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Safety of allergen injection immunotherapy in real life

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Though subcutaneous allergen immunotherapy (SCIT) is still considered the reference treatment of airborne allergies, many allergist today prefer the sublingual route due to its better safety profile. In effect, serious adverse reactions, near fatal or even fatal ones, have been reported in the past.(1, 2) Following trials comparing the safety profile of the two administration routes, some recent studies have re-assessed the real incidence of adverse reaction in SCIT (3, 4), trying to highlight the risk factors and the strategies to reduce the risk of adverse reactions.(5, 6) We report our data of adverse reactions with SCIT that we administer routinely in real life and compare our data with those from the current literature.
185 patients (M/F 50%/50%, mean age 29.5 years, rang 11-52 years) have been treated in our offices, receiving a total of 5625 shots from January 2001 to January 2010. Patients were admitted to Immunotherapy according to established criteria (7). Extracts and number of injections are summarized in Table 1.
All 5625 shots were given by the same treating physician specialized in Allergy and Clinical Immunology. Even if not directly recommended (8) the operator aspirated not only before, but also during the injection. We observed a total of 3 mild SRs (grade 1 and 2, according to the recent World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System(9)) occurring in 3 patients: this figure corresponds to 0,053% of the injections, and to 1.6 % of the patients. In keeping with some previous studies (10,11), and in contrast with other ones (12) no local reaction was observed at the previous injections in these 3 patients . Three patients had a large local reaction (LLR). No delayed reactions were reported. Two out of the three patients experiencing systemic reactions resumed the treatment at a lower dose, and were able to reach the maintenance dose; one patient refused to resume the treatment. The variability in the way SCIT-induced SRs are defined and reported has led to misinterpretations in evaluating the safety of this treatment and the true incidence of systemic reactions (9). Most previous studies used the 1993 EAACI grading system revised in 2006 (7). A new Systemic Reactions Grading System has been now published and accepted (9) and we used this system in the present report. Our result are in keeping with an earlier European large retrospective analysis covering 300.000 injections, reporting SRs in 0.061 % of injections and 2.1% of patients (10). In a recent multicenter Italian survey, reviewing 60785 injections given to 1738 patients over a three-year period, SRs were observed in 0,16 % of injections and 3,28 % of patients. (4)
The low figures in our survey don't allow to draw absolute conclusions. Nevertheless, some practical points deserve to be outlined. First 2/3 patients had asthma, a well-known major risk factor for SRs. (11). All systemic reactions occurred during the maintenance phase, at dosages that had been previously well tolerated. Both subjects with seasonal allergy experienced the systemic reactions outside the pollen season. In the survey by Schiappoli et al.(4) SRs were equally

Table 1 - Extracts composition and number of injections.

Composition	N° of extracts	N° of injections
Grasses	84	2740
House dust mites	38	1082
Birch	25	722
Parietaria	22	605
Cypress	3	51
Flour	5	225
Mix grasses/parietaria	6	184
Ribwort plantain	1	8
Ragweed	1	8

distributed between the build-up and the maintenance phase.

Interestingly, blood appeared during the aspiration in 2 of the 3 reactions. As stated before, it is a custom of the operator in this survey to make an aspiration approximately every 0.1 ml injected. The need for aspiration before injection has been a matter of debate, but there are few reports addressing the argument. In two retrospective and prospective surveys covering more than 30000 allergy shots Waibel concludes that "the absence of blood in the syringe during aspiration suggests that injection without aspiration is a safe practice". (12) But this conclusion has been challenged by others with anecdotic reports. (13, 14) Altogether , these data show the very good safety profile of SCIT, when carried on by expert physicians. The large diffusion of SLIT is mainly due to the supposed greater safety of route of administration although the systematic review by Radulovic et al. (15) found that 41 of 824 (5%) withdrew because of adverse events, and in two recent studies with grass tablets the discontinuation rates due to adverse events was 13 out of 175 treated children (7.4%) and 11 out of 213 adults (5.2 %). Two subjects in either study were treated with epinephrine. Furthermore, being SLIT a self-administered treatment, some adverse events could go unrecognized, and, more important, immediate medical intervention for severe reactions may not be available. In conclusion, our small survey confirms previous large epidemiological studies showing the safety of SCIT. Altogether, it does not seem rationale to choose SLIT instead of SCIT only because of a supposed better safety, as it seems the most frequent case today. Many different criteria (timing, costs, patient age, clinical characteristics, behaviour, adherence, and of course efficacy) must be taken into consideration, in order to give the right treatment to the right patient.

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