Safety and tolerability of a 3-hour build-up phase with Hymenoptera venom depot extracts: preliminary results

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Safety and tolerability of a 3-hour build-up phase with Hymenoptera venom depot extracts: preliminary results

RUNNING TITLE

Ultrarush venom immunotherapy with depot extracts

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KEY WORDS

Hymenoptera venom allergy; ultrarush venom immunotherapy; build-up phase; side effects.

CONFLICT OF INTEREST

All authors have no conflict of interest do disclose.

To the Editor,

Hymenoptera venom allergy may be responsible for systemic reactions ranging from urticaria to fatal anaphylaxis. Yellow jackets (*Vespula* spp.) and honeybees (*Apis mellifera*) are the most involved Hymenoptera[1]. Paper wasps (*Polistes* spp.) and hornets (*Vespa* spp.) are a frequent cause of systemic reactions in Southern Europe with *Vespa velutina nigrithorax* being the commonest cause of anaphylaxis in Spain[2].

Venom immunotherapy (VIT) is the only treatment that can prevent new reactions, and it is effective in 77-84% patients receiving honeybee venom and in 91-96% patients treated with vespid venoms.

VIT can be performed with both aqueous and depot extracts. Aqueous extracts are used during the build-up phase while depot extracts are preferred for the maintenance phase since they cause fewer local reactions[1].

Several regimens are available for the build-up phase, from ultra-rush, rush, cluster and conventional protocols. Conventional (12 weeks) and cluster protocols (7 weeks) are time consuming for both patients and physicians while rush (2-4 days) and ultra-rush (1 day) can give protection in less time. However, rapid protocols are at higher risk of systemic reaction during the buildup phase[1].

In our department we have used a 1-day, 3-hour ultra-rush build-up phase with aqueous honey-bee or *Vespula* spp. venom extracts according to a previously published protocol[3]. Since aqueous extracts are no longer available, we decided to use depot extracts adsorbed with aluminium hydroxide (Alutard ALK Abelló, Hørsholm, Denmark) for honey-bee and *Vespula* spp. and with tyrosine (Anallergo, Scarperia e San Piero, Florence, Italy) for *Polistes dominula* and *Vespa crabro* for the ultra-rush build-up phase. The protocol was approved by our local ethic committee and an informed consent was obtained by all patients.

Thirty-five (20 males) patients aged 29-74 years with a clinical history of a systemic reaction (grade 1-4 according to Mueller) to an Hymenoptera sting were included. Four patients underwent 2 VIT, 3 with *Vespula* and *Polistes dominula* venoms (we could not identify the culprit stinger after specific IgE, skin tests and basophil activation) test and 1 with *Vespula* and *Vespa crabro* venoms (he had a respiratory arrest after a hornet sting). Fourteen patients had a REMA score higher than 2 and 2 had previous diagnosis of systemic indolent mastocytosis. All patients reached the maintenance dose with no systemic reactions while 8 out of 12 with honeybee venom, 6 out of 14 with *Vespula* venom and 4 out of 12 with *Polistes dominula* venom had a late large local reaction (LLR) (>10 cm) which was treated with topical corticosteroids and/or oral antihistamines (Table 1).

Bee venom allergy seemed to be the only risk factor for LLRs after ultrarush VIT. High venom specific IgE, a REMA score [?] 2, high serum tryptase levels and the severity of the index reaction were not risk factors for both local and systemic reactions[4].

Even if the number of subjects is low, our data suggests depot extracts can be used also for ultra rush protocols with a good safety profile. The safety profile of depot extracts has been confirmed also by other studies with cluster (7 weeks)[5] and rush protocols (2 days for *Vespula* and 4 days for honeybee)[6], with a lower incidence of LLR.

However, ultra-rush protocols are less time consuming and can provide protection in a few hours reducing the risk of new field sting reactions when using conventional or cluster protocols.

As regards efficacy, only 2 patients were stung during the maintenance phase with no systemic reactions.

Larger studies are needed to assess the safety profile of this protocol and to put in evidence immunological changes after a rapid buildup phase.

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Table 1. Clinical characteristics of investigated patients

Culprit insect						

Culprit insect						
Bee	12					
Vespula spp.	10					
Polistes dominula	9					
Hornet (Vespa crabro)	1					
Unknown vespid	3					
Age						
Range	29-74					
Mean	53.6					
Sex (n)						
Male	20					
Female	15					
Venoms		HB	YJ	PW	YJ + EH	YJ + PW
	Total (n=35)	12	10	9	1	3
Treatment (n)	Total (n=4)					
Beta blockers	1	0	0	1	0	0
ACE-inhibitors	4	0	3	1	0	0
Grade of SR (Mueller classification)	Total (n=35)					
I	6	1	3	2	0	0
II	4	4	0	0	0	0
III	9	5	2	2	0	0
IV	16	2	5	5	1	3
REMA (n)						
	[?] 2 (n=14)	4	3	5	2	0
	< 2 (n=21)	8	7	4	1	1
Reactions during ultra-rush (n)						
No side effects	Total (n=21)	4	5	6	2*	4*
Large local reaction	Total (n=18)	8	5	3	0	2*
Systemic reaction	Total (n=0)	0	0	0	0	0
Reactions during maintenance dosing						
No side effects	Total (n=190)	84	40	47	3	16
Large local reaction	Total (n=10)	2	4	2	0	2
Systemic reaction	Total (n=0)	0	0	0	0	0

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YJ: yellow jacket (Vespula); PW: paper wasp (Polistes dominula); EU: European hornet (Vespa crabro); HB: honey-bee (Apis mellifera)

* with both venoms