Epidemiological characterization of ophidian accidents in a Colombian tertiary referral hospital. Retrospective study 2004-2014

Caracterización epidemiológica de accidentes ofídicos en un hospital de tercer nivel en Colombia. Estudio retrospectivo 2004-2014

Received: 30/11/2016. Accepted: 23/04/2017.

Karen Sarmiento1 • Ivonne Torres2 • Mariana Guerra3 • Carolina Ríos4 • Carlos Zapata5 • Fernando Suárez6

1 Pontificia Universidad Javeriana - School of Medicine - Department of Physiological Sciences - Bogotá D.C. - Colombia.
2 Hospital Central de la Policía - Hospitalization Service - Bogotá D.C. - Colombia.
3 Hospital Universitario San Ignacio - Research Office - Bogotá D.C. - Colombia.
4 Centro Médico Sura Sur - External Consultation Service - Bogotá D.C. - Colombia.
5 Hospital Universitario de La Samaritana Empresa Social del Estado - Surgery Service - Bogotá D.C. - Colombia.
6 Pontificia Universidad Javeriana - School of Medicine - Institute of Human Genetics - Bogotá D.C. - Colombia.

Corresponding author: Karen Sarmiento. Departament of Physiological Sciences, School of Medicine, Pontificia Universidad Javeriana. Carrera 7 No. 40-02, edificio: 31, office 3. Telephone number: +57 1 3208320, ext.: 2782. Bogotá D.C. Colombia. Email: ksarmiento@javeriana.edu.co.

DOI: http://dx.doi.org/10.15446/revfacmed.v66n2.61335

| Abstract |

**Introduction:** In Colombia, there are 5 000 cases of ophidism per year. This is a public health issue that causes mortality in 8% of cases and disability in 10% due to inadequate clinical attention.

**Objective:** To describe the clinical and epidemiological characteristics of patients diagnosed with ophidic accident in a tertiary hospital in Colombia.

**Materials and methods:** A review of clinical charts that included a diagnosis of ophidism during the 2004-2014 period was made at Hospital Universitario de La Samaritana Empresa Social del Estado. The frequency of the variables associated with snake bites, previous treatment and in-hospital management was analyzed.

**Results:** 42 medical charts were reviewed. Ophidism predominated in male farmers, who presented with bites in the lower limbs and were initially treated by medicine men/women. 90% of patients developed superinfections, 30% wound culture, 74% received antibiotics, 50% underwent fasciotomy and 95.2% were given antivenin.

**Conclusions:** Significant variability in the management of patients, discrepancy in antivenin dose and in classification of poisoning severity were observed throughout the study, as well as a high incidence of infections despite antibiotic schemes and surgical procedures. Medical management of ophidic accidents must be continuously updated to reduce disability and mortality in patients.

**Keywords:** Antivenins; Snake Bites; Tertiary Healthcare; Epidemiology; Public Health (MeSH).

| Resumen |

**Introducción.** En Colombia se presentan 5 000 casos de ofidismo anuales, un problema de salud pública que por manejo inadecuado provoca mortalidad en el 8% de los casos y discapacidad en el 10%.

**Objetivo.** Describir las características clínicoepidemiológicas de los pacientes diagnosticados con accidente ofídico en un hospital de tercer nivel en Colombia.

**Materiales y métodos.** Se realizó una revisión de las historias clínicas con diagnóstico de ofidismo del Hospital Universitario Del Samaritana Empresa Social del Estado, en el periodo 2004-2014, analizando la frecuencia en las variables asociadas a un mordedura de serpiente, el tratamiento previo y el manejo intrahospitalario.

**Resultados.** Se revisaron 42 historias clínicas. Predominó el ofidismo en hombres agricultores, con mordedura en miembros inferiores y asistidos inicialmente por curanderos. 90% de los pacientes presentó sobreinfección, 30% tuvo cultivo de la herida, 74% recibió antibiótico, al 50% se les realizó fasciotomía y al 95.2% se le suministró antiveneno.

**Conclusiones.** Se evidenció variabilidad en el manejo de los pacientes y discrepancia en la dosis de antiveneno y la clasificación de severidad del envenenamiento, alta incidencia de infecciones a pesar del esquema antibiótico y procedimientos quirúrgicos reevaluados en ofidismo. El manejo médico del accidente ofídico debe estar en continua actualización para disminuir discapacidad y mortalidad en los pacientes.

**Palabras clave:** Antivenenos; Mordeduras de serpientes; Atención terciaria de salud; Epidemiología; Salud pública (DeCS).
Introduction

The clinical picture triggered by the bite of a venomous snake is known as ophidiotoxicosis. (1) Every year, about 2.4 million people are bitten by venomous snakes around the world, causing between 94,000 and 125,000 deaths, as well as 400,000 secondary amputations and other complications such as infections, deformities, psychological sequelae and injuries derived from non-medical cultural practices to prevent the progression of poison. Such practices include the intake of hydrocarbons or alcohol, electrical burns, tourniquets, among others (2), which mostly have a negative impact on the work capacity of the people affected and, therefore, family and regional economy. (2,3)

Colombia is a tropical country characterized by high biodiversity, where venomous snakes are found mainly in areas below 2,500 m amsl, especially those that generate the greatest risk to populations. For this reason, ophidic accidents occur more frequently in rural areas, being farmers the most affected population, with a higher incidence in young adults and in males. (4)

According to statistics from the Instituto Nacional de Salud (National Health Institute) (1), between 2,000 and 3,000 ophidian accidents occur in Colombia every year, with an incidence of 6.2 cases per 100,000 inhabitants in less populated regions and 20 cases per 100,000 inhabitants in the most populated. (4) For the most part (90-95%), these accidents are caused by snakes of the Bothrops genus, and Antioquia and Chocó are the most affected departments. About 5-9% of the events in Colombia are fatal and 6-10% have sequelae. (4)

Although the epidemiological potential of snake bites is not greater than that of diseases transmitted by vectors or other infectious diseases, it is important to note that the impact of mortality caused by ophidiotoxicosis is greater than that attributed to diseases that have been recognized as unattended in tropical regions, which include dengue, cholera, leishmaniasis, chagas, etc. (5), thus turning ophidian accidents into a major public health issue.

In Colombia, some factors that hinder rapid attention of these patients have been identified, namely, geographical features, poor infrastructure for transportation from rural areas to care centers, inadequate cultural practices and lack of thorough medical management of ophidic accidents by health professionals. (6-9)

The treatment of ophidism should be comprehensive and timely, based mostly on the administration of polyvalent antivenin serum specific for the type of venom inoculated according to the genus of the snake. Clinical and paraclinical assessment performed by health personnel is highly important to correlate the etiology with the type and degree of poisoning and, thus, be able to administer sufficient antivenin vials in a timely manner. (5)

The severity of poisoning and the type of venom are determined by factors such as the age of the victim, the size of the bite and sensitivity to the poison, the time elapsed since the bite until receiving medical attention, the location and depth of the bite, the number of bites, the size of the snake and the amount of poison inoculated. (9,10)

Currently, Colombia has a Public Health Surveillance Protocol for Ophidic Accidents (1) and a Guide for the Management of Toxico logical Emergencies (5), which establish the basic guidelines for hospital care. However, there is still a high mortality rate and disability secondary to inadequate prehospital treatment.

Therefore, the objective of this study is to perform a clinical characterization of snake bite cases treated in a tertiary hospital in Bogotá between 2004 and 2014, making a comparison with the treatment recommended in national and international management guidelines and review articles, in order to analyze the factors that can provide a continuous improvement in the care of patients with this diagnosis.

Materials and methods

A descriptive, retrospective, cross-sectional study was carried out, with sampling at convenience and evaluation of secondary data sources. The evaluation was made on 42 clinical charts of patients diagnosed with poisonous and non-poisonous snake bites during the aforementioned period, and attended at Hospital Universitario de La Samaritana Empresa Social del Estado (HUS), located in Bogotá, Colombia. Clinical charts with pictures compatible with bites or stings by other animals, blunt trauma to the extremities and poisoning by chemical substances were excluded.

After receiving the authorization from the Ethics Committee, a format was used to collect information regarding the patient’s sex, age, geographical area where the bite occurred, occupation, previous morbidities, bite history and use of antiphidic serum, treatment prior to hospital admission, anatomical location of the bite, time of evolution of the condition, time elapsed between the bite and the administration of the antivenin serum, requirement of hospitalization and admission to the intensive care unit, classification of the severity of the ophidic accident, number of days of antibiotic treatment, need for surgical management, complications, antivenin serum side effects, paraclinical evolution of the patient, and alarming signs and symptoms at admission and discharge, such as findings on vital signs, pain, hemorrhages, neurological symptoms and fever.

Once data were collected, information was entered into a spreadsheet in Microsoft Excel 2013. Absolute and relative frequencies of the variables of interest were estimated and grouped into tables. Variables regarding the use of antibiotics and frequency of infections were compared with data from another national hospital-based study using a proportion comparison test. If p<0.05, a statistically significant difference was considered.

Results

The most significant results were that the average age was 41.3 years, 76% of the population was male, 42.8% were farmers from the region and Cundinamarca was the main geographical area where ophidian accidents occurred (80.9%). Regarding the anatomical place of the bite, 53% of the patients were bitten in the lower limbs and the remaining patients in the upper limbs (Table 1).

With respect to severity, numerical and (1, 2, 3 and 4) and status records (mild, moderate and severe) were obtained. Taking into account the most used classification, 63.3% of patients were classified in moderate stage, 28% in severe and 7% in mild. The time elapsed from the bite until initiation of medical attention ranged between 1 and 5 hours in 45.2% of the patients, of which 28.5% were in a moderate stage of poisoning.

Regarding the time elapsed from the bite to the administration of antivenin, antivenin was administered between 6 and 11 hours after the bite in 30.9% of patients, of which 21.4% were found in moderate stage, while two patients, with moderate and severe classification, respectively, were not administered any. In relation to previous attention at the HUS, 71.4% of patients were attended first by a medicine men/women and the most frequent procedure (35%) was tourniquet. Of the total patients, 41 required some type of surgical procedure; however, it should be noted that 70% underwent fasciotomy (Table 2).
Table 1. Characteristics of the studied population.

| Characteristics          | Female |  | Male |  | Total |  |
|--------------------------|--------|---|------|---|-------|---|
| Age                      |        |   |      |   |       |   |
| <15 years                | 1      | 2.3 | 0    | 0 | 1     | 2.3|
| 16-29 years              | 5      | 11.9| 12   | 28.5| 17    | 41 |
| 30-59 years              | 2      | 4.7 | 13   | 30.9| 15    | 35.7|
| >60 years                | 2      | 4.7 | 7    | 16.6| 9     | 21 |
| Total                    | 10     | 23.8| 32   | 76.2| 42    | 100|
| Geographical location of ophidism |      |   |      |   |       |   |
| Cundinamarca             | 8      | 19 | 26   | 62 | 34    | 81 |
| Boyacá                   | 1      | 2.3| 0    | 0 | 1     | 2.3|
| Vaupés                   | 1      | 2.3| 2    | 4.72| 3    | 7.5|
| Caldas                   | 0      | 0  | 1    | 2.3| 1     | 2.3|
| Guainia                  | 0      | 0  | 2    | 4.72| 2    | 4.6|
| Guaviare                 | 0      | 0  | 1    | 2.3| 1     | 2.3|
| Occupation               |        |   |      |   |       |   |
| Not registered           | 2      | 4.71| 6   | 14.3| 8    | 19 |
| Farmer                   | 1      | 2.3| 17   | 41 | 18    | 42.8|
| Household duties         | 4      | 9.36| 5  | 12  | 9     | 21.4|
| Student                  | 2      | 4.71| 1   | 2.3| 3     | 7.5|
| Environmental promoter   | 1      | 2.3| 0    | 0 | 1     | 2.3|
| Catechist                | 0      | 0  | 1    | 2.3| 1     | 2.3|
| Snake oil salesperson    | 0      | 0  | 1    | 2.3| 1     | 2.3|
| Merchant                 | 0      | 0  | 1    | 2.3| 1     | 2.3|
| Anatomical location of the bite | | | | | | |
| Upper limbs              | 3      | 7.14| 17  | 40.5| 20    | 47.6|
| Lower limbs              | 7      | 16.6| 15   | 35.7| 22    | 52.4|

Source: Own elaboration based on the data obtained in the study.

Table 2. Distribution of patients according to characteristics associated with the stage of severity.

| Characteristics          | Classification of poisoning severity |
|--------------------------|-------------------------------------|
|                          | Mild (%)  | Moderate (%) | Severe (%) | Total (%)  |
| Bite-medical care        |            |              |            |            |
| 1-5 hours                | 2 (4.76)   | 12 (28.57)   | 5 (11.9)   | 19 (45.2)  |
| 6-11 hours               | 1 (2.38)   | 9 (21.42)    | 1 (2.38)   | 11 (26.1)  |
| 12-23 hours              | 0          | 2 (4.76)     | 1 (2.38)   | 3 (7.14)   |
| 24-47 hours              | 0          | 3 (7.14)     | 3 (7.14)   | 6 (14.2)   |
| 48-71 hours              | 0          | 0            | 1 (2.38)   | 1 (2.38)   |
| >72 hours                | 0          | 1 (2.38)     | 1 (2.38)   | 2 (4.76)   |
| Bite-antivenin           |            |              |            |            |
| Not administered         | 0          | 1 (2.38)     | 1 (2.38)   | 2 (4.76)   |
| 1-5 hours                | 0          | 4 (9.52)     | 1 (2.38)   | 5 (11.9)   |
| 6-11 hours               | 1 (2.38)   | 9 (21.42)    | 3 (7.14)   | 13 (30.95) |

Source: Own elaboration based on the data obtained in the study.

A prevalence of 90% in in-hospital infectious complications was found, which includes those associated with intradermal and musculoskeletal infectious processes, and of those, 9.5% of the patients without treatment were classified as moderate and mild.)
When specifying the antibiotics used, 31 different schemes were observed. The most widely used drug was crystalline penicillin in 17 cases, followed by clindamycin in 16, ampicillin sulbactam in 14, and ciprofloxacin in 12. Additionally, records of patients who were administered piperacillin tazobactam, cefazolin, amikacin, meropenem, gentamicin, vancomycin, imipenem, among others were obtained.

76% of the patients presented some complications, being more frequent hematological and dermatological alterations (25%). The moderate stage included 42% of patients with complications, of which compartment syndrome was the most frequent, followed by dermatological, hematological and musculoskeletal alterations, while patients in severe stage presented multisystemic complications (hematologic, renal and pulmonary) by 33%. Table 3 shows the main complications observed by groups and those observed at least once in patients.

Table 3. Complications observed in patients.

| Complications                                      | Patients |
|---------------------------------------------------|----------|
| Compartment syndrome                              | 16       |
| Abscesses                                          | 9        |
| Soft tissue sepsis                                 | 9        |
| Cellulitis                                         | 8        |
| Rhabdomyolysis                                     | 3        |
| Necrosis                                           | 3        |
| Necrosing fascitis                                 | 3        |
| Surgical Site Infection                            | 1        |
| Infectious tenosynovitis                           | 1        |
| Disseminated intravascular coagulation             | 13       |
| Hemolytic anemia                                   | 8        |
| Hematemia                                          | 5        |
| Rectal bleeding                                    | 3        |
| Gynecologic hemorrhage                             | 3        |
| Septic shock                                       | 3        |
| Ischemic stroke                                    | 1        |
| Hypovolemic shock                                  | 1        |
| Thrombocytopenia                                   | 1        |
| Hyperbilirubinemia                                 | 1        |
| Deep vein thrombosis                               | 1        |
| Pulmonary edema                                    | 7        |
| Hypoxemia                                          | 6        |
| Pneumatocele                                       | 3        |
| Pulmonary embolism                                 | 3        |
| Pneumonia                                          | 1        |
| Acute renal failure                                | 8        |
| Emergency dialysis                                 | 5        |
| Proteinuria                                        | 3        |
| Myoglobinuria                                      | 2        |
| Urinary tract infection                             | 1        |
| Acute myocardial infarction                        | 3        |
| Encephalopathy                                     | 2        |

Table 4. Antivenin and side effects presented according to poisoning severity.

| Characteristics | Family | Mild (%) | Moderate (%) | Severe (%) | Total |
|-----------------|--------|----------|--------------|------------|-------|
| Ophidiotoxicosis| Viperidae | 3 (7) | 26 (61) | 12 (28.5) | 41 (97.6) |
| Mortality       | Viperidae | 0 | 1 (2.3) | 0 | 1 (2.3) |
| Antivenin vials | Viperidae | < 4 | 2 (4.6) | 5 (12) | 7 (16.6) |
|                | Viperidae | 5-9 | 1 (2.3) | 13 (31) | 15 (35.7) |
|                | Viperidae | 10-14 | 0 | 5 (12) | 7 (16.6) |
|                | Viperidae | >15 | 3 (7) | 6 (14.2) | 9 (21.5) |
| Antivenin side effects | Viperidae | 5-9 | 1 (2.3) | 1 (2.3) |
| No side effects | Viperidae | 2 (4.6) | 1 (2.3) | 3 (7) |
| Skin rash | Viperidae | 1 (2.3) | 6 (14) | 7 (17) |
| Hives | Viperidae | 1 (2.3) | 4 (10) | 2 (4.6) | 7 (17) |
| Fascication | Viperidae | 1 (2.3) | 4 (10) | 5 (12) |
| Increase of blood pressure readings | Viperidae | 2 (4.6) | 1 (2.3) | 3 (7) |
| Change in the electrocardiogram | Viperidae | 3 (7) | 1 (2.3) | 4 (10) |
| Anaphylactic shock | Viperidae | 4 (10) | 7 (16.6) | 11 (26.5) |
| Antivenin side effects | Elapidae | 1 (2.3) | 1 (2.3) |

Source: Own elaboration based on the data obtained in the study.

Discussion

Results reveal a scenario in which diverse medical, sociocultural and economic factors converge and lead to an outcome. Epidemiological data obtained from the population studied are similar to those found by some researchers in Colombia (7) and those recorded in the national report of ophidian accidents. (11)

Furthermore, similarities with other studies were found regarding cultural practices that are carried out in cases of ophidism, such as tourniquets, plasters, cuts, suction, burns and alcohol and petroleum intake.

With regard to in-hospital care, about 50% of the patients received antivenin in less than 6 hours after the accident, suggesting that the remaining 50% presented with advanced progression of systemic and local effects of the poison upon admission. (8) Based on the type of ophidian accident, management guidelines (5) and the consensus of
the review articles (6), initiating early antivenin administration is highly recommended to reduce vital organ involvement and mortality.

Fibrinogen uptake and coagulation times were found in 30% of the patients treated, as well as patients with moderate and severe classification who did not receive antivenin. According to the recommendation, coagulation and fibrinogen times should be measured on hospital admission, since the latter is the most useful parameter for determining the severity of poisoning by the Viperidae family and the number of initial antivenin vials. (5-7,10)

The most frequent side effect of the drug (antivenin serum) among the entire population was anaphylactic shock with 26.5%, followed by skin rash with 17% and hives in equal proportion. These data coincide with the findings of some researchers when comparing different types of antivenins. (12,13)

Fasciotomy was performed in 70% of the patients; however, this procedure is contraindicated in opifidian accidents due to the absence of a true compartment syndrome and high risk of superinfection. (6,14,15) The most frequent complication in 90% of the patients was local or systemic infection, followed by multisystem failure (50%). Broad spectrum antibiotics were established within the treatment.

Given that current guidelines recommend initiating prophylactic treatment with crystalline penicillin/clindamycin (5) and adjusting antibiotics based on the culture obtained from the affected site (15,16), a comparison of antibiotic management was made against a descriptive study conducted in Hospital Pablo Tobón Uribe (HPTU) of Medellín between 2000 and 2006. (17) Eight HPTU patients who presented with infectious complications were identified out of a total of 52 snake bites; they underwent microbiological isolation of the affected site and prophylactic and in-hospital antibiotic treatment established prior to the culture was observed. This study shows that the most prevalent bacterium in those for whom antibiotic therapy previously indicated was not adequate and also generated resistance was Morganella Morgagni and other Gram-negative bacteria. (17,18)

Additionally, a statistical comparison was made based on hospitals, taking into account the frequency of patients treated with penicillin or clindamycin prior to admission and, at in-hospital level, prior to culture (Table 5). Greater frequency was observed in the use of the recommendation at the HUS, but also greater infectious complications, at hospital level, were found with a statistically significant difference compared to the HPTU.

Table 5. Prophylactic antibiotic treatment used in the Hospital Pablo Tobón Uribe and the Hospital Universitario de La Samaritana Empresa Social del Estado.

| Treatment               | HPTU | HUS  | P  |
|-------------------------|------|------|----|
| Infectious complication | n=52 | n=42 | 0.0|
|                         | 8 (15%) | 38 (90%) |    |
| No previous antibiotic *| n=8  | n=38 | 0.5|
|                         | 4 (50%) | 23 (60%) |    |
| At least previous penicillin * | 3 (37%) | 34 (89%) | 0.0008|
| At least previous clindamycin * | 0 (0%) | 26 (68%) | 0.0|
| At least hospital penicillin *† | 1 (12%) | 17 (44%) | 0.08|
| At least hospital clindamycin *† | 3 (37%) | 17 (44%) | 0.7|

HPTU: Hospital Pablo Tobón Uribe; HUS: Hospital Universitario de La Samaritana Empresa Social del Estado.
* In a patient with an infectious complication.
† Previous to sampling.
Source: Own elaboration based on López et al. (17)

Conclusions
Ophidian accidents continue to be an important cause of morbidity and disability in Colombia; therefore, this is a public health issue with consequences that generate disability and limitations in the economic development of the communities. Training the rural population and health personnel is important to avoid secondary complications due to empirical treatments. (9,19,20)

Information regarding ophidian accidents reported in the 2004-2014 period at the HUS allowed to demonstrate variability in management, classification of severity, use of antivenin, examinations and antibiotic and surgical treatment in patients with respect to management guidelines and studies conducted in comparable hospitals.

Clinical management of poisoning by venomous animals should be personalized. (21) However, medical knowledge is part of a continuous updating process, based on studies with a high level of evidence from specialized centers, which promote the re-evaluation of medical practices within care centers for the sole purpose of reducing disability and mortality in patients.

Conflicts of interest
None stated by the authors.

Funding
None stated by the authors.

Acknowledgements
To Hospital Universitario de La Samaritana Empresa Social del Estado, especially to the team of the HUS Research Center: Cristian Espinosa, Marlene Ordoñez, Luz Marina Achuri and Monica Quemba, and the archive and statistics team: Gloria Bernal.

References
1. Colombia. Instituto Nacional de Salud. Protocolo de Vigilancia en Salud Publica. Accidente Ofidico. Bogotá D.C.: INS; 2014.
2. Organización Mundial de la Salud. Mordeduras de animales. Nueva York: Nota descriptiva No. 373; 2013 [cited 2016 Jul]. Available from: https://goo.gl/bKZ8Dj.
3. Kasturiratne A, Wickremasinghe AR, de Silva N, Gunawardena NK, Pathmeswaran A, Premaaratna R, et al. The global burden of snakes: a literature analysis and modelling based on regional estimates of envenoming and deaths. PLoS Med. 2008;5(11):1591-1604. http://doi.org/b39jmf.
4. León-Nuñez L. Informe Del evento accidente ofídico hasta el periodo epidemiológico V, Colombia, 2016. Bogotá D.C.: Instituto Nacional de Salud; 2016.
5. Ayerbe-González S, Rodríguez-Buitrago JR. Accidentes por animales venenosos y plantas tóxicas. In: Ministerio de la Protección Social. Guías para el manejo de urgencias toxicológicas. Bogotá D.C.: Ministerio de la Protección Social; 2008 [cited 2018 Jan 18]. p. 277-289. Available from: https://goo.gl/n1Ezot.
6. Sarmiento-Acuña K. Aspectos biomédicos del accidente ofídico. Univ. Méd. 2012;53(1):68-85.
7. Otero R, Tobón GS, Gómez LF, Osorio R, Valderrama R, Hoyos D, et al. Accidente ofídico en Antioquia y Chocó. Aspectos clínicos y epidemiológicos (marzo de 1989 - febrero de 1990). Acta Med Colomb. 1992;17(4):229-49.
8. Gil-Alarcón G, Sánchez-Villegas MC, Reynoso VH. Tratamiento prehospitalario del accidente ofídico: revisión, actualización y problemática actual. *Gac Med Mex*. 2011;147:195-208.

9. Rincon-Torres CE. Accidentes ofídicos por Micrurus, Colombia, 2011, una mirada desde la salud pública. Bogotá D.C.: Informe Quincenal Epidemiológico Nacional, Instituto Nacional de Salud; 2012.

10. Perú. Ministerio de Salud. Norma técnica sobre prevención y tratamiento de accidentes por animales ponzosos. Lima: MINSA; 2005.

11. León-Nuñez L. Informe final del evento accidente ofídico, Colombia, año 2014. Bogotá D.C.: Instituto Nacional de Salud; 2014.

12. Otero R, Nuñez V, Barona J, Díaz A, Saldarriaga M. Características bioquímicas y capacidad neutralizante de cuatro antivenenos polivalentes frente a los efectos farmacológicos y enzimáticos del veneno de Bothrops asper y Porthidium nasutum de Antioquia y chocó. *Iatreia*. 2002;15(1):5-15.

13. Vázquez H, Olvera F, Alagón A, Sevcik C. Production of anti-horse antibodies induced by IgG, F(ab’)2 and Fab applied repeatedly to rabbits. Effect on antivenom pharmacokinetics. *Toxicon*. 2013;76:362-9. http://doi.org/f5mwm6.

14. Pineda D, Ghotme K, Aldeco ME, Montoya P. Accidentes ofídicos en Yopal y Leticia, Colombia, 1996-1997. *Biomédica*. 2002;22(1):14-2. http://doi.org/cjhd.

15. Hurtado-Zuluaga OA, Urán-Arboleda JE, Villa-Arango JE. Protocolo de atención prehospitalaria para el manejo integral del accidente ofídico Bothrópico en Colombia [tesis]. Medellín: Universidad CES; 2013.

16. Muñoz-Porras A, Ovares-Arroyo C. Antibioticoterapia profiláctica en el accidente ofídico: evidencia actual. *Revista Médica De Costa Rica y Centroamérica*. 2010;67(593):251-4.

17. López N, Lopera C, Ramírez A. Características de los pacientes con accidente ofídico y complicaciones infecciosas atendidos en el Hospital Pablo Tobón Uribe entre los años 2000 y 2006. *Acta Med Colomb*. 2008;33(3):127-31.

18. Blándón-Marín G. Flora bacteriana asociada a la cavidad bucal en serpientes de la familia Viperidae [tesis]. Manizales: Universidad de Caldas; 2009.

19. Zambrano-Ospina AM. Accidente ofídico como evento de interés en salud pública en Colombia: aportes al diseño de estrategias de gestión [tesis]. Bogotá D.C.: Universidad Nacional de Colombia; 2012.

20. Lynch JD. El contexto de las serpientes de Colombia con un análisis de las amenazas en contra de su conservación. *Rev. Acad. Colomb. Cienc.* 2012;36(140):435-49.

21. Williams D, Gutiérrez JM, Harrison R, Warrell DA, White J, Winkel KD, et al. The Global Snake Bite Initiative: an antidote for snake bite. *Lancet*. 2010;375(9708):89-91.
