

INVITED COMMENT

Real-life safety of allergen immunotherapy in children and adolescents

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For more than a century, allergen immunotherapy (AIT) has been a part of anti-allergic strategies. The first studies in seasonal allergic rhinitis included adults only, although it is well known that the highest incidence for allergic rhinitis is observed in the first two decades of life. The first placebo-controlled trial was published by Frankland and Augustin in 1954 (1). It was not earlier than the last two to three decades, when national as well as European authorities requested careful documentation of efficacy and safety by clinical development plans which are nowadays considered a necessary prerequisite for allergenic extracts as they are for all drugs. A specific pediatric investigational plan (PIP) is in most drugs a mandatory component for new registration of allergenic products used for treatment (2).

In this issue, Rodríguez del Río et al. (3) report safety data for 'real-life immunotherapy' in children and adolescents which have prospectively been documented by 112 doctors from three European countries. A large number of children (1563) receiving sublingual (451) and subcutaneous (1127) AIT over one year have been included in this survey. The data obtained in this study are particularly interesting because they are not part of a clinical development program of a single allergen manufacturer for a single allergenic source.

In several European countries, AIT for children may be applied as a mixture of two, three, or more allergenic sources which is the case in more than 10%. These figures may differ from other continents, particularly Northern America, where it is still common practice to mix different allergenic sources in one treatment extract according to skin test results (4, 5).

Real-life AIT may also include concomitant injections of different components at the same day. It may include animal danders or other sources which are marketed, although they have never really sufficiently been registered for treatment.

Large studies regarding safety in children have so far not been published.

Real-life AIT includes sublingual and subcutaneous applications, which have not really been assessed head to head in comparative surveys. (6, 7)

In most countries, where AIT is widely used, a systematic reporting system documenting serious adverse effects which may be life-threatening or fatal is lacking. Therefore, occasional anecdotal information on these cases in adults and children is leaving us with the impression that underreporting may possibly bias the current knowledge.

It is reassuring that Rodríguez del Río and colleagues clearly demonstrate that systemic reactions (29 in 24 patients of 1563 cases) are possible (frequency 1.5%) but obviously are clearly rare. The survey suggests that severe systemic reactions after SCIT (23) are slightly more frequent than after SLIT (6, 5 drops, one tablet). It is also interesting to realize that allergoids as products with a reduced allergenicity obviously reduce the risk of severe side effects.

The careful assessment of each reported case of severe reaction and anaphylaxis is still suggesting that even among experience specialists, anaphylaxis seems to be undertreated: The use of epinephrine autoinjectors obviously was limited to very few life-threatening cases.

Reports like the survey by Rodríguez del Río, which has been supported by an expert group of EAACI, are clearly needed in addition to publications related to phase-two or phase-three studies of clinical development plans.

To optimize both efficacy and safety of all therapeutic interventions including AIT, allergen immunotherapy, in allergic children, more real-life studies like the published survey will be needed in the future.

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