes in nasal resistance expressed as C2/A2. The effects of the pharmacological agents on the nasal airway resistance in nasal provocation were evaluated by comparing C1/A1 (Control) with C2/A2. The amount of nasal secretion and the number of sneezes were compared with the values obtained from pretreatment of saline and those from pretreatment of drugs. Statistical analyses were performed by the two-tailed students test, paired t test or the chi square test.

RESULTS

Definitive effects appeared at the spray of α-agonist or choline agonist. Phenylephrine reduced the nasal airway resistance, phentolamine increased it although not significantly in statistical analysis, and methacholine increased the amount of nasal secretion. Phentolamine and methacholine each occasionally induced sneezes possibly due to stimulation of the irritant receptors. Neither β-agonist nor antagonist affected the nasal airway resistance. When the same experiment was repeated using increased doses of the same drugs (isoproterenol 600 µg, and propranolol 1 µg), the nasal airway resistances were unchanged (Table 2).

Statistically significant effects of drugs on nasal provocation reaction were noted as follows: decrease of nasal airway resistance by phenylephrine spray, increase of nasal airway resistance by both phentolamine and isoproterenol, increase of nasal

Table 2. Direct effects of autonomotropic drugs on the nasal mucosa.

drugs		number of cases	sneezes	nasal secretion	nasal blockage average of ratio of B/A
phenylephrine	3.2 mg	16	0	0	0.66 ± 0.24*
phentolamine	1 mg	13	2A	1B	1.55 ± 1.06
isoproterenol	400 µg	23	0	0	0.97 ± 0.20
propranolol	100 ng	25	0	0	1.01 ± 0.13
methacholine	6 mg	26	4A	16B*	1.11 ± 0.58
ipratropium	140 µg	13	0	0	1.00 ± 0.15
saline	0.26 ml	15	0	0	1.09 ± 0.32

A number of patients who showed sneezing.
B number of patients who showed increased nasal secretion of more than 0.26 gr.
* statistical significant ($P<0.01$).

Table 3. Effects of autonomotropic drugs on nasal provocation reaction.

		sneezes	nasal secretion	nasal airway resistance
phenylephrine	3.2 mg	n.e.	n.e.	decreased
phentolamine	1 mg	n.e.	n.e.	increased
isoproterenol	400 μg	n.e.	n.e.	increased
propranolol	100 ng	n.e	n.e.	n.e.
methacholine	2 or 6 mg	n.e.	increased	n.e.
ipratropium	140 μg	n.e.	decreased	n.e.

n.e.: not significantly effective

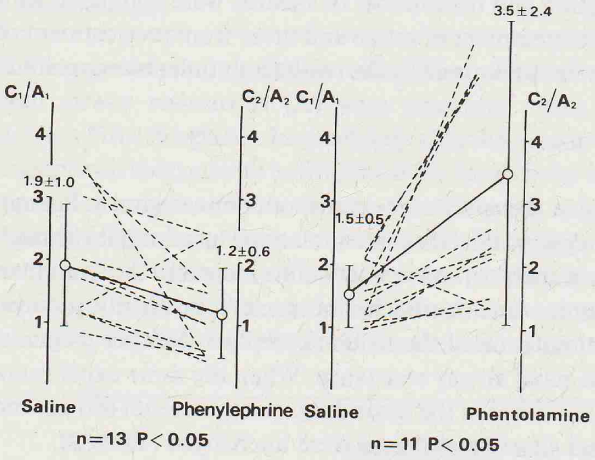

Figure 2.
Effects of α-adrenergic drugs on nasal airway resistance in nasal provocation.

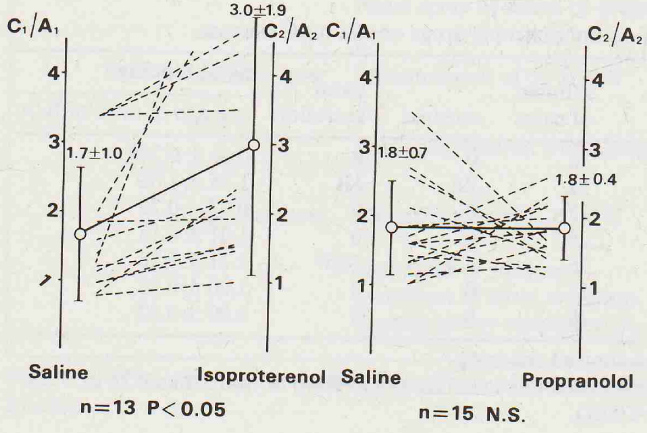

Figure 3.
Effects of β-adrenergic drugs on nasal airway resistance in nasal provocation.

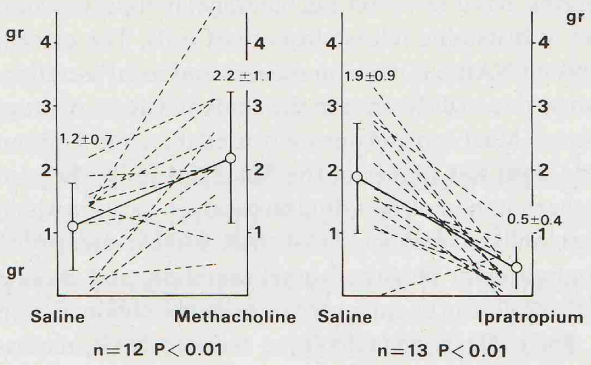

Figure 4.
Effects of cholinergic drugs nasal secretion in nasal provocation.

secretion by methacholine and decrease of secretion by ipratropium. None of the drugs, however, affected the number of sneezes (Table 3). Spray of phenylephrine or α-agonist decreased the nasal airway resistance from 1.9 to 1.2, whereas spray of phentolamine, or α-antagonist increased it from 1.5 to 3.5 (Figure 2).
Contrary to α-adrenergic drugs, the spray of isoprotenenol, a β-agonist, increased the nasal airway resistance from 1.7 to 3.0, while that of propanolol, a β-antagonist, induced no change in this value (Figure 3).
Methacholine, a choline agonist, increased nasal secretion from 1.2 to 2.2 grams, whereas ipratropium, a choline antagonist, decreased nasal secretion from 1.9 to 0.5 grams (Figure 4).

DISCUSSION

Different kinds of autonomotoric drugs directly affect the nasal mucosa in different ways. It is generally agreed that cholinergic stimuli increase nasal secretion. On the other hand, adrenergic influences on nasal secretion are less clear. Malm (1981, 1983) revealed that both α- and β-adrenoceptors involved nasal secretion, while we found no effect in the present study. It is also generally agreed that α-adrenergic stimuli reduce nasal airway resistance (NAR) due to vasoconstriction. Effects of β-adrenoceptors and cholinoceptors on NAR, however, are still controversial. After topical spray of different kinds of β-adrenoceptors, Schumacher (1981), Borum (1980), and MacLean (1976) found an increase of NAR, while Svensson (1986) as well as the present study revealed no effects. After sprays of cholinoceptors, Malm (1983) and MacLean (1977) found vasodilation, while Borum and our study (1978) found no effects.
These contradictions may be due to the different experimental conditions, i.e. different kinds and doses of drugs, and different methods of evaluation. Autonomotropic drugs also affect nasal reaction to allergens. As far is known except the β-stimulants few reports have been presented on this matter. Schumacher (1980), Borum (1980) and MacLean (1976) revealed that β-adrenoceptors inhibited all

three nasal symptoms (sneezing, nasal secretion and blockage) in nasal provocation through the inhibition of histamine release from mast cells. The present study, however, found effects on NAR but none on sneezes and nasal secretion. This contradiction may also be due to difference in the kinds and doses of drugs used. Of the reports mentioned, MacLean and our study used the same β-stimulants, isoproterenol, but the dose was higher in the MacLean study. We also examined the effects of another autonomotropic drug on nasal provocation which revealed that α-adrenoceptor inhibited the increase of NAR, while α- antagonist enhanced it. Moreover, cholinoceptor enhanced nasal secretion, and choline antagonist inhibited it. These results can be supported by evidence obtained from the present study that as direct effects phenylephrine reduced NAR, methacholine increased nasal secretion and ipratropium reduced nasal secretion.
In the present study it was revealed that different kinds of autonomotropic drugs affect the nasal mucosa in different ways. These suggest that nasal autonomic conditions influence nasal manifestation of allergy.

CONCLUSION

Adrenergic receptors are mainly distributed on the walls of the vessel, and cholinergic receptors mainly on the secretory glands. Pharmacologically induced changes of local autonomic nervous conditions affect the nasal response in allergy in different ways according to different conditons.

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T. Watase, M.D.
Dept. of Otorhinolaryngology
Nippon Medical School
1-1-5 Sendagi, Bunkyo-ku
Tokyo, Japan