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Symptomatic and pathophysiological observations in a modified animal model of allergic rhinitis*

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SUMMARY

There are many animal models for studying allergic rhinitis. However, they either need a too long establishment period or fail to show significant late allergic responses. In the model described in this paper, guinea pigs were sensitized and challenged intranasally with ovalbumin according to a modified protocol. As controls, antihistamine-treatment and non-sensitized, non-treatment groups were studied in parallel. Early and late symptoms, passive cutaneous anaphylaxis (PCA) reaction, nitric oxide synthase (NOS) immunoreactivities, pathological changes in nasal mucosa and nasal lavage fluid (NLF), and histamine, TXB_2 and p-LTs levels in NLF were evaluated. In contrast to the control groups, the model group exhibited typical symptoms, including late phase nasal blockage, and increased levels of IgG_1 and IgE. Considerable eosinophil infiltration and eNOS immunoreactivities in nasal mucosa, and increased levels of histamine, TXB_2 and p-LTs in NLF were also observed. This model was not only capable of showing satisfactory symptomatic and pathophysiological changes in allergic rhinitis but also showed good responses to antihistamine treatment. The model can be established in six weeks. For the first time, respiratory rate was employed as an index to reflect the nasal blockage of guinea pigs and it proved to be a reliable indicator.

Key words: allergic rhinitis, animal model, nasal blockage, nasal lavage fluid, nitric oxide synthase

INTRODUCTION

A wide variety of animal models of allergic rhinitis have been developed in the past 20 years. Guinea pigs have been the most widely used animal for allergy models, although other animals, such as rats, mice and rabbits have been occasionally used. The commonly used allergens were ovalbumin, cedar pollen extracts or toluene diisocyanate (TDI). The study periods of these models were quite diverse, varying from one week to 10 months [1-3]. Typical early symptoms, such as sneezing, nasal scratching, rhinorrhea and pathophysiological allergic reactions were usually induced after challenges; however, the late responses were seldomly addressed. As an allergen, TDI can give rise to both allergenic and non-specific stimulation, and so the symptoms induced may be the results not only of immunological reactions but also of physical stimulation. Rats and mice were good vehicles for the pathophysiological research into allergic rhinitis; however, to date, researchers have not been able to evaluate nasal blockages in rats and mice. In 1997, Nabe et al.[1] developed an allergic rhinitis model using Japanese cedar pollen as an allergen. This model was designed to monitor both the early and late phases of nasal blockage in allergic rhinitis [4]. It was the first animal model that showed a biphasic elevation of nasal blockage after allergen challenge. However, the study duration (15–30 weeks) was rather long. Moreover, Japanese cedar pollen is not easily available.

The present study aimed at creating a modified model that needs shorter development time and uses the readily available allergen, ovalbumin. This paper reports, for the first time, the use of respiratory rate (RR), which has a good correlation with the specific airway resistance (sRaw) in guinea pig models, to evaluate nasal blockage.

MATERIALS AND METHODS

Animals

Forty-six 8–12-week-old Hartley guinea pigs, weighing 400–650 g, were purchased from the Animal House of the Chinese University of Hong Kong. The animals were housed under specific allergen-free conditions. A standard laboratory diet and water were given ad libitum. The sensitization was started one week after they were housed. All procedures complied with the

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standards specified with the Animal Experimentation Ethics Committee (AEEC) of the Chinese University of Hong Kong.

Protocol of sensitization and challenge

Sensitization

Ovalbumin (OVA) (grade V, Sigma) was used as an antigen, which was absorbed on freshly prepared Al(OH)3 gel. Each dose of allergen consisted of 20 µg OVA/0.5 mg Al(OH)3 gel/100 µl saline. The whole sensitization process involved the instillation of one dose of allergen to each nostril, twice a day, for 10 consecutive days. In order to inhibit the movement of nasal cilia and so enable longer retention of the reagent, both nostrils of the animal were instilled with a drop of 4% lidocaine hydrochloride before the administration of sensitization reagents. The negative control (non-sensitized, non-challenged) group was sham sensitized with 0.5 mg Al(OH)3 gel/100 µl saline, and the nostrils of these animals were similarly anaesthetized with 4% lidocaine hydrochloride.

Challenge

After a five-day interval, the model (sensitized-challenged) group was challenged with 1% OVA saline solution, 100–150 µl/nostril once every three days, 11 times. The negative control (non-non) group was challenged with saline instead of OVA solution. The treatment control group was sensitized and challenged followed by daily treatment with 1.5 mg/kg desloratadine (Schering-Plough Corporation, Belgium), a second generation of H_1-receptor antagonist (antihistamine-treated group).

Measurement of respiratory rate (RR)

A good correlation between the increase in sRaw and the decrease in RR in the allergic rhinitis model of guinea pig had been demonstrated by Nabe et al. [4]. Therefore, RR was employed as the parameter to reflect the degree of nasal blockage. Because the guinea pigs are shy and the RR is subject to change with emotion and activity, RR was counted twice each time, without any disturbance to the animals. The average of the two readings was used as the final RR.

Sneezing and nasal scratching frequencies

The animal activities were recorded with a digital video camera (Sony, 420E, Japan), and the numbers of sneezing and nasal scratching events were counted in three consecutive 10-minute intervals after the first, third, fifth, seventh and ninth challenges.

Evaluation of the rhinorrhea

The nasal secretion was measured with a filter paper technique [5]. Ten minutes after the second, fourth, sixth, eighth and tenth challenges, the animals were restrained by hand, and a filter paper strip (2 mm x 80 mm) was continuously inserted into the nares and the secretion was absorbed with the pre-weighed paper during the second 10-minute interval after the challenges. The weight changes after the absorption indicated the quantity of secretion (mg).

PCA test

IgG1 and IgE are known to persist in the skin for up to four hours and three weeks, respectively, after allergen stimulation. IgG1, rather than IgE, is the main antibody in Type I anaphylaxis reaction in guinea pigs. Thus four-hour and seven-day PCA tests were performed to evaluate the titres of IgG1 and IgE according to the method of Levine [6]. Anti-OVA standard serum was obtained from a guinea pig, which was sensitized by i.p. injections of 20 µg OVA/2 mg Al(OH)3 gel/100 µl saline, once every two weeks for 10 injections. This serum was collected as the standard anti-serum for the PCA tests, and was stored at –80°C until use. The test sera were obtained five hours after the second, sixth and tenth challenges.

Pathological observations

After the last challenge, the animals were sacrificed and the nasal tissue was immediately fixed in 4% paraformaldehyde for 48 hours. Then, the fixed tissue was decalcified with 5% formic acid and embedded in paraffin wax, and 5 µm thick sections were prepared on poly-L-lysine pre-coated slides for haematoxylin and eosin (H-E) staining and immunohistochemical staining. In H-E staining, the intensity of eosinophil infiltration in the nasal mucosa was graded with an arbitrary scale: Grade 0, not present or not found; Grade 1, mild; Grade 2, moderate; and Grade 3, severe. To avoid bias, all slides were coded and blindly read by the observer. The bronchial and lung tissues were also processed as above to identify if there was eosinophil infiltration in the lower airways, which would indicate the existence of asthma.

Immunohistochemical staining

The NOS immunohistochemical staining was carried out using the avidin-biotinylated horseradish peroxidase complex (ABC) visualizing protocol. Briefly, the primary rabbit polyclonal antibodies of iNOS (1:1000, Santa Cruz, USA) and eNOS (1:200, Santa Cruz, USA) were applied to tissues, which were then incubated at 4°C overnight; then the slides were washed with PBS followed by incubation with biotinylated goat anti-rabbit immunoglobulin. The negative controls were given the normal rabbit sera instead of the primary antibody. Slides were examined with a Leica DM RXA2 (Wetzlar, Germany) microscope and the image analysis was performed with a semiautomatic imaging system. Images of the nasal tissue slides were acquired with a Leica DC500 camera from nine consecutive fields for each slide (magnification: x 400). The analysis was performed with a Dell computer using the MetaMorph Imaging System® (Universal Imaging Corporation, West Chester, USA) software. All specimens were blind to the observer.

Nasal lavage fluid (NLF) collection

NLF was collected according to the method previously reported [1]. Five hours after challenge, the guinea pigs were anesthetized with i.p. injections of ketamine (100 mg/kg) and xylazine (2 mg/kg) and then placed supine with their heads

extended. Then, 2 ml saline was instilled into one nostril with a speed of 1 ml/minute and the saline was slowly sucked out from another nostril with a hand-made silicon tube connected to a pump with slight negative pressure. With this method, the nasal cavity was thoroughly washed and 80–95% recovery of NLF was achieved. After the fluid had settled, 10 _l of NLF was placed in a haemocytometer chamber to be counted for total leucocytes, and the remainder was centrifuged at 800 g for 10 minutes. The resultant pellet of cells was smeared on a slide and stained with Giemsa-May for differential counting of leucocytes. At least 100 leucocytes were counted under the microscope in an attempt to identify the number of eosinophils. All slides were coded and blindly read to avoid bias.

Measurement of histamine, TXB_2 and p-LTs in NLF

The NLF for this assay was collected five hours after the tenth challenge and stored in a tube containing cyclo-oxygenase inhibitor indomethacin (10 µmol/l), 5-lipoxygenase inhibitor AA-861 (1 µmol/l) and EDTA (7.7 mmol/l). The histamine level in NLF was measured by the o-phthaldialdehyde spectrofluorometric procedure according to the method previously reported [7]. TXB_2 and p-LTs levels in NLF were measured by enzyme immunoassay using TXB_2 and leukotriene C4/D4/E4/ enzyme-immunoassay systems (Amersham Pharmacia Biotech, UK) according to the manufacturer's instructions.

Statistical analysis

The results are presented as means ± SEM. Statistical analysis was performed by one-way analysis of variance (ANOVA) followed by Dunnett's test or Student's t-test. All statistical calculations were performed in SPSS 10.0. A probability value of $p < 0.05$ was considered as statistically significant.

RESULTS

Time-course changes in RR

As shown in Figure 1, the non-non group showed no RR changes after each challenge for the whole time-course, whereas the sensitized-challenged group showed a sharp decrease in RR shortly after each challenge. The valley of RR was located at about 10 minutes after challenge and slowly rose thereafter until a second valley occurred at about eight hours after the seventh challenge, which implies a biphasic nasal blockage. Figure 1 shows the RR time-course changes of the antihistamine-treatment group in the first and the ninth challenge. At the beginning, this group showed no difference compared with the sensitized-challenged group but, at the ninth challenge, its RR decreased much less than did that of the sensitized-challenged group ($p < 0.01$ or $p < 0.05$) and no biphasic pattern was found.

Time-course changes in sneezing and nasal scratching frequencies

As shown in Figure 2, the animals sneezed frequently immediately after the challenges, with sneezing being most frequent during the first 10 minutes. During the second 10 minutes, sneezing frequency decreased rapidly, and sneezing was only

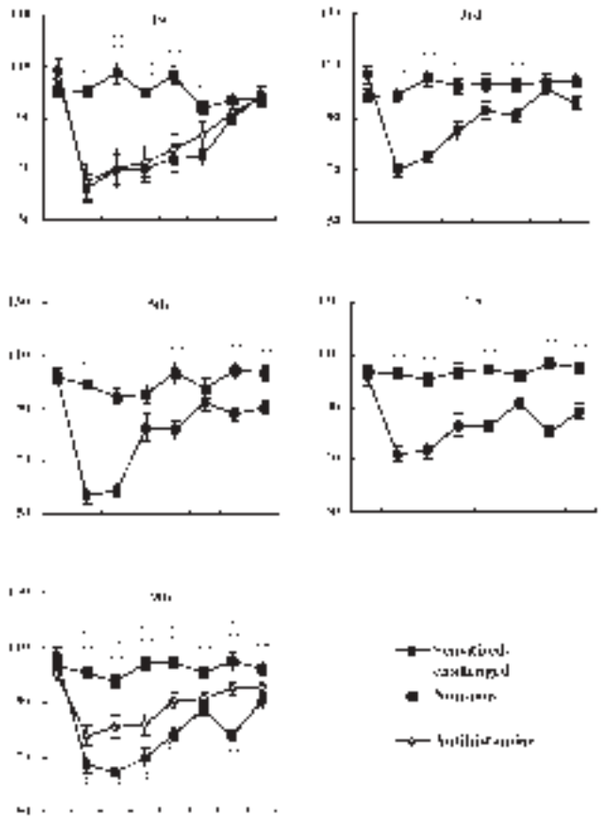

Figure 1. Time-course changes in respiratory rate (RR) after the first, third, fifth, seventh and ninth challenges with 1% ovalbumin in sensitized guinea pigs. Each point represents the mean ± SEM of 10–12 guinea pigs. *$p < 0.05$, **$p < 0.01$, compared with the sensitized-challenged group; †$p < 0.05$, ††$p < 0.01$, compared with the antihistamine-treatment group; $p < 0.05$, $p < 0.01$, comparison between sensitized-challenged and antihistamine-treatment groups.

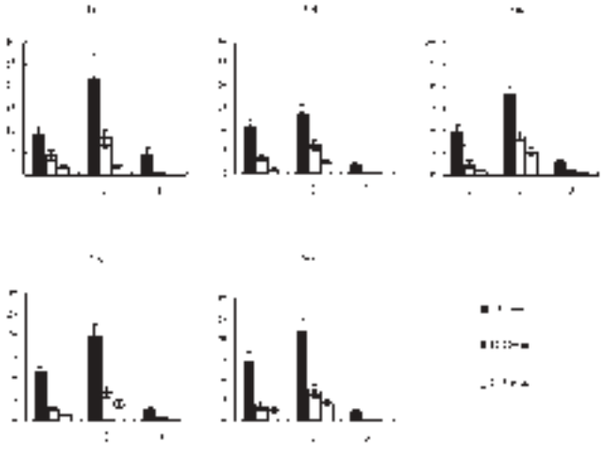

Figure 2. Time-course changes in sneezing frequency over three 10-minute intervals after the first, third, fifth, seventh and the ninth challenges respectively in antihistamine-treatment (1), sensitized-challenged (2) and non-non groups (3). Each column represents the mean ± SEM of 10–12 guinea pigs over 10 minutes. *$p < 0.05$, **$p < 0.01$, compared with the sensitized-challenged group.

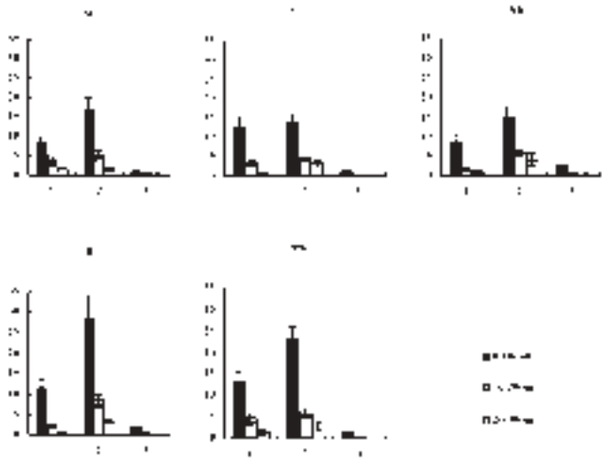

Figure 3. Time-course changes in nasal scratching frequency over three 10-minute intervals after the first, third, fifth, seventh and the ninth challenges in antihistamine-treatment (1), sensitized-challenged (2) and non-non groups (3). Each column represents the mean ± SEM of 10–12 guinea pigs over 10 minutes. *$p < 0.05$, **$p < 0.01$, compared with the sensitized-challenged group.

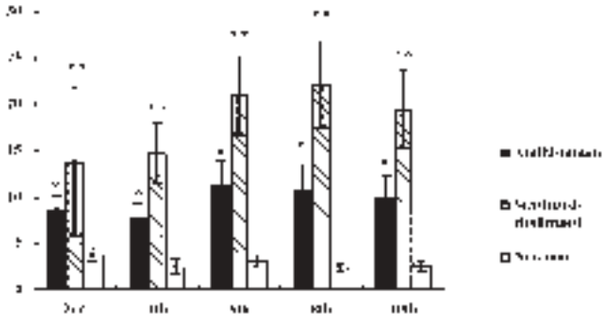

Figure 4. Time-course changes in rhinorrhea volume at the second, fourth, sixth, eighth and tenth challenges in antihistamine-treatment, sensitized-challenged and non-non groups. Each column represents the mean ± SEM of 10–12 guinea pigs. *$p < 0.05$, **$p < 0.01$, compared with the non-non group; and †$P < 0.05$, compared with the sensitized-challenged group.

occasional in the third 10 minutes. The frequency of the non-non group was much lower than that of the sensitized-challenged group ($p < 0.01$). For the antihistamine-treated group, this symptom was rather low but higher than that of the non-non group. In our study, the animals seldom sneezed half an hour post-challenge, although they occasionally did so up to several hours later (data not shown). The nasal scratching frequencies followed a similar pattern to the sneezing frequencies (Figure 3).

Volume of rhinorrhea

As shown in Figure 4, the volume of rhinorrhea from the sensitized-challenged group was higher than those from the other two groups ($p < 0.01$ or $p < 0.05$), and the antihistamine-treated group was higher than that of the non-non group ($p < 0.05$). From the sixth challenge, the volume of the sensitized-challenged group increased remarkably. The animals of the non-non group also had some rhinorrhea even though no real antigen challenge was given, possibly because of normal secretion and some remnants of the ovalbumin solution.

PCA test

As shown in Table 1, IgG_1 and IgE levels of each group were undetectable at the earlier challenge (second challenge). The IgG_1 levels in the sensitized-challenged and antihistamine-treated groups increased at the sixth challenge, with no significant difference between the two groups ($p > 0.05$). However, in the tenth challenge, the level in the sensitized-challenged group was significantly higher than that in the antihistamine-treated group ($p < 0.01$). The IgE level in the sensitized-challenged group was higher than in the antihistamine-treated group at the sixth and tenth challenges ($p < 0.05$). However, both antibodies were undetectable from the beginning to the end in the non-non group. The titres of IgG_1 and IgE in the antihistamine-treatment group increased moderately over the challenge time-course.

Cytology in NLF

As shown in Figure 5, in the sensitized groups, the total leucocytes in NLF decreased markedly in the sixth challenge compared with the second challenge, and moderately decreased in the tenth challenge. However, in the non-non group, the number of leucocytes increased during the course of the challenge. Antihistamine slightly suppressed the eosinophil infiltration into the NLF compared with the sensitized-challenged group ($p < 0.05$), and eosinophil infiltration was much greater for

Table 1. IgG_1 (4-hour) and IgE (7-day) titres of the sera from antihistamine-treatment, sensitized-challenged, and non-non groups in the PCA test. Sera were drawn at the second, sixth and tenth challenges. Titres are shown as geometric means ± SEM. *$p < 0.05$, **$p < 0.01$, compared with the sensitized-challenged group.

	IgG_1			IgE		
	2nd	6th	10th	2nd	6th	10th
Antihistamine	-	6.4±1.0	8.9±2.4 **	-	-*	2.2±0.6*
Sensitized-challenged	-	6.6±4.5	42.7±11.4	-	2.2±0.9	6.0±2.5
Non-non	-	-**	-**	-	-*	-**

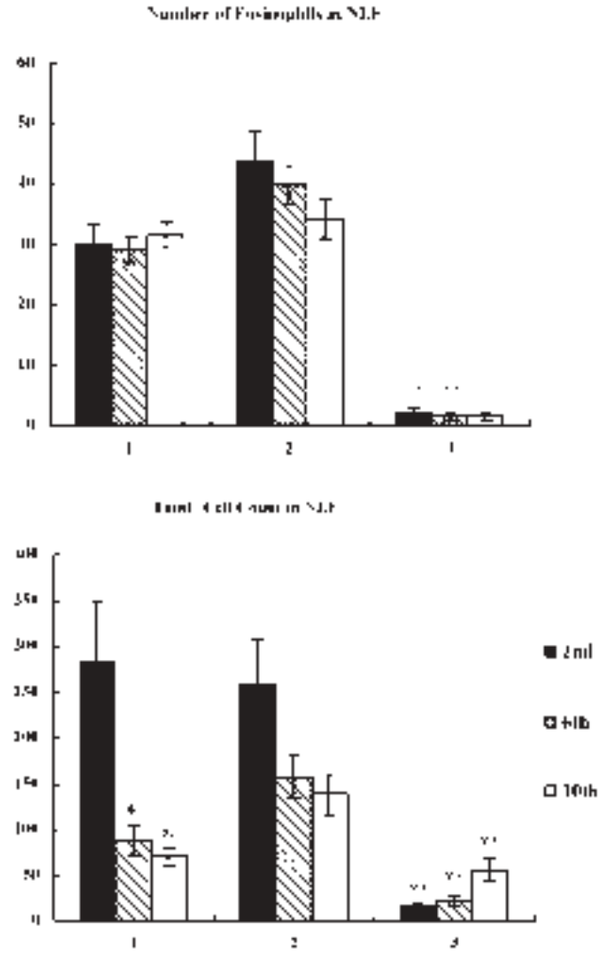

Figure 5. Time-course changes of total leucocyte number and eosinophil number per 100 leucocytes in the NLF collected after the second, sixth and tenth challenges in antihistamine-treatment (1), sensitized-challenged (2) and non-non (3) groups. Each column represents the mean ± SEM of 10–12 guinea pigs. **$p < 0.01$, *$p < 0.05$, compared with the sensitized-challenged group.

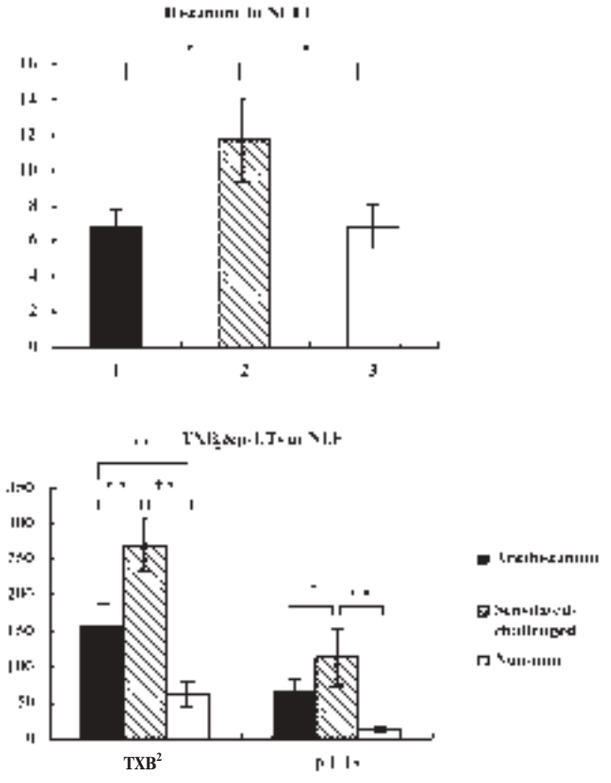

Figure 6. Histamine, TXB^2 and p-LTs levels in NLF at the tenth challenge in antihistamine-treatment (1), sensitized-challenged (2) and non-non (3) groups. Each column represents the mean ± SEM of 10–12 guinea pigs. *$p < 0.05$, **$p < 0.01$, comparison between groups.

both of these groups than for the non-non group ($p < 0.01$).

Histamine, TXB_2 and p-LTs levels in NLF

As shown in Figure 6, the histamine and TXB_2 levels in the sensitized-challenged group were higher than in the other two groups ($p < 0.05$ and $p < 0.01$). Moreover, the TXB_2 level in the antihistamine-treatment group was higher than in the non-non group ($p < 0.01$). The p-LTs levels in the sensitized-challenged group were significantly higher than in the antihistamine-treated ($p < 0.05$) and non-non groups ($p < 0.01$).

Pathological changes in nasal and lung tissues

As shown in Table 2 and Figure 7, the slides showed significant eosinophil infiltration into nasal mucosa after the last challenge. Eosinophil infiltration occurred in both the sensitized-challenged group and the antihistamine-treated groups, but was greater in the sensitized-challenged group. The eosinophil infiltrations in both groups were significant higher than in the non-non group ($p < 0.05$ and $p < 0.01$). However, no eosinophil infiltration was found in lung and bronchial tissues (figure not shown).

NOS expression in nasal tissue

The expression of eNOS was clearly observed in the nasal mucosa of the sensitized-challenged and antihistamine-treated groups, whereas, in the non-non group, it was weakly stained ($p < 0.01$ and $p < 0.05$). No significant difference between the sensitized-challenged and antihistamine-treatment groups in the expression of eNOS was detected ($p > 0.05$). There was no difference between groups in the expression of iNOS ($p > 0.05$). The immunoreactivities of eNOS and iNOS were localized to the cytoplasm of the submucosal glandular cells, epithelium and vascular endothelium. eNOS was also strongly stained in the goblet cells, whereas iNOS was not stained in the goblet cells (Figure 7, Table 2).

DISCUSSION

An ideal animal model should monitor not only the pathophysiological changes but also demonstrate the symptoms of allergic rhinitis of the animals and resemble the responses found in human patients. Acoustic rhinometry [8] and double-chamber plethymography [4] have been used to measure nasal

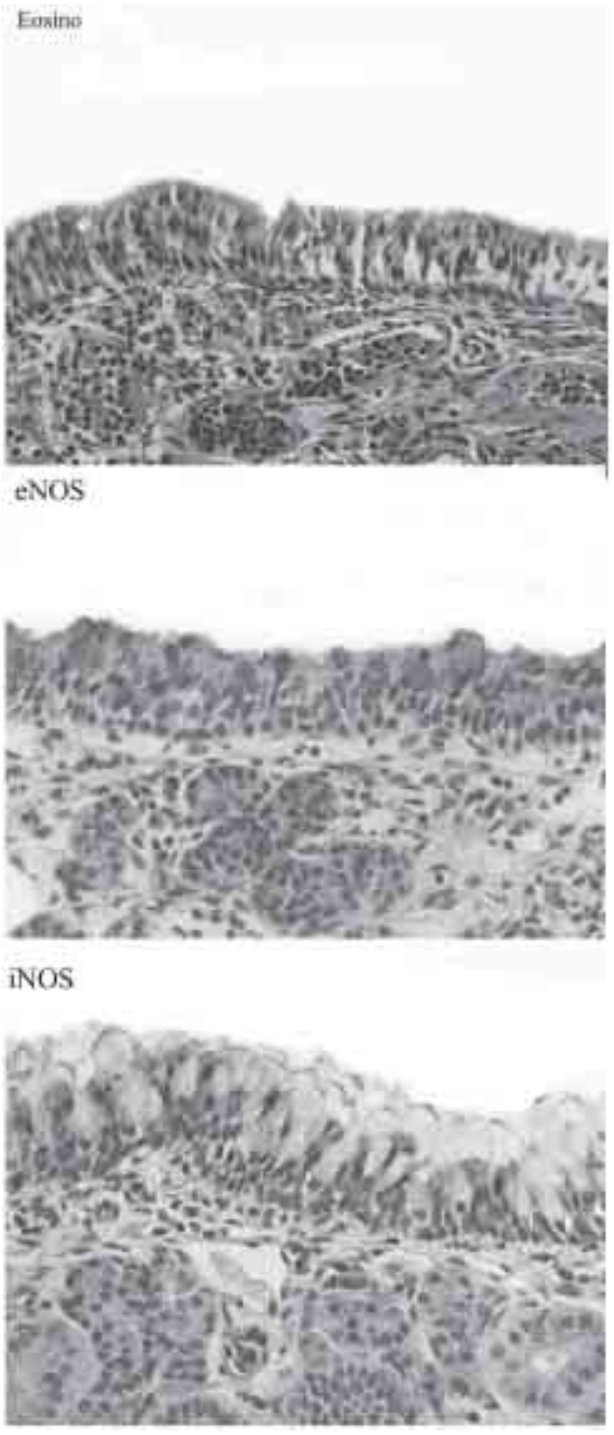

Figure 7. Light photomicrographs of NOS immunohistochemistry and H-E stained sections of nasal mucosa from sensitized-challenged guinea pigs after the last challenge. The slides show significant eosinophil infiltration into nasal mucosa after the last challenge. Cilia and epithelium necrosis, dilation of submucosal blood vessels and oedema of interstitial tissues were also observed in the slides. The stained eNOS and iNOS were localized in the cytoplasm of the submucosal glandular cell, epithelium and vascular endothelium. eNOS was also strongly expressed in the goblet cells while iNOS was not present (magnification: x 400).

blockage in animals; however, the equipment is usually expensive, taking measurements is time consuming and the accuracy of the measurements could easily be influenced by the activities and emotions of the animals. Guinea pigs are obligatory nose breathers and, when nasal blockage develops, the animals will naturally compensate by taking deeper breaths to raise the tidal volume. Nabe et al. [4] found that the RR decreased as the sRaw increased with a rather good correlation in their guinea pig model of allergic rhinitis. In our pilot study, the same phenomenon was observed. Therefore, RR was chosen as the indicator of upper airway resistance. This was the first time that nasal blockage was evaluated with RR as a parameter. Since counting RR involves no instrumentation, it should be less stressful for the animals and the results of measurements should be less affected. However, it is imperative that the application of this method is strictly confined to guinea pigs and only the nasal airway, and not lower airway, is affected. To confirm this, the bronchial and lung tissues of the animals used in our study were histopathologically examined, and no characteristics of asthma were detected. The local sensitization and challenge, with relatively high concentrations but small volumes of allergen solution, ensure that the lower airway will not be affected. With this method, we succeeded in observing a biphasic decrease of RR, which represents the early and late phases of nasal blockage. The appearance of a late phase of nasal blockage implies that a late response to the allergen challenge did occur. To date, only a few models allow the study of nasal blockages, especially both early and late phases. Desloratadine has been reported to alleviate nasal blockage in patients [9] and, in the present model, it also displayed a potent role in suppressing the decrease in RR after challenge; that is, in relieving nasal congestion. In addition, no second phase decrease in RR was observed in the treatment group. Therefore, it is appropriate and rather easy to investigate nasal blockages in allergic rhinitis by using this model.

The sneezing and nasal scratching frequencies observed in this model were similar to the phenomenon observed in patients with perennial allergic rhinitis [10]. It seemed that the stimulatory activities of the saline solution itself also stimulated the reflex because even the non-non group displayed the symptoms of sneezing, nasal scratching and rhinorrhea.

TXA_2 and p–LTs as well as histamine are involved in the pathogenesis of allergic nasal obstruction. These mediators were increased in NLF in allergic human patients after antigen challenge [11]. Their roles in the pathogenesis of the early and late phases of nasal blockage were demonstrated in an experimental allergic rhinitis [12], and recent reports have suggested that TXA_2 and p-LTs can increase the permeability of nasal mucosal blood vessels, leading to nasal blockage [13, 14]. TXB_2, which is the stable breakdown product of TXA_2, was detected in the NLF in other animal models as well as in patients with allergic rhinitis [11, 12]. In our model, the levels of TXB_2, p-LTs and histamine in NLF were significantly higher in the sensitized group than in the non-non group, and such an increase

Table 2. Results of image analysis for eNOS and iNOS expressions by immunohistochemical staining and eosinophil infiltration by H-E staining in the nasal tissue of guinea pigs. Values are means ± SEM from 10–12 subjects. *$p < 0.05$, **$p < 0.01$, compared with the non-non group; †$p < 0.05$, comparison between the antihistamine-treatment and sensitized-challenged groups. eNOS was found in the nasal mucosa of the two sensitized groups and it was obviously stronger than the non-non group. There was no significant difference in eNOS expression between the antihistamine-treatment and sensitized-challenged groups. There was a significant difference in iNOS between groups ($p > 0.05$). Eosinophil infiltration mainly occurred in the sensitized-challenged group and was inhibited by desloratadine, and it was significantly higher in these two groups than the non-non group.

	Antihistamine (n=12)	Sensitized-challenged (n=11)	Non-non (n=10)
eNOS	17.68 ± 2.41*	20.08 ± 2.05**	11.54 ± 1.47
iNOS	10.98 ± 1.68	11.45 ± 1.99	11.29 ± 2.53
Eosinophils	1.75 ± 0.22*	2.64 ± 0.15**	0.80 ± 0.20

could be partly suppressed by antihistamine, which probably contributed to the relief of nasal blockage. The above observations were consistent with the result of clinical trials, which demonstrated that loratadine suppressed not only the nasal allergy symptoms and eosinophil numbers in NLF but also the levels of histamine and p-LTs in patients' NLF [15, 16].

Nitric oxide (NO) plays an important role in the regulation of upper airway function. It is produced by the action of NO synthase (NOS). An increase of iNOS expression has been observed in nasal epithelium of allergic rhinitis patients [17], and a NOS inhibitor inhibited eosinophil infiltration into the airways of OVA-sensitized rats [18]. Nasal congestion and rhinorrhea are thought to be caused by increased NOS effects on vessel dilatation, and hyperfunction of submucosal glands. Strong eNOS and weak iNOS have been detected in the columnar epithelial cells of normal human respiratory epithelium [19]. In another study, it was demonstrated that iNOS, but no eNOS, presented in paranasal sinus epithelial cells and thus it was speculated that iNOS is a major isoform of NO production [20]. In the present model, eNOS levels were significantly different between sensitized-challenged and non-non groups, but there were no significant differences in iNOS between groups. This implies that, in contrast to allergic rhinitis human patients, in the allergic rhinitis model of guinea pigs eNOS rather than iNOS was the pathogenetic isoform. Moreover, both NOS isoforms were localized to the cytoplasm of the submucosal glandular cells, epithelium and vascular endothelium. eNOS was strongly expressed in goblet cells whereas iNOS was not expressed in goblet cells. This suggests that eNOS might play a more potent role in regulating the activity of goblet cells, and thus affect nasal secretion in allergic guinea pigs.

Infiltration of inflammatory cells into the nasal cavity is one of the characteristics and results of allergic rhinitis. In this model, eosinophil infiltration was significantly greater in the sensitized-challenged group compared with non-non group. Antagonists of TXA_2 and p-LTs were reported to inhibit antigen-induced eosinophil accumulation in nasal mucosa [11]. This was again confirmed by the present study, since the levels of TXB_2 and p-LTs in NLF correlated well with the accumulation of eosinophils in nasal mucosa.

The pathological changes in nasal tissue in response to allergen challenge were in good agreement with the clinical observations of allergic rhinitis. In patients with allergic rhinitis, the number of eosinophils in nasal secretions and washings reached maximal levels several hours after challenge [21]. In the sensitized-challenged animals, the intranasal ovalbumin challenge induced significantly more total leucocytes in NLF than that in both the non-non and antihistamine-treated groups. This was quite similar to the observations from another experimental model [22] and allergic rhinitis patients [23]. It is speculated that the number of leucocytes in NLF reached its highest level immediately after early challenges and, after repeated challenges, the numbers of neutrophils and/or monocytes together with the eosinophils were all reduced; however, the percentage of eosinophils remained stable.

In guinea pigs, an increase in IgG1 titres can aggravate nasal allergy-like symptoms, which reflects the allergy status in guinea pigs. In this model, after exposure to ovalbumin for several weeks, the titres increased dramatically in sensitized groups but not in the negative group, and antihistamine reduced the increase in the titres. This was consistent with other allergic rhinitis models of rats and guinea pigs as well as in human patients [24 – 26]. It is well known that the synthesis of IgE (for humans and mice) or IgG_1 (for guinea pigs) is influenced by the type of allergen contacted, TH cells and the cytokines produced. Desloratadine inhibits both IgE-mediated and non-IgE mediated generation of the cytokines IL-4, IL-13, IL-6 and IL-8 from basophils and mast cells. This may explain why, in our study, desloratadine inhibited IgE and IgG_1 levels.

CONCLUSION

In conclusion, the present, modified guinea pig model for studying allergic rhinitis has many advantages over other models. It is simple and easily available, and the whole process from sensitization, challenge and treatment analysis needs only six weeks. Despite the relatively short time frame, both the early and late phase reactions are captured. In addition, the respiratory rate was employed, for the first time, to evaluate nasal blockage and the biphasic change was observed. Moreover, the model showed good treatment reaction to the H1 antagonist. The corresponding symptomatic and pathophysiological changes that have reported in allergic rhinitis patients were fully observed in this experimental model. This is potentially very useful for testing the efficacy of new drugs.

However, it should be noted that there are also some disadvantages of the guinea pig model. The lack of species-specific immunological reagents makes it difficult to identify particular cell types, cytokines, etc. Guinea pig anaphylactic responses usually involve IgG_1 antibodies, although the model can be tailored for the production of IgE by additional adjuvants such as aluminium.

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