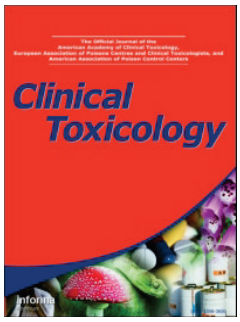

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LETTER TO THE EDITOR

Comment on "Antivenom for European Vipera species envenoming"

Dear Editor,

The article by Lamb *et al.* [1] gives a valuable review of the current needs for antivenom treatment of snakebite envenoming in Europe, the current practices in envenomation treatment across Europe, and the antivenoms' current availability, effectiveness and safety. However, we believe that some cited literature as well as experimental data should be differently interpreted.

Lamb *et al.* [1] state that five cases of patients' death have been reported after Zagreb antivenom use and provide five references [2–6] to support this. Those articles describe indeed six (not five) cases of envenomed patients' death; however, only two after Zagreb antivenom treatment. Lukšić *et al.* [2] described two deaths after *V. ammodytes* bites and Malina *et al.* [3] one fatal case after *V. berus bosniensis* bite. However, as stated in the papers, those three cases did not otherwise receive appropriate medical care due to military operations. Karlson-Stiber *et al.* [4] described 231 cases of *V. berus* envenoming in Sweden, among which 42 were treated with antivenom: 12 with Zagreb antivenom and 30 with ViperaTab. However, while the authors report on one death out of those 231 patients, they do not specify which antivenom the patient had received, or if he had received antivenom therapy at all. Only two reported fatalities after Zagreb antivenom treatment remain; a small baby bitten directly into the neck [5], and an old woman, who might have been otherwise over treated [6].

In Table 1, the authors compare different properties of European antivenoms. However, the data on antivenoms' neutralizing activities have been inconsistently presented. The obligatory minimal values are given for all antivenoms (as declared in products' specifications), except for ViperaTab. Instead, significantly higher values are given for this product, obtained experimentally for only one batch of ViperaTab. Such inconsistent presentation thus implies that ViperaTab is the most potent antivenom in Europe, even for the *V. ammodytes* bites. Further, in Figure 3A, the authors compare *in vitro* reactivity of Zagreb and ViperaTab antivenoms to different venoms, tested with ELISA, and conclude that ViperaTab is superior to Zagreb antivenom in recognizing different venoms, even the *V. ammodytes* venom. However, we believe that the results of those two different ELISA assays cannot be mutually compared. In the ELISA for assessment of ViperaTab's binding to different venoms the assay used commercial HRP-conjugated anti-sheep immunoglobulin, which recognizes sheep Fab. In the ELISA for the assessment of Zagreb antivenom binding to different venoms, the assay used commercial HRP-conjugated anti-horse immunoglobulin, which recognizes horse $F(ab')_2$. Although both antibodies were used in the same dilution in the two assays, the results cannot be directly compared, since those commercial antibodies differ in specificity and concentration and therefore affect both the absorbance intensity and the ELISA results. In conclusion, preclinical and clinical data available so far do not provide clear evidence on the neutralization efficacy of *V.berus*-specific antivenoms against *V. ammodytes* venom.

Disclosure statement

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