Efficacy and safety of a 7-week immunotherapy protocol with aluminium hydroxide absorbed hymenoptera venom

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To the Editor,

Hymenoptera venom allergy can cause life threatening anaphylaxis in patients sensitised to wasp and bee venom. Venom immunotherapy is effective in 77%-84% of patients treated with honeybee venom and in 91%-96% of patients receiving vespid venom[1]. Adverse events are usually rare and mild, and symptoms occur in only 4.3%-11.4% of patients during the updosing[1].

A variety of therapy regimes exist for the updosing phase, from conventional, rush, ultrarush or clustered modalities[1,2]. Current conventional protocols are time-consuming for patients, and some patients decline the potentially life-saving treatment due to the time commitment required for immunotherapy. Adverse events appear to be less frequent in conventional protocols during the updosing phase compared to rush and ultrarush protocols[1,2]; however, patients may remain unprotected for weeks as it takes considerable time to reach the maintenance dose.

The only licensed venom immunotherapy product in the UK is Alutard SQ® (ALK Abelló) for Vespula and Apidae venom. The SPC recommends updosing with a 7-week clustered protocol or 15- or 25-week conventional protocol.

To enhance the acceptance of treatment and increase compliance, we reduced the length of the SPC protocol. Another significant factor was the COVID-19 pandemic, which significantly reduced outpatient capacity to comply with social distancing.

Based on previous data using the same product[3], we introduced a shorter updosing protocol with 8 injections in 7 weeks and monitored its efficacy and safety. We used this in a wider age range of patients, including one patient with indolent mastocytosis and more patients with severe sting reactions.

Seventy-four patients aged 17 to 85 years with a history of a systemic sting reaction to vespid and apidae stings grade 2-4 were included (Table 1). Further information about patient selection and the updosing protocol is in supplementary file S1.

We managed to retain all the patients during updosing and maintenance, and no dose reduction was needed.

During updosing, there were no objective systemic adverse reactions recorded. Only one objective systemic adverse reaction was documented during maintenance, which was mild and limited to the skin. There were 6 incidences of mild and subjective systemic reactions during updosing and maintenance, which included symptoms of feeling hot, dizzy and itchy. The symptoms were treated with additional antihistamines with no change in regime required. We had a lower incidence of systemic reactions at 1.4% compared to Schrautzer et al[3], who reported objective systemic reactions in 3.9% of patients during just the updosing phase.

9.5% of our patient cohort reported large localised reactions throughout both the updosing and maintenance phase, which generally only occurred once or twice during the full treatment course.

The prevalence of cardiovascular disease and treatment with beta-blockers were not related to the occurrence of side effects.

Reactions to field stings were monitored to assess efficacy as sting challenges are not performed in the UK. 20 patients had field stings and all reported localised reactions. Some patients were stung by multiple insects (such as one patient who was stung by 19 insects at one time) and this was more common in beekeepers.

We have extended the work of Schrautzer et al[3] and demonstrated the efficacy and safety of their 7-week protocol in a large group of patients in a real-world setting. We have also demonstrated safety and efficacy of the 7-week protocol for Alutard SQ(r) apidae immunotherapy. Our data includes a larger group of patients with more severe reactions. Interestingly, our data also shows a lower number of reactions to immunotherapy treatment.

The quicker updosing protocol improved patients' acceptance of treatment and increased the efficiency of our immunotherapy clinic in terms of time and cost for patients, and medical staff.

Table 1

Demographic data and medical history (n=74) as well as frequency of adverse events (large local and systemic reactions during up-dosing and maintenance phase).

Age		
Range	17-85 years	17-85 years
Median	55 years	55 years
Sex	**Sex**	**Sex**
Female	39	52.7%
Male	35	47.3%
Insect	**Insect**	**Insect**
Bee	16	21.6%
Wasp	58	78.4%
Treatment	**Treatment**	**Treatment**
Beta blockers	3	4.1%
ACE- inhibitors	0	0%
Grade of SR	**Grade of SR**	**Grade of SR**
I	0	0%
II	20	27%
III	46	62.1%
IV	8	10.8%
Reactions during up-dosing (n=74)	**Reactions during up-dosing (n=74)**	**Reactions during up-dosing**
No side effects	67	90.5%
Large Local reactions	4	5.4%
Subjective systemic symptoms	3	4.1%
Objective systemic symptoms	0	0%
Total incidence of adverse reactions	7	9.5%
Reactions during maintenance (n=74)	**Reactions during maintenance (n=74)**	**Reactions during maintena**
No side effects	67	90.5%
Large Local reactions	3	4.1%
Subjective systemic symptoms	3	4.1%
Objective systemic symptoms	1	1.4%
Total incidence of adverse reactions	7	9.5%
Field stings	**Field stings**	**Field stings**

During up-dosing	**During up-dosing**	**During up-dosing**
Localised reaction	5	6.8%
Systemic reaction	0	0%
During maintenance	**During maintenance**	**During maintenance**
Localised reaction	15	20.3%
Systemic reaction	0	0%

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