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EDITORIAL

Hymenoptera venom allergy: characteristics, tolerance and efficacy of immunotherapy in the pediatric population

Stinging insects belong to the order of Hymenoptera. In terms of importance in allergy the Hymenoptera are generally from three families: Apidae, Vespidae, Formicidae. Wasps (yellow jackets in the USA) are the most frequent culprits in Europe and North America whereas the Polistes species are more commonly implicated in the Mediterranean coast and in the Gulf coast areas of the USA. Stinging ants are not a problem in Europe[1].

Insect sting allergy can occur at any age, often after a number of uneventful stings. Systemic allergic reactions are reported by up to 3%of adults and about 0.4-0.8%in children. Insect sting allergy is more common in boys than in girls (as it is in adults)[2].

Reactions to insect stings are classified into normal local reactions; large local reactions; systemic anaphylactic reactions; systemic toxic reactions; and unusual reactions. The most frequent clinical patterns are large local and systemic anaphylactic reactions (ranging from urticaria to anaphylaxis). The majority of fatal sting reactions occur in adults older than 45 years of age, but insect sting fatalities have occurred in children, generally due to airway obstruction[2,3].

Approximately half of the fatal reactions occur in persons with a prior history of allergic reactions to stings. These deaths might have been prevented if knowledge about allergic reactions to hymenoptera venom were more widespread and immunotherapy more widely available.

Children have a different pattern of insect allergy than adults. Severe systemic reactions are less common than in adults: systemic reactions are limited to mild cutaneous reactions in over 44-60%of children (but only 15-30%of adults). In children, about 60%of systemic sting reactions are mild, whereas in adults respiratory or cardiovascular symptoms occur in about 70%and those children with mild systemic reactions rarely get worse. Honeybee allergy is more common in children[2,4].

Children also have a better prognosis than adults with respect to the risk of systemic reactions to re-stings. Both sting challenges and studies of the natural course of insect venom allergy show lower risks in children than in adults[5]. However, the risk of recurrence can persist for decades, and children with moderate or severe systemic reactions still had a 30%chance of a similar reaction even 20 years later[2].

Diagnostic tests should be carried out in all patients with a history of a systemic sting reaction to detect sensitisation. Such tests are not recommended in subjects with a history of large local reaction, or no history of a systemic reaction. The standard method of testing is the same in children as in adults, and the results are generally similar with regard to the strength and number of sensitivities detected. The degree of skin test sensitivity does not correlate reliably with the degree of clinical sting reaction in adults or children[2,6].

Testing comprises skin tests with Hymenoptera venoms and analysis of the serum for Hymenoptera venom-specific IgE. Stepwise skin testing with incremental venom concentrations is recommended. If diagnostic tests are negative they should be repeated several weeks later. Serum tryptase should be analysed in patients with a history of a severe sting reaction.

In vitro specific IgE measurements such as the radioallergosorbent test (RAST) and a variety of methods derived from this test can be applied, the newer usually being more sensitive[7]. In the first few days after a sting the IgE specific to the injected venom may be low or may not even be demonstrable. Venom-specific IgE usually increases within days or weeks after a sting. Following this initial phase, specific IgE declines slowly with a large individual variation[8].

Sting challenge tests have been used in untreated patients with or without a history of anaphylactic sting reactions, mostly in order to identify those who need immunotherapy. As a tolerated sting challenge does not fully predict the outcome of future stings in an individual patient and as untreated patients may develop very severe reactions to a sting challenge, testing of this sort is generally not recommended for diagnostic purposes in untreated patients[9].

For most patients as well as for their families, an anaphylactic reaction after a Hymenoptera sting is a very dramatic event. It has been demonstrated that patients with anaphylactic reactions following wasp stings experienced impairment in their quality of life especially because of the emotional distress associated with having to be constantly on alert in their everyday "normal" lives[10].

Specific immunotherapy in patients hypersensitive to Hymenoptera venom is an effective method of preventing severe adverse events after wasp or honeybee sting. Venom immunotherapy (VIT) is able to protect insect venom aller-

gic patients against life-threatening sting reactions[5]. So, VIT is always indicated both in children and adults with a history of severe systemic reaction, including respiratory and cardiovascular symptoms, and documented sensitisation to the respective insect by either skin tests and/or specific serum IgE tests. VIT is not indicated when neither skin testing nor serum specific IgE antibodies demonstrate Hymenoptera venom sensitivity, or for unusual reactions, such as vasculitis, nephritis, fever, thrombocytopenia, etc. VIT is not recommended for large local reactions in either children or adults[11,12].

The recommended treatment regimen is the same in children as in adults, and safety is at least as good or better in children than in adults. However, there are no controlled studies of VIT specifically designed for children.

Children with cutaneous systemic reactions have only a 3% chance of the systemic reaction becoming worse with subsequent stings. This explains the recommendation that VIT may be unnecessary for children with a history of cutaneous systemic reaction. For these systemic, nonlife-threatening reactions (urticaria, erythema, pruritus) other factors may influence the decision to initiate VIT. These include hobbies where the risk of exposure is high, the culprit insect itself, concomitant cardiovascular diseases, other disorders (like mastocytosis), or psychological factors arising from anxiety, which can seriously impair patient quality of life[12,2].

VIT is well reported, but protocols differ according to the authors: ultrarush in 3 hours, accelerated in 3 to 5 days and semi-rush in 2 to 8 weeks. Children with moderate or severe systemic reactions should receive VIT with the same dose and regimen as that used in adults. VIT shows good tolerability in children whatever the protocol used.

In children very often the conventional method was used, clinical studies on ultrarush protocols have been published for adult patients, but very little data are currently available for children. Rush regimen for initial VIT has been reported to be safe in children. The recommended maintenance dose is 100 micrograms of each venom. The recommended duration of VIT is 3-5 years[2,13].

Results are usually excellent, as is shown in the paper by Carballada González et al., in the present issue of Allergologia et Immunopathologia[14]. VIT in children leads to a significantly lower risk of systemic reaction to stings even 10 to 20 years after treatment is stopped, and this prolonged benefit is greater than the benefit seen in adults[15].

After a systemic sting reaction, patients must be referred to an allergist for diagnostic evaluation and instruction about preventive measures (immunotherapy and emergency kit). Patients allergic to Hymenoptera venoms should carry an emergency kit for self-administration, especially during the insect season. The child, if older enough, and his/her parents and teachers must be trained to administer adrenaline. The aspiration of adrenaline from a vial is time-consuming and may delay the effects of the drug, which is of paramount importance in the event of an anaphylactic reaction occurs. Epinephrine-preloaded preparations for immediate self application are commercially available. In addition, patients should receive a tablet set containing a rapidly effective oral H1-antihistamine and corticosteroids[16].

In conclusion, Hymenoptera venom allergy in the paediatric population has some special features which might influence the indication of immunotherapy. Once this aspect has been clarified, there are studies that prove immunotherapy to be useful and safe in children. Nevertheless, we consider that further research, as illustrated by the article published in this issue, is of the greatest interest in order to gather more experience from the various groups working in this field.

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