

## Antidote treatment in Viper envenomation in Italy: a comparison between two antivenoms during four-year experience

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**Objective:** EU marketed viper antivenoms differ for pharmaceutical characteristics, equine/ovine origin, viper spp. neutralizing activity, dosage and registered route of administration. In Italy, hospital availability of 5 different antivenoms influence their use. Aim of this study was to evaluate the clinical response in envenomed patient treated with the two antivenoms (Zagreb and Biomed) mainly used in the last 4 years. There are no differences for host animal and fragment type [F(ab')<sub>2</sub>]; regarding the specific activity, Zagreb is declared active against *Vipera aspis*, *ammodytes*, *berus*, *labetina* and *xanthine*, Biomed only against *Vipera berus*.

**Methods:** All viper bitten patients treated with one of the two antivenoms (administered according to manufacturer recommended dose) from 2013-Sep2016 were retrospectively assessed for sex/age, site of bite, time elapsed between bite and ED admission/antivenom administration, antivenom administered and acute/delayed adverse effects (ADR). Grading-Severity-Score (GSS) was applied at admission, at antivenoms administrations, and after 6-hours. Improvement was defined as amelioration/no evolution of local effects and/or no appearance of systemic effects (including neurological symptoms). Patients were follow-upped until discharge.

**Results:** 66 patients (age  $44.3 \pm 27.2$  y-o; male 70%) were included; 16 were paediatric (1-15 y-o). Considering geographical distribution, *Vipera aspis* spp. was mainly involved. Upper and lower limbs were involved in 88% and 12% of cases, respectively. Average time between bite and admission was 4 hours (15min-23hours); an average of 9 hours (40min-26hours) elapsed between bite and antivenom administration in patients with GSS 2 or 3. Both antivenoms were administered intravenously: Zagreb in 31/66 (47%) and Biomed in 35/66 (53%) cases. Clinical improvement was registered in 94% (29/31) and 57% (20/35) of patients treated respectively with Zagreb and Biomed ( $p=0.0007$ ). Considering two subgroups [ $\leq 15$  (n =16) or  $>15$  (n=50) years old], Zagreb increases the probability of clinical improvement in both with more evidence in paediatric group (Zagreb=85.71% vs Biomed=22.22%, OR=16,  $p=0.041$ ). Acute adverse reactions occurred after Zagreb (3 cases; angioedema, pruritus, bradycardia) and Biomed administration (1 cases; vasovagal syncope). Serum sickness (3 weeks later) occurred in 1 case (Biomed).

**Conclusion:** An apparent less efficacy seem to exist for Biomed, both considering all patients and the paediatric sub-group, but these results should be cautiously evaluated because of the small paediatric population. Intravenous administration is usually safe (even if off-label used for Biomed). It remains difficult to ascertain which species of viper is responsible of the envenomation, and Biomed performance is probably influenced by the activity only against *V. berus*.