

Sublingual immunotherapy

A long-term solution to allergic rhinitis

Allergic rhinitis affects about 25% to 30% of the population. The symptoms of rhinorrhoea, nasal obstruction, sneezing, post-nasal drip have been shown to affect the quality of life (QOL) of many patients.¹ Patients of all ages are affected although they tend to be generally younger. In Singapore, the most common inhalant allergen is house dust mites (HDM). Up to 80% of all patients who are allergic have HDM allergy. Uncontrolled symptoms of allergy can lead to headaches, snoring, poor sleep quality, reduced ability to concentrate and other associated symptoms such as persistent or recurrent sore throat, cough and hoarseness. A recent Japanese study² related the effect of seasonal pollen allergy to reduced concentration. Half of the patients also reported a 25% reduction in productivity. Significant predictors were itchy eyes and use of anti-allergy medications. This can lead to reduced work productivity and loss of manhours. In children, untreated allergies can even lead to behavioural changes such as irritability and frustration. Of greater significance, studies have linked a higher incidence of asthma in adult patients with allergic rhinitis.³ This begs the question: Will control of allergic rhinitis decrease the prevalence of asthma?

Pathogenesis of allergic rhinitis

In a sensitised patient, exposure to the allergen causes a rise in immunoglobulin E (IgE) levels specific to the allergen. This specific IgE coats the surface of mast cells, which are present in the nasal mucosa. When the specific protein (eg, a specific pollen grain) is inhaled into the nose, it can bind to the IgE on the mast cells, triggering the immediate and delayed release of a number of mediators. The mediators that are immediately released include histamine, tryptase, chymase, kinins and heparin. The mast cells quickly synthesise other mediators, including leukotrienes and prostaglandin D₂. These mediators, via various interactions, ultimately lead to the symptoms of rhinorrhoea, such as nasal congestion, sneezing, itching, redness, tearing, swelling, ear pressure and post-nasal drip. Mucous glands are stimulated, leading to increased secretions. Vascular permeability is increased, leading to plasma exudation. Vasodilation occurs, leading to congestion and pressure. Sensory nerves are stimulated, leading to sneezing and itching. All of these events can occur in minutes; hence, this reaction is called the early or immediate phase of the reaction. Over 4 to 8 hours, these mediators, through a complex interplay of events, lead to the recruitment of other inflammatory cells to the mucosa, such as neutrophils, eosinophils, lymphocytes and macrophages. This results in continued inflammation, termed the late-phase response. The symptoms of the late-phase response are similar to those of the early phase, but there is less sneezing and itching, and more congestion and mucus production. The late phase may persist for hours or days.

Shortfalls of treating allergy

Treatment for allergic rhinitis is mainly based on the principles of allergen avoidance and adjuvant pharmacotherapy. Millions of

dollars are spent every year on dehumidifiers, air purifiers, proof covers and anti-mite bedding. The aim is to reduce exposure to potential allergens such as house dust mites, fungi and cockroaches. Unfortunately, it is impossible to totally avoid inhalant allergens. Pharmacotherapeutic agents such as nasal steroid sprays, mast cell stabilisers, oral antihistamines, topical decongestant nose drops or sprays work at different levels of the allergic cascade. Steroid sprays reduce the inflammatory reaction produced by histamine release; mast cell stabilisers prevent release of histamine; and antihistamines block the action of histamine on nasal mucosa. Although these measures are effective in controlling the symptoms of allergic rhinitis, patients are required to continue with these measures as long they desire to remain symptomfree. Questions such as "How long do I need to take the medications?", "Do you mean I need to take this medication forever?", and "Isn't there a cure for my allergies?" are commonplace. Unfortunately, the painful truth of anti-allergy medications can lead to some degree of frustration, misplaced concerns of long-term side effects of steroid sprays, subsequent reduction in compliance and eventual return of symptoms.

Immunotherapy

Grass pollen was first identified in the 1870s. Skin prick testing became accepted in the 1910s. Immunoglobulin E was only identified in 1965. The science of immunotherapy has only been studied and understood in the last 10 to 15 years. This sequence clearly shows how science has lagged behind the clinical application of immunotherapy in the management of allergic rhinitis. Immunotherapy, also known as "allergy shots", come in the form of injections. This involves subcutaneous injections of an allergen extract. Initially, injections are given once weekly. When immunity builds up, the injections may be given less frequently. Immunotherapy works by inducing the body to produce immunoglobulin G (IgG). Like IgE, IgG can also bind to receptors found on the surface of mast cells. Unlike IgE, binding of IgG to the receptors does not result in degranulation of mast cells and release of histamine. In effect, IgG acts as a "competitor" to IgE for receptor sites on mast cells. When IgG levels build up significantly, all or nearly all of the receptors on mast cells would be occupied by IgG. Thus, exposure of that particular allergen to the nasal mucosa will not cause histamine release as the allergen will not have the opportunity to bind to its IgE antibody on mast cells.

Sublingual immunotherapy (SLIT)

More recently, immunotherapy has been administered sublingually. The reagents are applied daily under the tongue for 2 minutes and then swallowed. This removes the need for painful subcutaneous injections. Studies have shown that SLIT is extremely safe and no adverse reactions have been reported with more than 50 million doses administered.

Although long-term studies are still in progress, patients can expect an 80% to 85% chance of significant reduction in symptoms without the dependence of medication.

Immunotherapy is suitable for patients who

- Do not respond to medical therapy
- Do not want to depend on medical therapy

- Have severe symptoms for more than 3 months a year

SLIT is also suitable for children 5 years and above. Aside from the benefits of symptom control, studies have shown that long-term control of allergic rhinitis with immunotherapy reduces the incidence of development to asthma.⁴ This is especially so for children suffering from dust mite or *Alternaria* (a fungus) allergy. It was also found that institution of immunotherapy in monosensitized (single sensitivity) children decreases the development of additional sensitivities in that child over time. Fatalities have been reported with immunotherapy. They occur with injection immunotherapy in children who have poorly controlled asthma. The risk occurs during the build up phase and with the first injection from a new vial. Injections at home or at a clinic with inadequate supervision are also at increased risk of a fatal outcome should an adverse event occur. As mentioned earlier, sublingual immunotherapy has been found safe thus far with no fatalities reported. Common side effects of SLIT include perioral tingling, tongue swelling and gastric discomfort. Allergic rhinitis is a very common condition that affects patients of all ages. It is closely associated with asthma. There are many treatment options, each with their own shortcomings. Immunotherapy has been used clinically in the control of allergic symptoms. The advent of sublingual immunotherapy has increased safety profile without compromising success. It is suitable for children over 5 years old and offers an attractive option in the management of allergic rhinitis.

References

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