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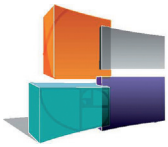

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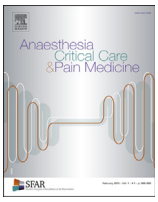

Letter to the Editor

Snake envenomations in French Guiana: First clinical assessment of an antivenom imported from Mexico

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Snakebites in French Guiana can lead to life-threatening situations as a recent publication shows 4 reported deaths in the Cayenne Hospital between 2007 and 2015 [1]. Moreover, the mortality is probably underestimated because illegal gold miners from neighbouring countries are certainly victim of snakebites without consulting a hospital. An antivenom was used for the first time in French Guiana during the 1980s, but immediately abandoned in consequence of severe side effects. Since then, and despite a high number of human envenomations, no specific antidotes have been made in order to treat envenomed patients in French Guiana. The classical management is symptomatic (disinfection of the site of the snake bite, analgesic drug, hydration, antibiotics, supportive care for organ failure). In some cases, extensive resections, and amputations have to be taken using a multidisciplinary approach.

In November 2014, collaboration between the Saint Laurent du Maroni Hospital (SLdMH) and the Western France Poison Control Centre (WFPCC) began in order to establish a protocol to use an available and efficient antivenom in French Guiana. Antivipmyn-Tri® was chosen: it is the only antivenom authorised in French Guiana by the French Health National Authorities because it fulfils the World Health Organization (WHO) recommendations [2]. Antivipmyn- Tri® is made with horses immunised with the venom from 3 species of snakes: *Bothrops asper, Crotalus durissus* and *Lachesis muta*. Because of cross-reactivity, Antivipmyn-Tri® is an effective antivenin for treating venom from the main South American *Crotalinae* species (*Viperidae* family) such as *Bothrops atrox*, *Bothrops brazili*, *Crotalus durissus*, *Lachesis muta*, *Bothrops bilineatus*... [3]. A preclinical study, challenging several marketed and experimental antivenins, showed a good neutralisation of venoms from French Guiana snakes [3]. The purpose of our study is to assess the tolerability and efficacy of this immunotherapy.

This prospective and observational study includes all *Crotalinae*-related snakebite patients admitted to the SLdMH between November 2014 and June 2016, requiring advice from the WFPCC. Immunotherapy with Antivipmyn-Tri® was recommended from grade II onwards in the protocol. Immunotherapy was performed at the SLdMH and the pharmacy prescribed the antidote with the patients' consent.

Thirty cases were included (Table 1): no grade 0, one grade I, 24 grade II and 5 grade III. The most common clinical signs were hemotoxic syndrome with extensive swelling. The biological disorders where mainly the consequence of major haemostasis disturbances, frequently observed during *Crotalinae* bites in the Americas [4]. The period between the bite and hospitalisation was recorded in 27 cases and varied from 1–41 hours, with an average of 9.6 hours and the median length between bite and hospitalisation was 4-hour.

The clinical feature of 29 patients was severe enough to indicate immunotherapy (grade II or III) but only 26 of them were treated with Antivipmyn-Tri®. For these 26 patients who received the antivenom the clinical symptoms decreased and a significant biological improvement was confirmed (prothrombin time (PT) and fibrinogen). Our data showed that Antivipmyn-tri® was most effective when given early after a bite with a better clinical and biological improvement (Mann-Whitney, $P = 0.023$). No death was reported during this study compared to the snakebite mortality in French Guiana (0.274/100,000 persons/year (95%IC 0.071–0.477)) [1]. No cases of severe anaphylactic reactions were reported during this study.

Lengths of hospital stays were short considering the clinical and biological examinations upon admission, with a mean of 4 days (average 6 days). Patients hospitalised longer than the mean length of hospital stay suffered from serious local complications that required surgery for example on necrotic tissue or on abscess.

In the present case series the antivenom therapy for treating envenomed patients in French Guiana seems to be both effective and well tolerated. The results of this study are in line with the WHO and the national French authorities recommendations: antivenin must be used for the treatment of moderate to severe envenomation after snakebites, and when it is indicated the correct dose must be administered intravenously as soon as possible [5]. However, our results should be interpreted with caution due to the small sample size. Placebo controls are not justified. Indeed, antivenin treatment's beneficial effects have been well documented in several other studies in South America. The presentation of this study of both structures (SLdMH/WFPCC) to the French Health authorities and the report of a new case of death in Cayenne where no antivenoms were available were in the beginning of 2017 at the origin of the decision to generalise the use of the Mexican antivenom in all of French Guiana (Antivipmyn-Tri® is now available in the 3 main hospitals of French Guiana).

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Table 1
Description of population: 30 patients included.

Age (years)	Grade	Antivenom	Time between bite and antivenom (hours)	Clinical signs[a] before immunotherapy	Coagulation before immunotherapy		Coagulation after immunotherapy		Side effects	Hospitalization	
					PT (%)	Fibrinogen (g/L)	PT (%)	Fibrinogen (g/L)		Duration (days)	Emergency/ICU (hours)
32	III	Multiple dose	20	P/E3/H/HD/IR	< 10	1.7	68	6.6	No	34	96
34	II	Single dose	12	P/E2	< 10	< 0.6	79	–	No	6	36
37	II	Single dose	38.5	P/E2	21	< 0.6	43	0.7	No	5	24
11	I	0	–	P	74	2.5	–	–	–	4	–
11	II	Multiple dose	5.5	E1/	< 10	< 0.6	47	0.6	No	4	36
48	II	0	–	P/E1	57	0.8	72	–	–	6	24
44	II	0	–	P/E2/HD/D/IR	< 10	< 0.6	50	1.4	–	5	48
44	II	Single dose	12.5	E2/H/D	10	< 0.6	39	1.3	No	1	–
37	III	Single dose	22	P/E2	22	0.6	62	–	No	4	48
17	II	Single dose	9	P	34	< 0.6	39	–	–	6	24
38	II	Single dose	38	P/E2/H	–	–	–	2.9	Pruritus	9	24
42	II	Single dose	39	P/E2	–	–	86	2.9	No	3	–
38	II	Single dose	–	E2	< 10	–	44	1.8	Urticaria	4	24
16	II	Single dose	3	P/E2	44	0.6	54	2.6	No	8	48
6	II	Single dose	6	P/E2/H	< 10	< 0.6	55	2.7	No	4	24
48	II	Multiple dose	9	P/E2	< 10	< 0.6	63	–	No	2	12
73	II	Single dose	–	P/E2	20	< 0.6	51	0.8	No	1	–
10	II	Single dose	6	P/E2	55	1.6	64	2.3	No	2	12
47	II	Single dose	3.5	P/E2/HD	< 10	0.7	59	3.8	No	4	24
53	III	Single dose	42	P/E3/H/IR	45	–	68	–	–	3	24
44	III	Single dose	12	P/E3/H	–	–	–	–	–	5	48
34	II	0	–	P/E1	< 10	2.6	56	0.7	–	3	24
18	III	Single dose	19	P/E2	< 10	0.6	59	2.5	–	4	48
4	II	Single dose	–	E2	< 10	0.6	56	1.5	No	7	24
17	II	Single dose	4	P/E2/H	20	< 0.6	28	3.8	–	28	72
31	II	Single dose	13	P/E2	< 10	< 0.6	72	1.1	Pruritus	1	–
45	II	Single dose	11.5	P/E2/H	18	< 0.6	87	2.4	No	3	24
7	II	Single dose	6	P/E2	17	< 0.6	75	3.2	Skin reaction, hypotension	10	48
8	II	Multiple dose	10	E2	27	< 0.6	67	–	No	6	60
30	II	Single dose	3	P/E2	< 10	< 0.6	81	–	No	2	12

Moderate haemorrhage: H; Haemodynamic signs: HD; Digestive signs: D; Impaired renal function: IR.
[a] Pain: P; Oedema: E (E1: not exceeding the overlying joint; E2: beyond the overlying joint; E3: greater than or equal to the root of the limb).

Disclosure of interest

The authors declare that they have no competing interest.

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