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Adverse reaction to sublingual Parietaria vaccine following an ultra-rush induction

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KEY WORDS

SLIT; asthma; adverse effects; Pellitory; Parietaria

Summary

In the treatment of respiratory allergies Sublingual Immunotherapy (SLIT) represents a valid alternative to Subcutaneous Immunotherapy (SCIT) for its better safety profile. We describe a case of acute severe asthma following the first maintenance dose of SLIT in a boy allergic to Parietaria pollen. At the initiation of therapy, the patient was in healthy condition and his asthma appeared to be under control. An ultra-rush induction had given no reaction. Despite the good safety profile of SLIT, clinicians should be aware of the risk of adverse effects when prescribing SLIT for respiratory allergies.

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Introduction

Allergen-specific immunotherapy (AIT) represents the only treatment of allergic disorders that is capable of both improving symptoms and modifying the natural course of illness in children. There is evidence that SIT is effective in patients with allergic rhinitis and mild asthma (1). Sublingual allergen-specific immunotherapy (SLIT) has been proven to be clinically effective in children with asthma (2) or rhinitis (3) and has been widely proposed as an alternative to SCIT (4) due to its better safety profile in respect to SIT.

SLIT doses are administered at home following the manufacturer instructions, but there at home several problems can arise. Parents often fear making dosage mistakes. They are aware of possible (but highly unlikely) adverse reactions since they are reported in the instruction books. In order to reduce these problems and to improve adherence to the therapy, some of us have

recently experienced an ultra-rush method of induction that has demonstrated to be safe and well tolerated (5). In the described case, a severe adverse event occurred at the beginning of the maintenance period. This is the first time in our experience that we had to stop SLIT therapy because of adverse effects.

Case report

S.L., a seven-year boy, has been affected by allergic asthma since he was three. He was seen in our hospital for the first time in 2009 and on that occasion an IgE-mediated allergy to Parietaria pollen was demonstrated. Prick test (ALK-Abellò) resulted in an 8 mm wheal (mean diameter) and the serum specific IgE was 28 KU/l (CAP FEIA, Phadia, n.v. < 0.35). He was treated with Fluticasone 50 mcg b.i.d. from March to the beginning of July. During the following summer months he was completely free of symptoms. In September, therapy with fluticasone was restarted.

Clinical conditions were good and spirometric data were within the normal range for the age. We prescribed SLIT for Parietaria judaica (SLIT-1, ALK-Abellò, Madrid, Spain). Contents of container: 18 sealed aluminium bags, each bag containing a strip of 5 single-dose containers for a total of 90 single-dose containers. Each single dose container contains 0.2 ml (extractable volume) that correspond to 200 STU per dose, which is the maintenance dose to be administered at home three times weekly.

After having obtained informed consent from the patient's parents, we admitted the patient to Day Hospital for routine preliminary exams, after which we began the ultra-rush induction (Day 1). At 40 minutes intervals we administered two 100 S.T.U. doses and a third dose of 200 STU. The patient was kept under observation for four more hours and eventually discharged with written instruction. No adverse events were observed. The patient's prescription called for him to take one 200-STU container every other day.

The following day (Day 2), the patient reported no problems. On Day 3, an hour after taking his first dose at home, the patient presented acute severe bronchial asthma. He was subsequently taken to the emergency room where he was found to have oxygen saturation of 88%. The situation was alleviated with prednisone per os and nebulized albuterol per aerosol. Within two hours, clinical conditions had sufficiently improved, enough so that the boy was sent home with a prescription of albuterol as an "emergency" medication in case of an asthma attack. The day after the episode (Day 4), the patient reported no problems, however on Day 5, after taking a 200 STU dose, the patient again suffered the same acute episode of asthma as he did after the first 200 STU dosage. The following day (Day 6) there were no problems. On Day 7, the patient again took his 200 STU dose, and had another identical acute asthma episode as he had had on Days 3 and 5. At this point, the parents informed us of the events of the previous week during a scheduled check-up, and therapy was discontinued.

At present the patient is still a patient of our outpatient ambulatory and his asthma is well controlled.

Discussion

Asthma has long been recognized as a risk factor for systemic reactions in patients treated with injective immunotherapy (SCIT). A recently published survey found that 15 of 17 patients who had a fatal reaction had preexisting asthma (6), and as such allergens should not be administered to patients with a forced expiratory volume in 1 second (FEV1) under 70% of predicted or to those who have unstable or symptomatic asthma (7).

SLIT, which has been proposed as an alternative to SCIT due to the ease of its administration at home and its better safety profile, has shown a good safety profile concerning severe systemic reactions in children (8). Most of the reactions are localized to

the oral mucosa, and very few systemic reactions have been reported, nevertheless severe adverse reactions to SLIT may still occur. The entire topic was recently reviewed by Calderon et al (9). It has been noted that most adverse reactions occur in patients who had already experienced side effects with SCIT. Eleven anaphylactic reactions have so far been reported in the literature, three of which occurred in paediatric age. One of these reactions occurred in an 11 year-old boy, who had asthma as the first and most relevant symptom of adverse reaction to the vaccine (10). Another case of acute asthma as an adverse reaction to the first doses of SLIT was described in an adult woman (11). In our experience, one child presented acute severe short-lasting asthma as an adverse reaction to SLIT for Parietaria. No serious adverse reaction had until then been observed in our Allergy Unit among our patients treated with SLIT. This experience will not change our behaviour going forward, however at the same time it is important to stress the concept that an allergen-specific vaccine, even when taken by means of sublingual drops or tablets, can represent a risk for the allergic patient. Clinicians who prescribe such therapy should be aware of the possibility of serious adverse reactions and should take all the preventive measures in order to ensure the patient's safety.

It is important to highlight the need for a standardization of allergenic extracts. The trend in immunotherapy is toward molecular or even epitopic, peptide therapy. In two large SLIT trials that utilized sublingual tablets and were carried out in paediatric patients, treatment protocol started directly at the target dose (12,13). Results were encouraging and the need for a build-up period in SLIT should likely be reconsidered. Moreover, we advise clinicians to be extremely careful when administering SLIT in patients with a previous history of systemic side effects after SCIT. Asthmatic patients whose disease is less than optimally controlled appear to be at highest risk (6). Finally, we wish to emphasise that the first dose of SLIT should be taken in a doctor's office with an observation period of at least 30 min.

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