Reactions to Sublingual Immunotherapy: An Analysis of a Group of Patients Who Developed Adverse Events over a Period of 5 Years

by Diego Saporta, MD

Introduction

Immunotherapy can be administered either by injections (subcutaneous injection immunotherapy; SCIT) or by the oral route (sublingual immunotherapy; SLIT). SLIT reactions (SRs), also called adverse events (AEs), are generally mild, but they appear to occur more frequently than reactions to SCIT. For example, SLIT AEs are reported with a variable rate of 9.6%, 20%, 23%, or even 78%, while systemic reactions after SCIT administration occur with a variable rate of 0.05 to 0.23 per 100 injections.[1–7]

In the last few years, several cases of severe reactions after SLIT administration have been reported wherein patients suffered asthma attacks, in some cases severe enough to require hospital care.[8–11] Despite these reports, SLIT safety is undisputed. While SCIT carries a risk of severe reactions, including mortality, there has not been a single report of mortality due to SLIT administration for the treatment of inhalant allergies.[12–16]

Usual reported AEs include labial or buccolingual edema, itching in oral cavity or other parts of the face, throat irritation, rhinoconjunctivitis, and gastrointestinal (GI) problems.[14–18] AE management usually involves dose adjustment or symptomatic treatment.[1,16,19,20] Treatment discontinuation because of SRs has been reported as less than 7% in several randomized controlled trials using oral tablets but as high as 31% despite symptomatic improvement in a clinical trial when using sublingual drops.[16,17] It has been reported that the majority of AEs occur during the induction phase and with low doses of allergen.[3,17,20]

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Methods

For a period of 5 years, records of any case where SLIT administration elicited any problems were collected. A brief analysis of those AEs is presented here (see below). Patients were adults or children of either sex with nasal allergy symptoms with or without asthma treated with SLIT according to our protocol.[21]

Results

Sixty-two patients were identified for analysis, 20 of them under 13 years old. AEs developed mainly during administration of the first treatment bottle. Two cases developed during the second bottle, 7 during the third bottle, and 6 during maintenance.

Reported Symptoms

Sixty two patients reported 39 symptoms. Table 1 shows those symptoms arranged according to their frequency of presentation for a total of 103 complaints.

Table 1: Reported Symptoms Arranged by Incidence

Rash skin	14	Cold sweat	1
Itchy skin	11	Diarrhea	1
Itchy throat	6	Dizziness	1
Stomach pain	6	Dry/chapped lips	1
Cough	5	Eczema	1
Tight chest	5	Feels weird	1
Headaches	4	Insomnia	1
Vomiting	4	Itchy lips	1
Itchy eyes	3	Lip tingling	1
Itchy face	3	Lips swollen	1
Nausea	3	Mood changes	1
Rash face	3	Nasal obstruction	1
Shortness of breath	3	Smell perversion	1
Throat tight	3	Sore throat	1
Swollen eyes	2	Throat burn	1
Tired	2	Throat dry	1
Taste	2	Tongue burn	1
Palpitations	2	Tongue tingling	1
Sneezing	2	Wheezing	1
Behavioral changes	1		

The first 5 symptoms in the table, involving the skin, oral area (OP), and GI system, account for 40.8% of the complaints (42/103). Itching/rash of the skin is by far the most common complaint and it is not necessarily limited to the perioral area.

Patient Management

AE management was based mainly on dose adjustment. The specific interventions included:

1. decreasing and subsequently increasing treatment dose
2. discontinuing and restarting treatment
3. diluting treatment bottle
4. dividing treatment dose in smaller a.m.-p.m. doses

Final Outcome

Defining "completion of the treatment" as 36 months, it was found that 53/62 (85.4%) of the patients did not complete the treatment after onset of AEs and that 23/53 (43.4%) of the patients who quit did so within 3 months after AE onset.

Conclusions

The most common complaints in this series are related to skin (reported as skin itching or skin rash).

The majority of the AEs occurred during the administration of the first bottle.

There were no life-threatening events.

This review suggests that patients who develop an AE during SLIT administration probably will quit the treatment.

Discussion

This is a retrospective analysis of all of the AEs developed during a certain period of time. While most of the published literature addresses the issue that in a certain group of SLIT patients a certain percentage will quit, this appears to be the only report that analyzes a group of patients who had already developed AEs, and it strongly suggests that once an AE develops, chances of quitting treatment are high.

The percentage of patients quitting SLIT is reported as no more than 7% in randomized control trials but up to 31% for patients attending an allergy clinic.[16,17] To further evaluate these figures, we reviewed 100 random SLIT charts and found a discontinuation rate of 27% to 34%. Certainly not having a prospective study with a control group is a shortcoming, but comparing figures of 27% to 34% of "spontaneous" discontinuation with almost 86% of AE-related discontinuation increases the possibility that the development of an AE will be a strong factor to determine treatment termination.

Our reported symptoms, in agreement with published literature, mainly involved the skin, OP, and GI tract.[14,15,17,18] In our case, itching of the skin was by far the most common complaint during SLIT administration. We also report symptoms (usually not reported in the literature) that occurred only once. We think that the length of time over which this sample was collected is a determining factor in recording infrequent occurrences.

Notes

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