ARTICLE

Tear IgE concentrations in allergic conjunctivitis

KEIKO NOMURA, ETSUKO TAKAMURA

Abstract

Purpose **Tear IgE has been considered to play an important role in allergic conjunctivitis and the measurement of tear IgE concentrations can help to diagnose this condition. Locally produced IgE levels have been shown to be the largest contributor to the severity of allergic conjunctivitis.**

Methods **One hundred and thirteen allergic conjunctivitis patients (70 seasonal allergic conjunctivitis (SAC), 21 perennial allergic conjunctivitis (PAC), 22 vernal keratoconjunctivitis (VKC)), 14 bacterial conjunctivitis (BC) patients, 13 epidemic keratoconjunctivitis (EKC) patients and 18 normal controls were recruited. Tear samples were collected using the microcapillary method and tear IgE levels were measured using an immunoenzyme assay.**

Results **Tear IgE concentrations showed significant increases in the VKC (322.2 ± 45.7 ng/ml), SAC (194.7 ± 21.7 ng/ml) and PAC (134.8 ± 23.1 ng/ml) groups when compared with controls (52.1 ± 9.7 ng/ml, $p < 0.01$). No significant difference was found between EKC (97.2 ± 11.7 ng/ml) and BC (92.6 ± 13.8 ng/ml) groups and controls ($p = 0.1$).**

Conclusions **Tear IgE concentrations showed a significant increase in allergic conjunctivitis patients when compared with controls. Our results suggest that measuring tear IgE concentrations can help to diagnose allergic conjunctivitis.**

Key words Allergic conjunctivitis, Tear IgE, Serum IgE, Eosinophils

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Allergic conjunctivitis is a type I allergic reaction caused by immunoglobulin E (IgE).[1,2] The diagnosis of allergic conjunctivitis is based mainly on clinical features, for example itching, hyperaemia or the presence of papillary formation on the conjunctiva. However, there is no one diagnostic technique that can be used reliably to confirm the presence of allergic conjunctivitis.[3] Eosinophils in conjunctival scrapings are helpful in confirming the diagnosis,[4-10] but positive detection rates are not very high.[11,12]

IgE has been considered to play an important role in allergic reactions in the eye;[13] thus it may be very important to be able to detect local allergic reactions so that they can be used in diagnosing allergic conjunctivitis.[14-16] Usually, diagnosis is performed by measurement of serum IgE concentrations.[17] However, these do not differentiate between local and systemic levels. Locally produced IgE has been shown to be the largest contributor to the severity of the disease.[18,19] Thus, tear IgE measurements could provide a much better way to diagnose allergic conjunctivitis. This study was undertaken to measure tear IgE concentrations in allergic conjunctivitis by means of enzyme-linked immunosorbent assays.

Patients and methods

Patients

The 113 allergic conjunctivitis patients in this study were divided into three groups: seasonal allergic conjunctivitis (SAC; $n = 70$), perennial allergic conjunctivitis (PAC; $n = 21$) and vernal keratoconjunctivitis (VKC; $n = 22$). There were 43 male and 70 female patients. The mean age was 34.6 years. All allergic patients were diagnosed on past history, symptoms of ocular itching, and clinical presence of redness and papilla in the conjunctiva. For patients and controls we measured the total IgE using the radioimmunosorbent test (RIST) and the specific IgE with an enzyme immunoassay (AlaSTAT). From the results of AlaSTAT, the categories were as follows: SAC patients showed cedar pollen sensitivity only. PAC patients showed household dust or mite sensitivity. VKC patients showed typical clinical features: the presence of recurrent symptoms of itching, tearing, associated with cobblestone lesions in the upper tarsal conjunctiva, corneal ulcers, plaque and mucous discharge. VKC patients showed not only household dust or mite sensitivities, but additionally seasonal allergen sensitivity.

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The 14 bacterial conjunctivitis (BC) patients initially presented with discharge; clinical evaluation documented the presence of redness in the conjunctiva and finding of the causative bacteria in bacterial tests of the discharge from the conjunctival sac. Moreover eosinophils were not detected in the conjunctiva.

Epidemic keratoconjunctivitis (EKC) was diagnosed by acute follicular conjunctivitis, hyperaemia, discharge, preauricular lymph node swelling, the formation of pseudomembranes on the conjunctiva or a positive reaction on the enzyme-linked immunosorbent assay for adenovirus. Also, eosinophils could not be detected in EKC patients. The definitive diagnosis for EKC is the positive reaction for adenovirus separation. However, this procedure requires rather a long time to complete. Recently the Adenoclone kit, which is an enzyme-linked immunosorbent assay, has been introduced, and a positive test for this is considered the definitive diagnosis of EKC.

The 18 normal controls had no history of allergic disease or any other conjunctivitis. Moreover they had no clinical symptoms and no eosinophils or bacteria were detected.

Informed consent was obtained from all patients and controls. The research followed the tenets of the Declaration of Helsinki.

Tear sampling

Tear samples were collected using the microcapillary method without local anaesthesia and samples were taken from the temporal meniscus. During sampling the patient was requested to look in the opposite direction and not to blink their eye (Fig. 1).

Tear IgE measurement

After collecting tear IgE, it was measured using an enzyme-linked immunosorbent assay performed by the Touch Tear Micro Assay System. The minimal detection limit was 5 ng/ml. The normal detection limit was 50 ng/ml. Average test completion time was 6–7 min.

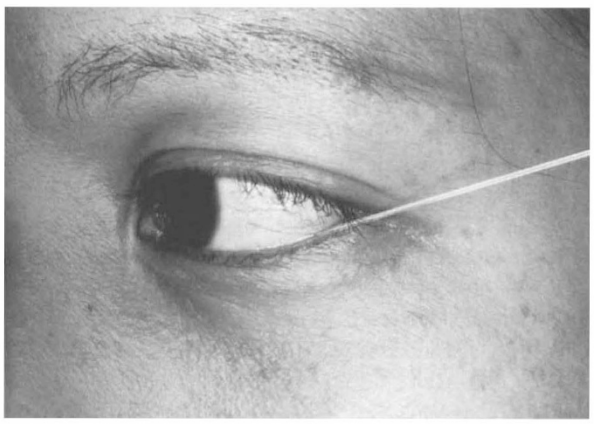

Fig. 1. *Collection technique using the microcapillary method. Samples are taken from the temporal meniscus without using local anaesthesia.*

Serum IgE measurement

Serum samples were collected and analysed using the AlaSTAT allergen-specific IgE test system. Total IgE were measured by RIST.

Statistical analysis

Statistical analysis of the tear IgE data was performed using Scheffé's multiple comparison. Values are given as the mean ± standard error. Differences were assumed to be significant at $p < 0.05$.

The relationship of tear IgE and serum IgE concentrations in each allergic conjunctivitis patient was compared using Spearman's correlation coefficient. Differences were assumed to be significant at $p < 0.05$.

Results

The tear IgE concentrations were significantly higher in the VKC (322.2 ± 45.7 ng/ml), SAC (194.7 ± 21.7 ng/ml) and PAC (134.8 ± 23.1 ng/ml) groups compared with controls (52.1 ± 9.7 ng/ml). In contrast, concentrations in the EKC (97.2 ± 11.7 ng/ml) and BC (92.6 ± 13.8 ng/ml) groups were not different from controls (Fig. 2).

There was a correlation between serum IgE and tear IgE levels for the VKC group ($p = 0.013$, $r = 0.572$). On the other hand, no such correlation was found for the SAC ($p = 0.137$, $r = 0.182$) and PAC ($p = 0.495$, $r = -0.158$) groups.

Discussion

Using this method, tear IgE concentrations can be measured in small samples very rapidly and easily.

Diagnosis of allergic conjunctivitis in patients who have no systemic atopic disease is difficult because of low serum IgE concentrations. Previous studies,[18,19] however, have reported that IgE is suspected of being produced locally. In addition, it has been documented[20]

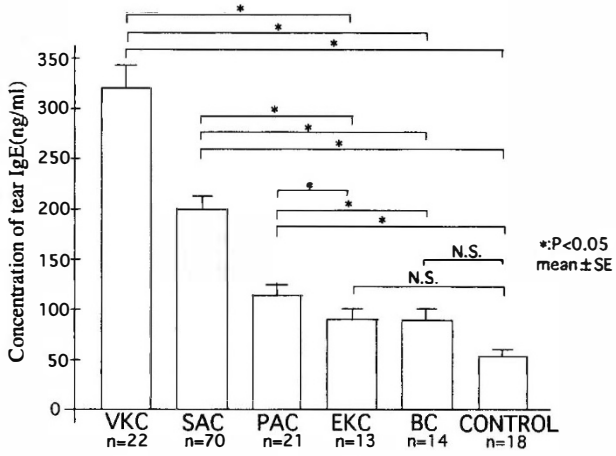

Fig. 2. *Tear IgE levels in different types of conjunctivitis. Concentrations were significantly higher in the allergic conjunctivitis groups (VKC, vernal keratoconjunctivitis; SAC, seasonal allergic conjunctivitis; PAC, perennial allergic conjunctivitis) than in the control group or those with epidemic keratoconjunctivitis (EKC) or bacterial conjunctivitis (BC).*

that IgE-positive cells are present in the subconjunctival layer in all cases during the exacerbation phase of the disease. In our study we were able to measure tear IgE using the microcapillary method, and we found high levels of tear IgE in SAC, PAC and VKC subjects confirmed to have allergic reactions in the conjunctiva. Conversely, tear levels of IgE in the EKC and BC groups were no different from those in normal controls and were significantly lower than in the allergic conjunctivitis patients. This method can therefore distinguish allergic conjunctivitis from other forms of conjunctivitis.

Currently, in ophthalmic practice, serum IgE levels are used in the diagnosis of allergic conjunctivitis. But often IgE levels in the serum are low, even though a positive diagnosis of allergic conjunctivitis can be made based on the evidence of eosinophils in conjunctival scrapings. However, eosinophils can not always be detected in all cases of allergic conjunctivitis. Abelson *et al.*[10] found eosinophils in only 45% of their patients. Thus, a better diagnosis might be obtained by mixing methods, i.e. clinical findings (itching, redness), the presence of eosinophils, and IgE measurement in tears and serum.

Locally produced IgE combines with the antigen and attaches to the surface of local mast cells. Subsequently, these cells migrate into the systemic circulation. And while local concentrations of IgE may be high, systemic concentrations will be very low. Recently it has been shown that IgE synthesis can be induced by the interaction of B cells with mast cells and basophils in the presence of interleukin-4.[21] This suggests that inflammatory cells have a very important role in regulating IgE production at local levels in reactions such as allergic conjunctivitis. We feel that the interaction between the immunoglobulins from the subconjunctival layer and antigens present at the local level is the mechanism responsible for the findings in this study.

We are concerned that differences between serum IgE and tear IgE measurements may cause confusion or lead to an incorrect diagnosis. In case of serum IgE measurements, it is quite easy to obtain large volumes of serum for testing; however, the methodology necessary to detect the smaller concentrations of IgE requires much longer analysis times. Conversely, while obtaining tear IgE samples is difficult due to the limited sample volume available, IgE quantitation can be done quickly and easily. In fact, in mild to moderate cases of allergic conjunctivitis eosinophils are sometimes not detected locally and therefore can not be used as the basis for diagnosis, although tear IgE levels are measurable. Thus tear IgE measurements may provide a much better way to diagnose allergic conjunctivitis.

The authors wish to thank Prof. M. Kogure, of the Ophthalmology Department, Tokyo Women's Medical College, for her helpful comments, and J. Eudeikis, M.S., for his kind advice.

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