

Safety of venom immunotherapy administered by a cluster schedule

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The goals of immunotherapy are to reach rapidly an allergen dose inducing the protection of patients with the lowest rate of SRs. Thus, not only the optimal maintenance dose should be reached but the schedules of allergen administration should be adapted. VIT is now well documented, and the maintenance dose of 100 µg is usually recommended.¹ In contrast, many different schedules have been proposed from very slow protocols to 1-day rush protocols.¹⁻³ The rate of SRs is usually low with YJV but increases with some rush protocols or with HBV and wasp venoms.^{1, 3, 4}

After several years of VIT and the treatment of several hundreds of patients, we tested several schedules. We devised a three-session step protocol that appeared optimal and tested its safety in a prospective study performed in 100 patients sensitive to HBV, YJV, and/or wasp venom.

MATERIAL AND METHODS

One hundred patients, ranging in age from 6 to 70 years (mean $\pm$ SD, 38.8 $\pm$ 19.3 years; 57 men), were included in the study after informed consent. The patients were included in the study without any particular selection, and no patient was excluded. The diagnosis criteria were previously described in detail.⁵ All patients had experienced SRs ranging from grades 1 to 4 according to the method of Mueller⁶ and had positive skin tests to one or several of the three venoms tested (HBV, YJV, and/or wasp venom, Stallergènes Laboratories, Fresnes, France) at a venom concentration of 0.1 or 1 µg/ml. Patients who had a positive skin test for a concentration of 1 µg/ml were only desensitized when the RAST (Phadebas RAST, Pharmacia Diagnostics AB, Uppsala, Sweden) to the corresponding venom was positive. The RAST levels before immunotherapy ranged from 0.75 to 17.5 PRU/ml. Median RAST levels were 2.4 $\pm$ 1.7 PRU/ml for HBV and 1.9 $\pm$ 1.4 PRU/ml for YJV.

Specific VIT was performed with venoms (Stallergènes Laboratories) according to a step protocol, making it pos-

Abbreviations used

SR:	Systemic reaction
VIT:	Venom immunotherapy
YJV:	Yellow jacket venom
HBV:	Honeybee venom
PRU:	Phadebas RAST unit

TABLE I. Protocol of venom immunotherapy

Day 1 (µg)	Day 7 (µg)	Day 14 (µg)
0.1	30	100
1	30	
5	30	
10		
20		

sible to reach the maintenance dose in three sessions (Table I). The maintenance dose for each venom was 100 µg. Since wasps are present in our area, many of vespid venom-allergic individuals received a mixture of YJV and wasp venom administered during the same injection.

All patients were carefully monitored before and between each injection and were followed for up to 2 hours after the last injection. In particular, the pulse rate and blood pressure were checked, and patients were always examined carefully before each injection for possible wheezing or urticaria.

RESULTS AND DISCUSSION

Fifteen patients had VIT with HBV, 23 with YJV, and five with wasp venom, and the other patients received YJV and wasp venom. The mean severity of SRs was similar in all four groups of patients (mean $\pm$ SD, 3.01 $\pm$ 0.8, score of Mueller⁶). Twenty-five patients had experienced one or more anaphylactic shocks. All patients were able to reach the maintenance dose of 100 µg of venom, and no patient experienced an SR during the course of VIT.

The efficacy of this treatment was not controlled by challenge stings, but 42 patients subsequently had field stings without any reported severe SR. Two patients had mild SRs. Venom-specific IgG levels rose to levels similar to those observed with previous VIT schedules.

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The VIT schedule proposed in the present study was found to be safe in all treated patients, including 15 HBV- and five wasp venom-allergic individuals. This is, to our knowledge, the first study reporting no SR in patients treated with HBV. Previous studies attempted to reach the dose of 100 µg of HBV within a day, but between 36% and 100% of patients had an SR.^{1, 3, 6} In contrast, with YJV, rush protocols are safer. The protocol proposed is simple, can be performed routinely, and, for HBV, represents an alternative to more rapid schedules used safely with YJV.

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