

Compliance to Immunotherapy for *Hymenoptera* Venom Allergy

Improvements Through Switching from Aqueous to Depot Extract in the Maintenance Phase

by Federico Reccardini, Paola Puccinelli, & Samuele E. Burastero

Immunotherapy is effective and potentially life-saving for *Hymenoptera* venom-allergic patients. We investigated whether the long maintenance phase can be performed with an easier-to-handle depot extract also in patients who began immunotherapy with a short rush induction schedule. This switch proved successful, opening up new opportunities for improving compliance with treatment by reducing side effects and enabling treatment to be performed outside specialist centers.

Keywords: *Hymenoptera* venom, immunotherapy, adverse effects, aqueous extract, depot extract

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venom-allergic patients [1, 2]. In contrast to therapy for hypersensitivity to inhalant allergens, aqueous extracts are preferred in the induction phase, since they allow the maintenance dose to be reached with rush schedules [3]. This treatment is usually only carried out at selected allergological centers, due to the possibility of severe side effects, including anaphylactic shock. Patients therefore often have to travel far from home, which may induce them to decide against treatment. Here we investigate whether the long maintenance phase of treatment can be performed with an easier-to-handle depot extract in patients who began immunotherapy with an aqueous extract.

Our study comprised 30 patients allergic to *Hymenoptera* venom; their characteristics are indicated in Table 1. Immunotherapy was performed with Pharmedgen aqueous extract (ALK Abellò, Milan, Italy) as represented in

Table 2. One year later, patients switched to the Alutard SQ depot extract of the proper allergen, produced by the same manufacturer. This preparation is aluminum hydroxide-adsorbed and depleted of contaminating vasoactive amines and of other nonimmunogenic component, which reduces the frequency and severity of adverse effects [4].

The frequency of adverse effects, local and/or systemic (malaise, urticaria, itching, migraine), in the induction phase (see Table 3) was similar to reported data [1]. No severe reactions were observed and only one patient had to have an antihistaminic drug administered as a premedication. In the maintenance phase, the aqueous extract induced nonsevere adverse reactions in a proportion of patients, which diminished ($p = .0011$ at Fisher's exact test) after switching to the depot extract (see Table 4).

In conclusion, the depot formulation of the *Hymenoptera* venom extract was safely used in patients who started immunotherapy with an aqueous extract. This approach represents an opportunity to improve compliance with treatment since it reduces side effects and allows venom immunotherapy to be carried out at centers that routinely perform ordinary vaccinations to treat hypersensitivity to inhalant allergens.

TABLE 1
PATIENT CHARACTERISTICS

Sensitization	N	Mean age (range)	Gender (f/m)
<i>Apis mellifera</i>	6	(39.5) 25–68	2/4
<i>Vespula</i> spp.	24	(41.4) 11–76	7/17
Total	30	(41) 11–76	9/21

TABLE 2
TREATMENT SCHEDULE

Induction phase (aqueous, rush modified)						
day	visit	vial	µg/ml	time	µl administered	µg administered
1	1	1	1	0h 0 min	0.1	0.1
		1	1	0h 30 min	0.25	0.25
		3	10	1h 0 min	0.1	1.0
		3	10	1h 30 min	0.25	2.5
		4	100	2h 0 min	0.05	5.0
		4	100	2h 30 min	0.1	10.0
5	2	4	100	0h 0 min	0.05	5
		4	100	0h 30 min	0.1	10
		4	100	1h 0 min	0.3	30
		4	100	1h 30 min	0.5	50
10	3	4	100	0h 0 min	0.5	50
		4	100	0h 30 min	0.5	50
Maintenance phase, first year (aqueous)						
		vial	µg/ml	time	µl administered	µg administered
every 30 days		4	100	0h 0 min	1.0	100
Maintenance phase, after 1 year (depot)						
		vial	µg/ml	time	µl administered	µg administered
every 30 days for 1 year		4	100	0h 0 min	0.3	30
every 60 days for 1 year		4	100	0h 30 min	0.7	70

TABLE 3
ADVERSE REACTIONS DURING THE INDUCTION PHASE

		No. of patients (%)
Early reactions	Local	6 (2.4)
	Systemic	9 (3.6)
Late reactions	Local	33 (13.4)
	Systemic	4 (1.6)
Frequency per number of injections (N=390) with aqueous extract		

TABLE 4
ADVERSE REACTIONS DURING THE MAINTENANCE PHASE

		Aqueous extract No. of patients (%)	Depot extract No. of patients (%)
Early reactions	Local	3 (10)	1 (0)
	Systemic	1 (3.3)	0 (0)
Late reactions	Local	7 (23.3)	1 (3.3)
	Systemic	0 (0)	0 (0)
	Total	13 (43.3)	2 (6.6)

Number of patients (N=30) who suffered adverse reactions in at least one visit during the 1-shot-a-month maintenance phase (12 injections)

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Samuele E. Burastero, MD (to whom correspondence should be addressed) is with the San Raffaele Scientific Institute, 58 via Olgettina, 20132 Milan, Italy (tel. +39 02 2643-4730/-4736, fax +39 02 2643-4723, e-mail burastero.samuele@hsr.it). Federico Reccardini, MD, is with U.O. Pneumology and Respiratory Physiology, A.O. Santa Maria della Misericordia, Udine, Italy, and Paola Puccinelli, MD, is with ALK-Abellò, Lainate (MI), Italy.