**INTRODUCTION**

In the southeastern parts of Europe *Vipera a. ammodytes* (V. a. ammodytes) and *Vipera berus* (*V. berus*) are the only medically important poisonous snakes. Differentiation of their bites based on pharmacokinetic data is essential for optimal management. In the southeastern parts of Europe *V. a. ammodytes* and *V. berus* are venomous snakes, and their antivenom availability is a major concern. The aim of this study was to present cases of *V. a. ammodytes* and *V. berus* snakebites and to evaluate the pharmacokinetics of ViperTAb® (MicroPharm Limited, UK), composed of ovine Fab fragments as active principle against the venom of *V. berus* only. Its therapeutic use was to determine the optimal schedule for the administration of antivenom to patients. In the southeastern parts of Europe, *V. a. ammodytes* and *V. berus* snakes were successfully treated with ViperTAb® and Viperfav™, respectively.

**RESULTS**

**Case No. 1**

- A 60-year-old man was bitten in the thenar of the hand by *V. a. ammodytes*.
- Upon hospitalisation the patient was bent, dizzy, confused, tachycardic (100/min) and hypotensive (85/50 mmHg). Edema of the affected hand was extending up to a fifth of his forearm.
- The patient was somnolent, tachycardic (100/min), normotensive (110/80 mmHg) and tachypneic (30/min). He felt strong pain in the bite site. Local edema with erythema extended up to a half of his forearm. Laboratory tests showed leukocytosis (25×10^9/L), thrombocytopenia (20×10^9/L) and coagulopathy (prothrombin time: 0.41). However, d-dimer (10469 μg/L) and thrombocytopenia (21×10^9/L) were noted. While coagulopathy improved with antivenom, it increased on the 7th post-bite day.
- The initial laboratory tests showed leukocytosis (25×10^9/L), thrombocytopenia (20×10^9/L), slight rash and coagulopathy (prothrombin time: 248 μsec). Platelet number normalised (177×10^9/L), while coagulopathy improved with prothrombin time reaching 0.53. Local edema and erythema extended further to the shoulder and the patient developed neurological signs (bilateral ptosis, ophthalmoplegia and dysphagia).
- ELISA analysis of serum samples taken 4 h after the bite revealed the venom level of 40 ng/mL.
- Platelet number normalised (177×10^9/L) again, while coagulopathy improved with prothrombin time reaching 0.53. However, local edema and erythema extended further to the shoulder and the patient developed neurological signs (bilateral ptosis, ophthalmoplegia and dysphagia).
- ELISA analysis of serum samples taken 7 h after the bite revealed the venom level of 160 ng/mL. The Atxs® (100) and Viperfav™ (5428 μg/L) serum concentrations are presented in Table 1. Antivenoms ViperTAb® and Viperfav™ serum concentrations measured by ELISA are presented in Fig. 1, while ViperTAb® pharmacokinetic data is summarised in Table 1.

**Case No. 2**

- An 83-year-old man was bitten in the dorsal side of the right foot by *V. a. ammodytes*. Immediately after the bite he felt pain and within a few minutes the right foot started to swell.
- Upon hospitalisation the patient was in extreme pain, confused, tachycardic (124/min) and hypotensive (100/50 mmHg). Local edema, lymphangitis and haemotoma were extending up to a third of the lower leg. There were no neurological symptoms. The initial laboratory tests showed leukocytosis (25×10^9/L), thrombocytopenia (20×10^9/L), slight rash and coagulopathy (prothrombin time: 0.70). Platelet time was at lower normal value (0.70).
- Platelet number normalised (135×10^9/L), while coagulopathy improved with prothrombin time reaching 0.53. However, local edema and erythema extended further to the shoulder and the patient developed neurological signs (bilateral ptosis, ophthalmoplegia and dysphagia).
- ELISA analysis of serum samples taken 4 h after the bite revealed the venom level of 40 ng/mL. Serum concentrations are presented in Fig. 2. None of the analysed sera samples for Atxs in this patient gave absorbance values higher than those obtained for the same snake and control. Antivenom ViperTAb® serum concentrations measured by ELISA are presented in Fig. 2, while ViperTAb® pharmacokinetic data is summarised in Table 1.

**CONCLUSIONS**

In *V. a. ammodytes* bitten patients ViperTAb® application induces *V. a. ammodytes* venom level decrement, but it does not affect serum concentration of neurotoxic Atxs. ViperTAb® doses in *V. a. ammodytes* bites should be higher and given repeatedly despite its maximum 55-hour long elimination half-life.

No adverse effects of ViperTAb® were noticed in *V. a. ammodytes* bitten patients.

**AIM**

For the first time we present cases of several *V. a. ammodytes* snakebites that occurred in Slovenia and were treated with ViperTAb® and *V. berus*-specific antivenom, whose pharmacokinetics has been measured and correlated with clinical picture.

**MATERIALS AND METHODS**

*V. ammodytes* venom, neurotoxic ammodytoxins (Atxs) and Fab fragment levels in sera samples of three patients envenomed by *V. a. ammodytes* snakebite and treated with ViperTAb® were determined by the respective in-house ELISA assay.

In addition, the pharmacokinetic analysis of the antivenom Fab fragments was carried out. Pharmacokinetic analysis of the measured concentrations was performed using PKSolver add-in software (version 2.0, China Pharmaceutical University, Nanjing, China) for Microsoft Excel. Concentration-time data was fitted either to one-, two- or three-compartment model. Akaike information criterion (AIC) and Schwarz criterion (SC) were used for comparison of goodness of their fit [2].