

Differential responses to various classes of drugs in a model of allergic rhinitis in guinea pigs

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Abstract

Different drugs from various pharmacological classes were compared for their ability to protect against the nasal effects of acute allergen challenge in a guinea pig model. In the model, sneezing and nose rubbing were recorded after an initial allergen challenge in guinea pigs previously sensitized to egg albumin. Four days later the same guinea pigs were re-challenged a second time when anesthetized. In these anaesthetized animals, nasal airway pressure, pulmonary inflation pressure and cellular infiltration into nasal lavage fluid were measured. The drug tested were autacoid antagonists (mepyramine—3 mg/kg, cetirizine—3 mg/kg and montelukast—10 mg/kg), L-NAME (10 or 20 mg/kg), heparin (20 mg/kg) and dexamethasone (20 mg/kg) given either intraperitoneally or intravenously; all were given shortly before challenge.

Sneezing induced by allergen challenge was statistically significantly reduced by mepyramine, cetirizine and dexamethasone whereas only cetirizine reduced nose rubbing. Changes in nasal airway pressure due to allergen exposure were reduced by cetirizine, montelukast, L-NAME, and heparin, but not by mepyramine, nor dexamethasone. In the presence of L-NAME, nasal airway pressure actually changed in the opposite direction. Cellular infiltration, as assessed by cytometry in nasal lavage fluid 60 min after acute allergen challenge, was reduced by montelukast and heparin but not by antihistamines, L-NAME nor dexamethasone.

This pattern of effects of the drugs, given by doses and routes previously described in the literature as being effective was not completely consistent with expected responses. The lack of effect of dexamethasone probably reflects the fact that it was given acutely whereas in the clinic chronic administration is used. The two antihistamines were not identical in their actions, presumably reflecting the fact that cetirizine has therapeutic actions not entirely confined to blockade of H1 receptors. Montelukast has not been reported to have major effects on sneezing and itching in the clinic but reduces nasal obstruction (lower nasal airway pressure or nasal patency). Montelukast's effects on cellular infiltration indicate the possible involvement of leukotrienes. Heparin has actions on inflammatory cell infiltration. This could explain its profile of reducing both cellular infiltration, and increased nasal airway pressure.

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1. Introduction

Allergic rhinitis is a common health problem whose treatment with drugs is not ideal. The major signs and symptoms of allergic rhinitis include sneezing, itching, rhinorrhea and nasal congestion, accompanied by infiltration of the nasal mucosa by eosinophils [1]. There are two temporal phases to allergen challenge in sensitized subjects.

The earliest response consists mainly of sneezing, itching and rhinorrhea whereas nasal congestion and cellular infiltration occurs later [2].

Histamine is considered to play an important role in allergic inflammation. Nasal challenge with histamine causes sneezing, pain, pruritus, rhinorrhea and nasal blockade [3] and histamine concentrations in nasal lavage fluid increase with allergen challenge [2]. Furthermore, H1-antihistamines administered orally, or topically, reduce some of the signs and symptoms of both seasonal and perennial allergic rhinitis [1]. Other autacoids, e.g. leukotrienes, also play a

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role. Antagonists of cysteinyl leukotriene LTD₄ receptors (montelukast) reduce some of the signs and symptoms of allergic rhinitis [4]. Nitric oxide (NO), the cell-signaling molecule, has been implicated in a wide range of physiological and pathophysiological events in numerous cell types and in patho-physiological processes including the immune system. Interestingly, NO concentrations in exhaled air are elevated in allergic rhinitis patients compared to normal [5].

Anti-inflammatory drugs moderate many of the symptoms of allergy. Topical glucocorticoids are used routinely to treat allergic rhinitis. Steroids are routinely used chronically, but they have not been well investigated when given acutely in models of allergic rhinitis. Heparin, in addition to its anticoagulant properties, has anti-inflammatory actions that reduce the signs and symptoms of allergic rhinitis [6].

We have recently reported a combined conscious/anesthetized guinea pig model for studying allergic rhinitis [7]. The aim of this study was to expand our understanding of the model by testing therapeutic or experimental drugs including antihistamines, montelukast, heparin, L-NAME and dexamethasone.

2. Materials and methods

2.1. Animals

Male Dunkin–Hartley guinea pigs (Charles River Laboratories, Canada), weighing from 300 to 400 g during the sensitization period and 400–600 g at times of challenge, were used. They were housed at $23 \pm 2^\circ\text{C}$ and $55 \pm 5\%$ humidity, on a 12 h light/dark cycle, with food and water *ad libitum*. Animal experiments were approved by the University of British Columbia Animal Care Committee.

2.2. Drugs

The actions of various clinical or experimental drugs in the treatment of allergic rhinitis were assessed in terms of effects on sneezing, nose rubbing, nasal congestion, or patency as reflected by nasal airway pressure, and leukocyte infiltration into nasal lavage fluid. The drugs (see Table 1 for doses and routes) were selected on the basis of their general or particular effectiveness in the allergic rhinitis seen in humans and/or experimental animals. The drugs included first

(mepyramine) and second (cetirizine) generation antihistamines, a leukotriene D₄ antagonist (montelukast), a nitric oxide synthase inhibitor (L-NAME), and a glucocorticosteroid (dexamethasone), as well as heparin. Doses and routes of administration were chosen from the literature on the basis of their effectiveness in various animal models. Drugs were given intraperitoneally (i.p.) 15 min prior to ovalbumin challenge while intravenous drugs were given 5 min before.

2.3. Sensitization and assessment of sneezing and nose rubbing

The methods used in this study were recently described [7]. Briefly, the same animal was used for measurement of sneezing and nose rubbing (while conscious) and 2 days later (while anesthetized) for measurement of nasal airway pressure, lung inflation pressure and leukocyte infiltration into nasal lavage fluid. The sensitization procedure first described by Yamasaki et al. [8] was used with modifications. Initial exposure was to 1% ovalbumin (Grade V, Sigma, Germany) in saline twice (7 days apart) as an aerosol generated by ultrasonic nebulizer (ULTRA-NEB 99, DeVILBISS Co., Canada) and applied with a ventilation pump at 4 ml/stroke, 70 strokes/min via a nose cone. On days 14, 15 and 16 boosters of 1% ovalbumin in saline (20 μl /nostril/day) was instilled intranasally.

The first challenge, 21 days after beginning sensitization, was given to conscious guinea as 2% ovalbumin in saline to both nostrils 20 μl /nostril (treated groups plus an untreated control groups), or 20 μl saline alone (unsensitized group). Following challenge, guinea pigs were observed individually for sneezing and nose rubbing using standardized observations in a randomized blind fashion for 30 min post challenge. Sneezes were characterized by explosive expiration just after a deep inspiration. A nose rub was characterized by an external peri-nasal scratch with the animal's forelimbs. It was taken to be an index of nasal itching. Thereafter animals were left to recover for 4 days prior to a second challenge in anaesthetized animals for the measurement of nasal and lung pressures, as well as cellular infiltration in the nasal cavities of anaesthetized animals.

2.4. Assessment of specific nasal airway pressure

Guinea pigs were anaesthetized with pentobarbital (35 mg/kg intraperitoneally, plus more as appropriate), and cannulated for blood pressure measurement, intravenous injections, as well as nasal and lung inflation pressures. Nasal airway pressure was measured by a modification of the method of Mizuno et al. [9]. A catheter was passed from the trachea, through the laryngopharynx and the oropharynx, toward the nasopharynx, ending about 1 mm before the posterior nares. A ventilation pump (Harvard Apparatus Limited) was used to deliver air at a rate of 8 ml/stroke, 72 times/min directed toward the nares. In order to prevent air leakage, the buccal (oral) cavity was filled with epoxy-soaked cotton wool and the

Table 1
Drugs used in this study together with dose and route of administration

Drug	Dose (mg/kg)	Route of administration
Mepyramine	3	Intraperitoneal
Cetirizine	3	Intraperitoneal
Montelukast	10	Intravenous
L-NAME	10	Intravenous
Heparin	20	Intravenous
Dexamethasone	20	Intraperitoneal (for sneezing), intravenously (for nasal airway pressure)

oesophagus ligated. Intranasal pressure, as an index of nasal airway resistance, was recorded via a pressure transducer. A second ventilation pump was used to ventilate the lungs using the above ventilation protocol while the pressure in this circuit was also recorded.

Following their preparation, guinea pigs were allowed time to equilibrate with respect to a stable blood pressure, nasal airway pressure and lung inflation pressure. Thereafter, the nasal ventilation pump was disconnected so as to allow 0.5 ml of 2% ovalbumin challenge to be infused from the tracheal side toward the nasal cavity for 5 min. At the end of this 5 min infusion period, the ventilation pumps were reconnected and the animal was observed for 1 h as previously described by Sakairi et al. [10]. At the end of the 60 min observation period, a nasal lavage technique (see below) was used to assess leukocyte infiltration.

2.5. Leukocyte infiltration

Nasal cellular infiltration was used as an index of extravasation of leukocytes as part of the inflammatory response to allergen challenge. Total and differential leukocyte counts in nasal washings were made. The anaesthetized animals, described previously, were monitored for 60 min after allergen challenge before nasal lavage was performed. Nasal lavage was with a 2 ml wash of pre-warmed saline infused from the tracheal side, and collected from the anterior nares. Total and differential leukocyte counts were made of the lavage fluid immediately after sample collection.

The total cell count was by standard haemocytometer methods. Methylene blue was used for cell staining and clarity of counting. Leukocytes were counted under a light microscope at power $40\times$ using standard procedures. To perform differential cell counts, 100 μ l of nasal lavage was centrifuged using a cytospin (Shandon Cytospin 1) at a speed of 1500 rpm for 5 min. The sample was then stained with a solution of Wright's stain (Fluka, D89555, Steinheim, Germany) for 5 min. Leucocytes (eosinophils, neutrophils, basophils, monocytes and lymphocytes) were identified and their presence counted.

2.6. Statistical analysis

Data are expressed as mean $\pm$ SEM. A one-way analysis of variance (ANOVA) was used in data analysis with the Bonferroni significant differences test for multiple comparisons applied to the analysis, as well as unpaired Student's *t*-test when appropriate. Statistical significance was regarded as $p < 0.05$.

3. Results

3.1. Antihistamines (Fig. 1A–E)

In this experiment, as well as in those whose results are described in Figs. 2 and 3, control unsensitized guinea pigs challenged with saline or ovalbumin failed to give

significant responses. Control values were similar in all cases. Challenge with ovalbumin in these non-sensitized animals produced no statistically significant changes from pre-challenge readings. Saline alone did not produce changes in sensitized animals (data not shown). Because of these findings a saline treatment group was not included in all of the three experimental groups (Figs. 1–3) studied.

Treatment with mepyramine and cetirizine in sensitized guinea pigs inhibited ($p < 0.01$) ovalbumin-induced sneezing in sensitized guinea pigs as compared with sensitized untreated guinea pigs (Fig. 1A). Cetirizine treatment resulted in a reduction in nose rubbing, whereas mepyramine did not (Fig. 1B). Cetirizine also attenuated ($p < 0.05$) ovalbumin-provoked increases in nasal airway pressure whereas mepyramine did not (Fig. 1D). Both drugs failed to attenuate allergen-induced nasal leucocyte infiltration, or alter the types of leucocytes found in the lavage fluid. By far the majority of these cells were eosinophils (Fig. 1E).

3.2. Montelukast and heparin (Fig. 2A–D)

Treatment with montelukast or heparin failed to inhibit sneezing and nose rubbing (Fig. 2A and B). However, as shown in Fig. 2C, both treatments statistically significantly ($p < 0.01$) inhibited allergen-induced increases in nasal airway pressure. Both treatments also significantly ($p < 0.01$) reduced leukocyte infiltration (Fig. 2D). There were insufficient numbers of other leukocytes in lavage fluid, as compared to eosinophils, to make it possible to detect possible differences (data not shown).

3.3. L-NAME and dexamethasone (Fig. 3A–E)

As shown in Fig. 3A and B, dexamethasone given acutely, statistically significantly ($p < 0.001$) inhibited sneezing but not nose rubbing, whereas L-NAME had no effect on either. On the other hand, L-NAME ($p < 0.001$) markedly attenuated the nasal airway pressure change induced by ovalbumin challenge in sensitized guinea pigs whereas there was no obvious effects of dexamethasone. Of interest was the fact that L-NAME reversed the change in nasal airway pressure despite the fact that L-NAME did not have this effect in non-sensitized control animals (Fig. 3C). L-NAME and dexamethasone both failed to inhibit leukocyte infiltration, as shown by a lack of effect on total counts (Fig. 3D). However, differential counts were changed by L-NAME since it statistically significantly ($p < 0.001$) stimulated both eosinophil and neutrophil recruitment as compared with all of the other treatments studied. In particular, this effect of L-NAME was not seen in control non-sensitized non-sensitized guinea pigs (Fig. 3E).

4. Discussion

The purpose of this study was to ascertain the effects of various clinical and experimental drugs in a model of allergic rhinitis so as to further assess the value of the

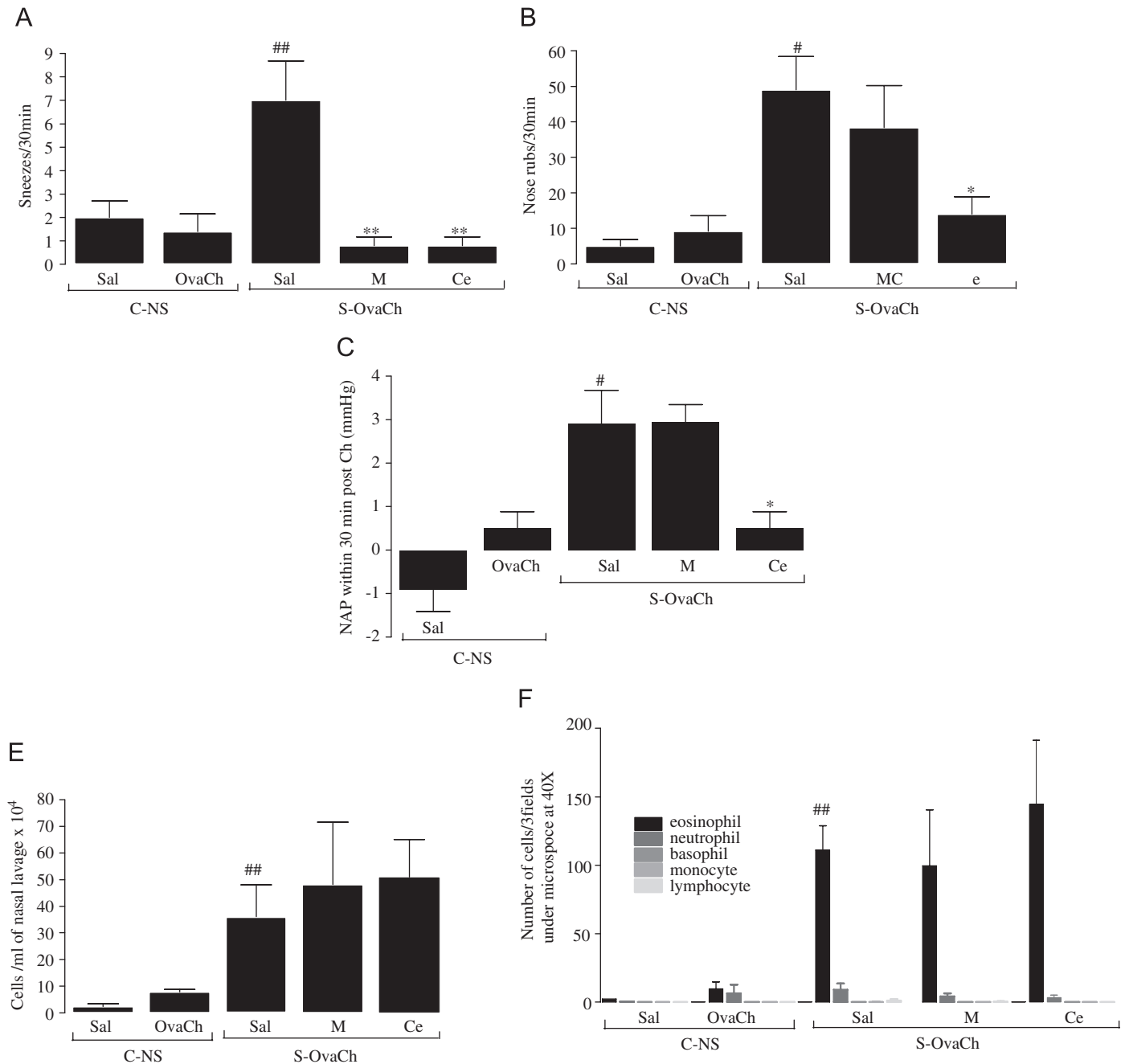


Fig. 1. (A–E) Effect of mepyramine (M) and cetirizine (Ce) (3 mg/kg i.p.) on (A) total sneezes in 30 min, (B) nose rubs in 30 min in conscious control non-sensitized (C–NS) and sensitized (S) conscious guinea pigs. (C) Shows nasal airway pressure changes (NAP–mmHg), (D) total cell count $\times 10^4$ /ml in nasal lavage fluid and (E) differential cell count in anesthetised guinea pigs. In A and B guinea pigs (S and NS) were challenged (Ch) with ovalbumin (2% ovalbumin (Ova) or saline (Sal) given as 20 μ l/(S) to each nostril in A and B. Treatments were administered i.p. 15 min prior to challenge. Anesthetised guinea pigs (C–E) were challenged with ovalbumin (Ova–Ch); 0.5 ml infused for 5 min through the nasal cavities. Nasal airway pressure (C) 30–35 min post challenge was expressed as a change from pre-challenge. Challenge (Ova–Ch) in sensitized animals produced increases in sneezing and nose rubbing compared with the two unsensitized controls. Mepyramine (M) or cetirizine (Ce) reduced sneezing (A) but had lesser effect on nose rubbing with only the reduction with cetirizine was statistically significant. Increases in nasal airway pressure (C) following challenge were reduced by cetirizine but not mepyramine. The amount or distribution of leukocytes in nasal lavage fluid induced by allergen was not reduced by mepyramine or cetirizine. In this, and all other figures, data are means ($n = 5$) and vertical bars $\pm$ SEM (standard error of mean). The sensitization status for different groups is indicated by horizontal bars indicating non-sensitized or sensitized. Statistical differences: # and ## for $p < 0.05$ and < 0.01 are difference in saline-treated sensitized animals or * or ** for difference of treated animals from sensitised saline control. Note: A common format and abbreviations are used for as well as for Figs. 2 and 3 apart from the abbreviations used for drugs.

model, advance knowledge of possible new treatments, and investigate the possible role of NO. In the following discussion the effects of each class of drugs is examined in individual sections.

4.1. Effects of antihistamines

While both cetirizine and mepyramine are selective H1 receptor antagonists cetirizine is less potent on

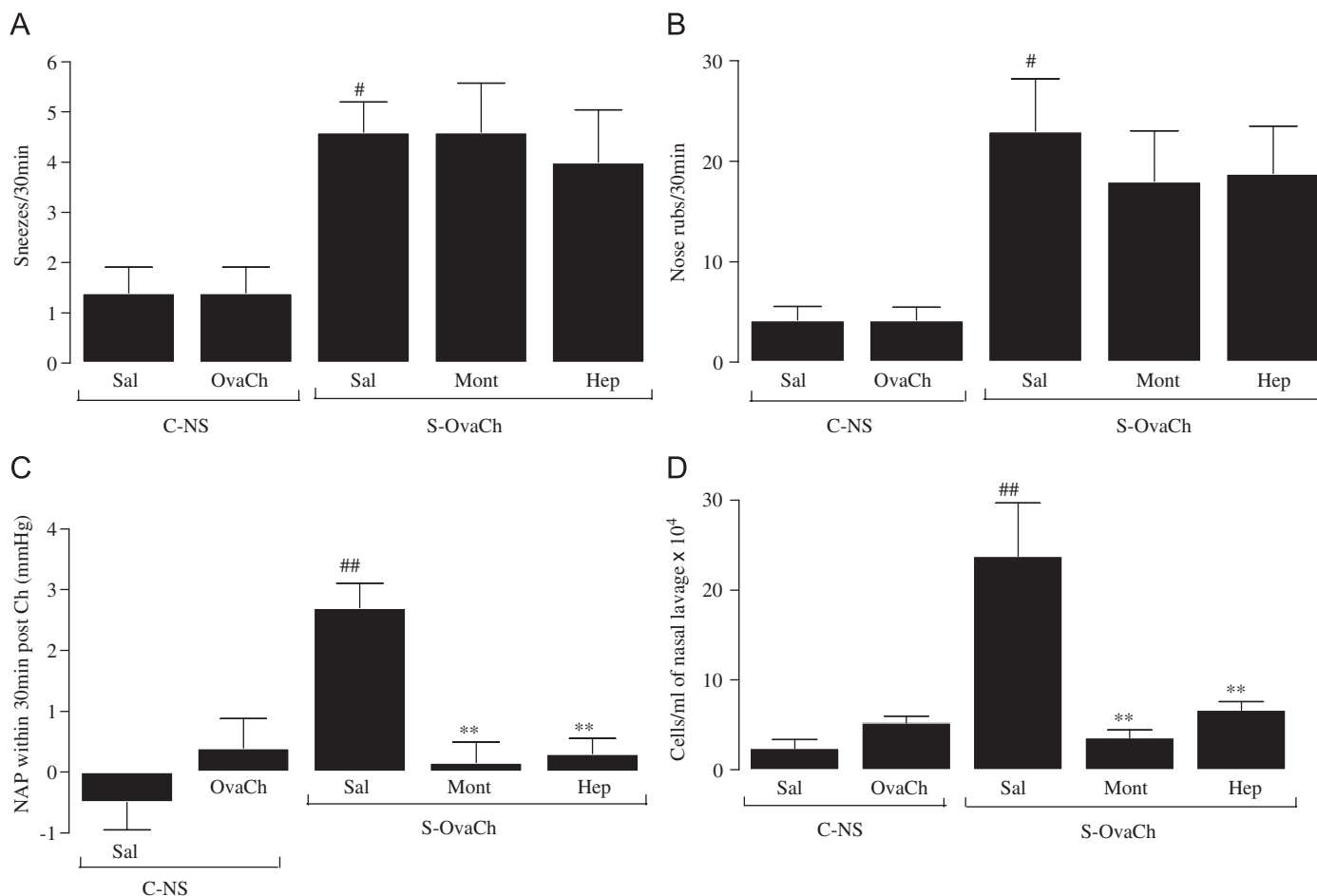


Fig. 2. (A–D) Effect of montelukast 10 mg/kg (Mont) and heparin 20 mg/kg (Hep) i.v. on sneezing (A) and nose rubbing (B) induced by 2% ovalbumin challenge (Ova–Ch) in conscious sensitized (S-) guinea pigs. Ovalbumin challenge (Ova–Ch) in sensitized (S) animals induced a marked increase in sneezing and nose rubbing when compared with the two control groups and this was not reduced by montelukast or heparin treatment. In only sensitized (S) animals did ovalbumin challenge (Ova–Ch) increase nasal airway pressure (NAP) (C) and the number of cells in nasal lavage fluid (D) when compared with the non-sensitized (C–NS) controls. However, both treatments statistically significantly reduced the change in nasal airway pressure (C) and the number of leukocytes (D) found in nasal lavage fluid. A differential count for leukocytes was not done since the reduced number of cell due to drug treatment precluded an accurate differential count. As in Fig. 1, data are means of five guinea pigs while vertical bars represent $\pm$ SEM (standard error of mean). Statistical differences are indicated by the symbols # and ## for $p < 0.05$ and < 0.01 respectively for difference in saline-treated sensitized animals and by * or ** for difference of treated animals from their saline control for sensitized guinea pigs.

muscarinic receptors [11]. As expected, both mepyramine (first generation antihistamine) and cetirizine (second generation) reduced allergen-induced sneezing. However, cetirizine, but not mepyramine, inhibited nose rubbing. Effects on sneezing were consistent with the accepted role of histamine in mediating allergen-induced sneezing [12]. The role of histamine in nose rubbing is less clear although some studies report inhibition by antihistamines [13]. Nose rubbing is considered to be due to itching and H1 receptor antihistamines are not as effective in alleviating itching due to allergy [14]. If histamine-induced itching is mediated via H4 receptors [15], this could explain a lack of effect of mepyramine. On the other hand, the effectiveness of cetirizine may reflect other types of actions such as antiallergic and anti-inflammatory actions, independent of H1-blockade

[16]. Thus our results are partly consistent with those of others [17].

In an analogous manner to nose rubbing, cetirizine but not mepyramine, reduced allergen-induced changes in nasal airway pressure (nasal patency). Previous studies have suggested a role for histamine in allergen-induced changes in nasal airway pressure [16,17] but not all antihistamines prevent this increase [18]. Previous studies have also been reported failure of antihistamines to inhibit increases in nasal airway pressure in guinea pigs [19]. However, Murata et al. [20] has previously shown that, similar to the finding in this study, that cetirizine was effective in preventing increases.

The different effect of the two antihistamines on nasal airway pressure is not readily explained. However, as discussed above, while all H1-antihistamines share

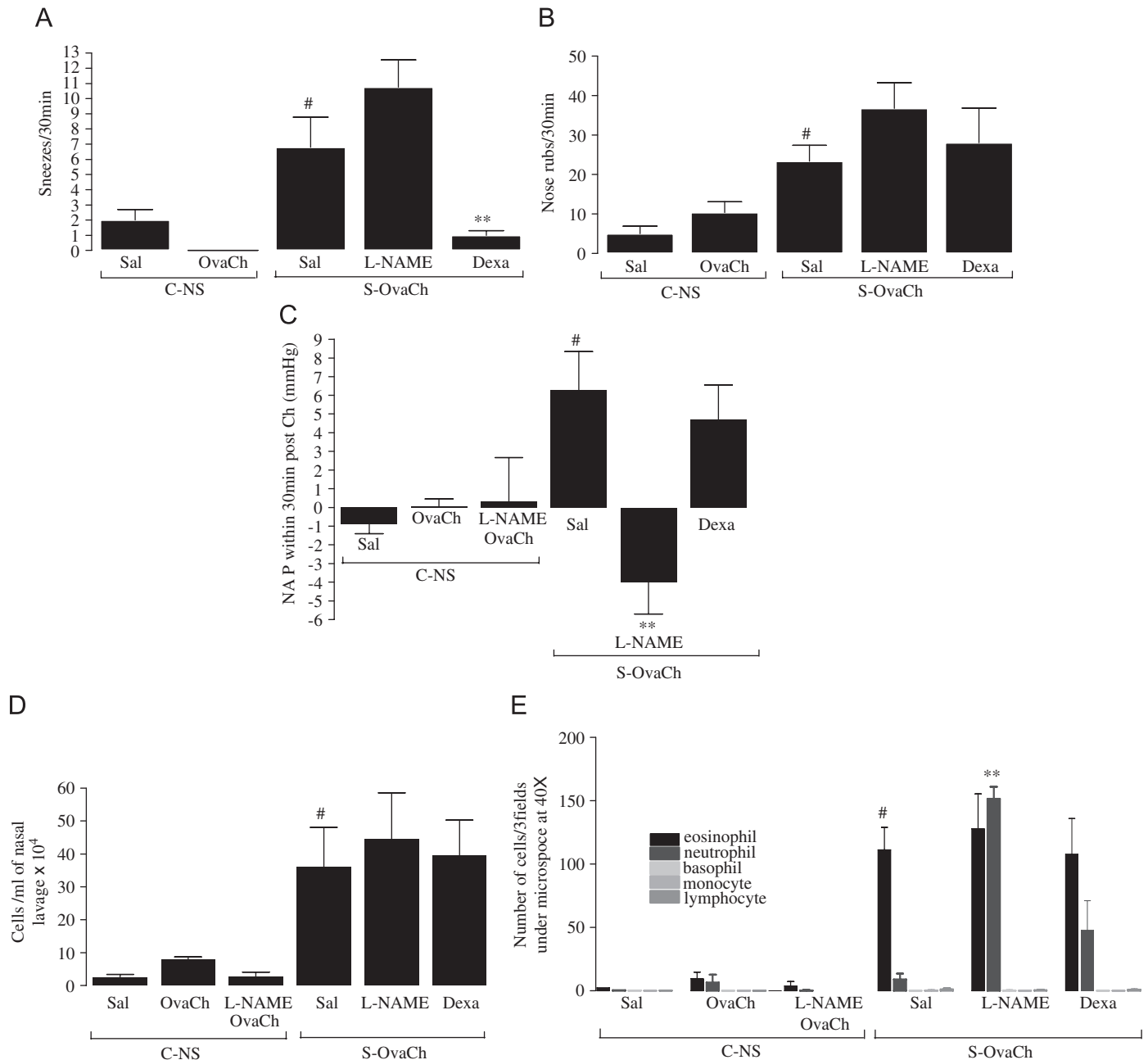


Fig. 3. (A–E) Effects of dexamethasone 20 mg/kg i.p. (Dexa) and L-NAME 10 mg/kg i.v. (L-NAME) on sneezing (A) and nose rubbing (B) shown as in the previous two figures. As in the previous experiments ovalbumin challenge (Ova-Ch) produced the expected changes in sneezing and nose rubbing. L-NAME treatment did not statistically significantly change sneezing or rubbing. In fact the number of these events tended to increase. Sneezing was reduced by dexamethasone treatment whereas it had no effect on nose rubbing. Dexamethasone failed to statistically significantly change either nasal airway pressure (NAP) (C) or cell count (D) in sensitized (S) animals. However, there appeared to be a change in the differential count with Dexa but this did not reach statistical significance because of the large variance. On the other hand L-NAME treatment in sensitized (S) animals not only reduced the change in nasal airway pressure due to challenge, but actually reversed the direction of change. However, L-NAME failed to produce a similar change when given to non-sensitized (C-NS) guinea pigs challenged with ovalbumin. Another notable effect of L-NAME treatment was the effect on differential count (E) where despite the non-statistically significant increase in total counts, the distribution of cells changed such that many more neutrophils were present. As in Figs. 1 and 2 data are means of five guinea pigs while vertical bars represent $\pm$ SEM (standard error of mean). Statistical differences are indicated by the symbols # $p < 0.05$ for difference in saline-treated sensitized animals, and by * or ** for difference of treated animals from their appropriate saline control for sensitized guinea pigs.

the common property of blocking H1 receptors they vary in their other pharmacological actions. Thus different H1-antihistamines can have different effects on different aspects of the allergic inflammatory response. For example,

cetirizine inhibits allergen-induced eosinophil accumulation, eosinophil migration and infiltration [21], reduces intercellular adhesion molecule 1 (ICAM-1) expression [22], and inhibits monocytes and T lymphocytes [23].

4.2. Effects of montelukast

Montelukast's effects in a guinea pig model of allergic rhinitis have not been previously described although it has been demonstrated (using different *cysLT1* receptor antagonists) that *CysLTs* (especially *LTD₄*) are involved in nasal congestion [24,25]. In allergic seasonal rhinitis [26] montelukast reduces symptom scores. Our results are consistent with the findings that nasally applied *LTD₄* did not induce sneezing in humans [27], nor in guinea pigs [28]. The involvement of *cysteinyl LTs* in allergic rhinitis is illustrated by findings such as increased levels in nasal lavage fluid [29] and vasodilator effects on nasal blood vessels [30]. In accordance with these findings there were marked effects on nasal airway pressure found in this study.

The reduction found in eosinophil infiltration with montelukast is consistent with previous findings in guinea pigs [28] and with the finding that *cysteinyl LTs* induces eosinophil infiltration in humans [31]. Interestingly *LTD₄* has been reported to have no chemotactic effects on guinea pig eosinophils [24], unlike in human eosinophils. Therefore the inhibitory effect in guinea pigs might be indirect. In conclusion, while the results of the present study do not support an involvement of *cysteinyl LTs* in sneezing or nose rubbing they do support a role in cellular infiltration and nasal obstruction.

4.3. Effects of heparin

The experiment with heparin was based upon the previously described protective effects of intranasal heparin on allergic rhinitis in man [6], the fact that heparin prevents AMP-induced nasal mucosa mast cell degranulation as well as inhibiting mast cell/endothelial cell interactions [32]. This study has added to those observations by showing that while heparin did not influence sneezing or nose rubbing induced by allergen challenge it inhibited both changes in nasal airway pressure and leukocyte infiltration.

Various findings have been used to explain the findings with heparin and a number of mechanisms might be involved. However, the anti-inflammatory effects of heparin are not well understood and their putative mechanisms still speculative. Despite lack of information regarding a mechanism, the results of this study lend encouragement to the thesis that heparin has anti-inflammatory actions in allergy that are of potential clinical usefulness, especially if such actions could be separated from anticoagulant actions.

4.4. Effects of L-NAME

The only significant actions of L-NAME in this study were its marked effects on nasal airway pressure, and the large increase in neutrophils found in nasal lavage fluid (Fig. 3C and D). Previous work has shown NO involvement in nasal airway pressure increases after allergen

challenge in guinea pig with allergic rhinitis [13,33]. The lack effect of L-NAME on eosinophil infiltration would negate these cells as being involved.

L-NAME has vascular actions and these might explain its effects on the nasal airway pressure response. NO induces microvascular leakage as a result of indirect vasodilatation [34] plus vasodilation and such actions might be expected to increase nasal patency as measured by nasal airway pressure. What is striking is that L-NAME actually reversed nasal airway changes after allergen challenge, despite failing to have any such action in control non-sensitized animals (Fig. 3C). The only correlate with this finding was the large increase in neutrophil infiltration. While L-NAME treatment did not statistically significantly increase the number of cells found in nasal lavage fluid there was a marked increase in neutrophil infiltration. This was the only example of any change in the distribution of leucocytes seen in this study into the effects of six different drugs. This effect on neutrophils was not due to L-NAME alone since it did not occur in L-NAME treated non-sensitized animals exposed to ovalbumin challenge. One explanation of the observations would involve allergen challenge releasing two substances (one of which is NO) which act in opposition to each other in terms of their effects on nasal patency and neutrophil infiltration. If NO acted as a brake on the second substance being released, and that this other substance acted to increase nasal patency and neutrophil infiltration, removal of the “NO brake” would result in a marked increase in nasal patency and neutrophil infiltration. Via its vasodilator actions NO would be expected to increase vascular congestion and thereby decrease nasal patency. NO is known to limit leukocyte recruitment while L-NAME promotes leukocyte adhesion [35] but exposure of venular endothelium and neutrophils for 60 min to L-NAME *in vitro* does not induce neutrophil–endothelial cell interactions [36]. However, such an *in vitro* observation may be a result of the absence of other types of leucocytes in the experimental system used. When mast cells are closely apposed to the vasculature and are activated, neutrophil–endothelium interactions are promoted [37]. Inhibition of NO synthesis causes mast cell degranulation *in vivo* and this induces leukocyte recruitment. Indeed, stabilization of mast cells prevents degranulation and subsequent neutrophil adhesion which is generally observed to occur with L-NAME [35]. Thus, the increase in neutrophil infiltration caused by L-NAME may be a result of mast cell degranulation due to L-NAME and subsequent induction of neutrophil adhesion and eventually infiltration.

4.5. The effects of dexamethasone

Clinically, glucocorticosteroids are effective when given chronically in allergic rhinitis but their actions in the acute phase of rhinitis have not been extensively studied. Therefore, in this study we thought it of interest to test for acute effects of dexamethasone. Interestingly, sneezing,

but not nose rubbing, was reduced (Fig. 3A and B). Acute dexamethasone administration also failed to ameliorate nasal blockade or cellular infiltration, responses inhibited by chronic administration. Inhibition of sneezing by corticosteroids has been previously demonstrated in a rat model of allergen-induced rhinitis after allergen challenge [38]. It is commonly accepted that responses to corticosteroids involving anti-inflammatory actions are expected to develop over a period of hours and days, presumably as a result of its underlying intracellular mechanism of action. The absence of acute effects of glucocorticoids cannot of course be proven completely and so it is of interest to repeat this observation of preferential effects on sneezing, and to investigate the possible mechanisms involved.

5. Conclusions

In conclusion, we have examined the action of a spectrum of drugs in our model of the acute phase of allergic rhinitis in guinea pigs. The reference drugs did not always have the actions expected while experimental drugs showed interesting spectra of actions. Thus, by using a model of rhinitis, and examining a range of responses to different drugs, one gains insights into the complexity of the acute phase of responses to allergen challenge in guinea pigs, a species used routinely in the study of airway allergy.

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