## **CAN YOU CURE ALLERGIES?**

## CORINA PORR<sup>1</sup>

<sup>1</sup>County Clinical Emergency Hospital Sibiu

**Keywords:** specific immunotherapy, allergy, anti-allergy vaccine Abstract: Specific immunotherapy is the administration of graded amounts of an allergen vaccine in an allergic individual in order to achieve a dose that ameliorates the symptoms associated with exposure to sensitizing allergen. Anti-allergy vaccine is used to treat allergies, by modifying the immune response. Anti-allergy vaccine is indicated in many allergic diseases. Specific immunotherapy can reduce the use of symptomatic treatments, the number of consultations for disease flare-ups.

Cuvinte cheie: imunoterapia specifică, alergie, vaccin antialergic Rezumat: Imunoterapia specifică este administrarea gradată a unor cantități dintr-un vaccin alergenic la un individ alergic, pentru a atinge o doză care ameliorează simptomele asociate expunerii la alergenul sensibilizant. Vaccinul antialergic este utilizat în tratamentul alergiilor, prin modificarea răspunsului imun. Vaccinul antialergic este indicat în multe afecțiuni alergice. Prin imunoterapia specifică, se reduce mult utilizarea tratamentelor simptomatice, scad numărul de vizite pentru puseele de exacerbare a bolii.

This is the questions that one in four persons has in mind, given that the incidence of allergic diseases has increased in the last years. Allergen vaccine immunotherapy is the only curative treatment of allergy and asthma.

What is immunotherapy with allergen vaccine? The European Society of Allergy and Clinical Immunology (EAACI) defined allergen-specific immunotherapy (SIT) to be the gradual administration of vaccine amounts of allergen in an allergic individual to achieve a dose that improves the symptoms associated with exposure to sensitizing allergen. Anti-allergy vaccine is an allergen solution obtained by a special method of preparation of the allergens, which allows the extraction of the active constituents of animal or plant which may then be used in the treatment of allergy, by modifying the immune response.(1)

Who can receive an anti-allergy vaccine?

Anti-allergy vaccine is indicated in:

- 1. Hymenoptera venom allergy;
- 2. Allergic rhinitis (moderate, severe);(2)
- 3. Allergic conjunctivitis (moderate, severe);
- 4. Asthma (mild, moderate, persistent);
- 5. Allergy to pollen (birch, Ambrose etc.);
- 6. Allergy to house dust mites;
- 7. Allergy to cats;
- 8. Food allergy;
- 9. Allergy to drugs.

In Hymenoptera venom allergy, allergen-specific immunotherapy is indicated in the following cases:

- 1. The existence of moderate or severe allergy reaction;
- Re-exposure likelihood (beekeepers and their relatives):
- 3. Minimum age 5 years (no maximum);
- Diagnostic tests positive: skin tests or specific IgE (RAST, CAP-system).

SIT is not performed in patients with severe reaction, but negative specific IgE (in this case, anaphylactoid reaction). It is only done by subcutaneous injection. The method of SIT

until reaching the maintenance dose is classical (lasting months), rush (which takes days) ultra rush (24-48h) and only with the patient's hospitalization. ITS duration for Hymenoptera is over eight years, and the success rate is of 95%

SIT major indication in allergic rhinitis is for moderate/severe allergic rhinitis. Symptoms MUST be present more than two consecutive seasons (3,4,5,6,7,8) with pollen (birch, Ambrose, olive etc.); the success rate is of 90-95%.(9) In house dust mites allergy, the success rate of SIT is of 60-70%.(10) In moderate / severe allergic conjunctivitis, the results are less spectacular as compared with allergic rhinitis.

Food allergy has no major indication, except cases of severe anaphylactic events (milk, peanuts).(11-15) It is preferred that the vaccine containing the allergen be altered by enzymatic action, in which case, it is called the enzyme-potentiated desensitization).

The allergic medication is recommended to be replaced by another class of drugs. SIT is carried out only if specific IgE-mediated reaction and tolerance is achieved in hours or days. Dose administration is increased every 20-30 min during hospitalization and only with the written consent of the patient. There is a risk of anaphylactic reactions (30-80% penicillin).(16) Other drugs undergoing SIT: biseptol, antibiotics, chemotherapy, sulfasalazine, nonsteroid anti-inflammatory drugs.(17)

Atopic dermatitis is not a major indication of SIT. Favourable results have been obtained in a small number of children in the case of mites and those associated with asthma.

In the allergy to moulds (Alternaria, Cladosporium), SIT is indicated if they cannot be avoided and pharmacotherapy does not lead to satisfactory results, but studies are few.

The latex allergy is not treated by SIT, avoidance and replacement of latex products is recommended.

But SIT has absolute contraindications:

1. When there is not a condition subject to an allergen;

<sup>1</sup>Corresponding author: Corina Porr, Str. Reşiţa, Nr. 95/12, Sibiu, România, E-mail: corina\_sibiu@yahoo.com, Tel: +40723 083974 Article received on 20.02.2014 and accepted for publication on 28.04.2014 ACTA MEDICA TRANSILVANICA June 2014;2(2):202-204

## **CLINICAL ASPECTS**

- 2. The existence of severe illness (cancer, cirrhosis, hepatitis, cardiovascular disease, kidney);
- 3. The presence of autoimmune diseases;
- 4. The presence of immunodeficiency;
- 5. Disease at high risk for serious reactions to the administration of epinephrine, using β-blockers, ACE;
- 6. Asthma unstable;
- 7. Patient refusal;
- 8. Repeated severe reactions.

Relative contraindications are:

- Age <5 years for subcutaneous ITS and <2 years for sublingual;
- 2. Age > 50 years, especially if the patients have cardiovascular disease;
- 3. In the period before or during pregnancy and lactation;
- Patients on β-blockers may be switched to a different class of antihypertensive drugs, then SIT may be initiated.

The success of the SIT lies in the selection of patients. They must meet certain conditions

- Be allergic and with documented conditioning between the allergen exposure and symptoms;
- Present allergen-specific IgE (skin tests or serum dosage);
- 3. The allergen cannot be avoided;
- The disease is not lengthy prior to SIT or has not reached the stage of tissue remodelling;
- 5. It is initiated when the disease is controlled;
- Patients who do not respond adequately to standard therapy;
- 7. Patients to be compliant;

Who administers the anti-allergy vaccine?

SIT can be applied only by the allergologist as only this one can decide in what patients can apply it and in case of adverse effects, the allergologist is the most indicated person to treat them.

Ways of managing SIT are:

Table no. 1. SIT administration ways

| SIT mode of            | SIT characteristics            |
|------------------------|--------------------------------|
| administration         |                                |
| Subcutaneous           | Named as classic. It was first |
| (parenteral)           | used and is the most           |
|                        | commonly used                  |
| Sublingual (swallow or | Favourable results (pollen)    |
| spit)                  | New                            |
| Oral                   | Useful for adults. The effects |
| Nasal inhalation       | on children not known          |
|                        | Under evaluation               |
| Bronchial inhalation   | For Hymenoptera                |
| Intraganglionary (3    |                                |
| months)                |                                |

EAACI proposed for treatment only subcutaneous and sublingual (oral) routes.

Modes of administration of SIT are

- 1. Slow: 3-5 months (each scheme adapts to each patient);(18)
- 2. Rush: 1-2 weeks (insects, drugs);
- 3. Ultra-rush: 1-4 days (insects, drugs).

The maintenance dose for sublingual administration is daily, and in the subcutaneous one, the monthly duration is 3-5 years.

What happens if I do not make the vaccine?

Allergy does not go away and the patient needs chronic therapy to control the symptoms. Without therapy, the disease can become more severe or new allergen sensitization may appear. It is known that allergic rhinitis is a risk factor for asthma or untreated asthma can go from mild to severe one.

When will I feel better?

Vaccination is made for 3 years at minimum and the reduction of the medication starts usually 6 months later, sometimes later. If there is not response to the anti-allergic vaccine after 6 months, it is considered that the dose of allergen in the vaccine is not sufficient, the allergen to which a vaccine is not relevant to the patient's symptoms.

When to stop the anti-allergic vaccine?

Allergic vaccine should be usually discontinued after 3-5 years if IgG4 protector antibodies are proved and in case of Hymenoptera, the cutaneous tests could be made which should be negative.

What are the possible side effects?

These may be local, syndrome, or systemic.

Local reactions at the injection site, redness, warmth, itching, swelling, or pain occurring immediately or a few hours of the shot. They are the most common and totally harmless and are usually treated with cold compresses and second generation antihistaminic medication.

Figure no. 1. Local reaction at the injection site



Syndrome reactions consist of nasal and bronchial symptoms.

Systemic reactions can be anaphylactic shock, generalized urticaria, severe asthma attack, severe angioedema (larynx). These are rarer than the local reactions and occur within the first 30 minutes when administering the vaccine. Surveillance in the surgery is the first 30 minutes after vaccine administration.(19)

What are the benefits allergic vaccines?

This results in reducing allergy symptoms, reducing the need for medication, quality of life, improved functional status, cost reduction, it prevents progression from allergic rhinitis to asthma (20-24), prevents multi-sensitization.(25,26)

ITS mechanism is shown in the figure below:

Factors that negatively influence the effectiveness of SIT are lack of patient's compliance, patient awareness amendment, and intolerance of an optimal dose, lack of accurate diagnosis

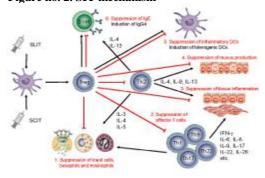
What are the costs?

SIT vaccine is expensive in price, it addresses specialized medical service, and it has long period of treatment. But an SIT is cheaper for a period of six months, compared with daily administration in the same period of a non-sedating antihistamine as a single dose.

Through SIT, symptomatic treatments may be reduced, as well as the number of visits for exacerbation of disease flares.

In conclusion, SIT may be a cheaper alternative in the therapeutic program of an allergic patient.

Figure no. 2. SIT mechanism



Source: Fujita et al. Clinical and Translational Allergy 2012 2:2 doi:10.1186/2045-7022-2-2

## REFERENCES

- Dumitrașcu D. Imunoterapia specifică. In Dejica D (ed). Tratat de imunoterapie; 2006. p. 268-297.
- Jacobenson L, Moller C, Dreborg D et al. Five-year follow on the PAT-study: a 3-year course of specific immunotherapy (SIT) results in long-term prevention of asthma in children. Allergy 2003;58 (Suppl 74):S3.
- Bousquet J, Lockley RF, Malling HJ. WHO Position Paper-Allergen Immunotherapy; Therapeutic vaccines for allergic diseases. Allergy 1998;54 (Suppl):S1066-1088.
- Dolz I, Martinez-Cocera C, Bartolome JM et al. A doubleblind placebo-controlled study of immunotherapy with grass-polen extract Alutard SQ during 3-year period with initial rush immunotherapy. Allergy 1996;51:489-500.
- Varney VA, Gaga M, Frew AJ et al. Usefulness of immunotherapy in patients with severe summer hay fever uncontrolled by anitiallergic drugs. BMJ 1991;302:265-269.
- Maasch BJ. Double-blind, placebo-controlled immunotherapy with mixed grass-pollen allergoids II. Comparison between parameters assessing the efficacy of immunotherapy. J Allergy Clin Immunol 1988;82:439-446.
- Ortolani C, Patorello EA, Incorvaia C et al. A double-blind, placebo-controlled study of immunotherapy with an alginate-conjugated extract of Parietaria judaica in patients with arietaria hay fever. Allergy 1994;49:13-21.
- Ross RN, Nelson HS, Finegold I. Effectiveness of specific immunotherapy in the treatment of allergic rhinitis: an analysis of randomized, prospective, single or double-blind, placebo-controlled studies. Clin Ther 2000;22:342-350.
- Abramson R, Puy R, Weiner J. Allergen immunotherapy for asthma (Cochrane Review) in The Cochrane Library, Issue 3, Oxford: Update Software. Systematic Cochrane meta-analysis of the efficacy of immunotherapy in asthma; 2003.
- Kuehr J, Brauburger J, Zielen S. Efficacy of combination treatment with anti-IgE plus specific immunotherapy in polysensitized children and adolescents with seasonal allergic rhinitis. J Allergy Clin Immunol 2002;109:274-280.
- 11. Helson HS, Lahr J, Rule R. Treatment of anaphylactic sensitivity to peanut by immunotherapy with injections of

- aqueous peanut extract. J Allergy Clin Immunol 1997;99:744-751.
- Bannon GA, Cockrell G, Connaughton C. Engineering, characterization and in vitro efficacy of the major peanut allergens for use in immunotherapy. Int Arch Allergy Immunol 2001;124:70-72.
- 13. Wild LG, Lehrer SB. Immunotherapy for food allergy. Curr Allergy Rep. 2001;1:48-53.
- Xiu-Min Li, Sampson HA. Novel approaches for the treatment of food allergy. Curr Opin Allergy Clin Immunol 2002;2:273-278.
- Stark BJ, Earl HS, Gross GN sa. Acute and chronic desensitization of penicillin-allergic patients using oral penicillin. J Allergy Clin Immunol 1997;79:523-532.
- Lockey RF. Allergen Immunotherapy. Its origin and future. Allergy Clin Immunol Int 2004;16:107-111.
- Frew AJ, Norman PS, Golden DBK, Adelman DC. Immunotherapy. In: Holgate ST, Church MK, Lichtenstein LM (eds). Allergy: Mosby; 2011. p. 175-185.
- Cools M, Van Bever HP, Weyler JJ. Long-term effects of specific immunotherapy, administered during childhood, in asthmatic patients allergic to either house-dust mite or to both house-dust mite and grass pollen. Allergy 2000;55:69-73.
- Mahmoudi M, Naguwa SM. Immunotherapy. In Naguwa SM, Gershwin ME, (eds) Allergy and Immunology Secrets. Questions you will be asked. Philadelphia: Hanley& Belfus Inc; 2001. p. 225-232.
- Moller C, Dreborg S, Ferdousi HA. Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study). J Allergy Clin Immunol 2002;109:251-256.
- 21. Jacobsen L, Moller C, Dreborg D. Five-year follow on the PAT-study: a 3-year course oh specific immunotherapy (SIT) results in long-term prevention of asthma in children. Allergy 2003;58 (Suppl 74):S3.
- Grembiale RD, Camporota L, Naty. Effects of specific immunotherapy in allergic rhinitis individuals with bronchial hyperresponsiveness. Amm J Respir Crit Care Med 2010;162:2048-2052.
- Simons FE. Allergyc rhinoconjunctivitis: the asthma allergic rhinitis link. J Allergy Clin Immunol 1999;104:534-540.
- 24. Pajno GB, Barberio G, De Luca F. Prevention of new sensitization in asthmatic children monosensitized to house dust mite by specific immunotherapy. A six-year follow-up study. Clin Exp Allergy 2010;31:1392-1397.
- Grembiale RD, Camporota L, Naty S. Effects of specific immunotherapy in allergic rhinitis individuals with bronchial hyperresponsiveness. Am J Respir Crit Care Med 2010;62:2048-2052.
- Des Roches AD, Paradis L, Menardo JL. Immunotherapy with a standardized Dermatophagoides pteronissinus extract. VI. Specific immunotherapy prevents the onset of new sensitizations in children. J Allergy Clin Immunol 2007;99:450-453.