SNAKE VENOM POISONING IN THE PLOVDIV REGION FROM 2004 TO 2012

Yanko T. Iliev*, Stoilka G. Tufkova, Marin Y. Zagorov, Stanka M. Nikolova

Clinic of Toxicology, St. George University Hospital, Plovdiv, Bulgaria

INTOXICATION WITH SNAKE VENOM IN THE PLOVDIV REGION FROM 2004 TO 2012

Yanko T. Iliev*, Stoilka G. Tufkova, Marin Y. Zagorov, Stanka M. Nikolova
Clinic of Toxicology, St. George University Hospital, Plovdiv, Bulgaria

ABSTRACT

Introduction: Envenomation by poisons of biological origin is very common globally in the tropical and subtropical areas mainly, where the biological diversity of the species clearly leads to evolution of highly toxic species. The weather warming trend in Bulgaria, whether cyclic or permanent, allows for a change in the biological response of reptiles and insects inhabiting the temperate zone by a possible migration of biological species from the subtropical zone towards the temperate zone because of the new environmental conditions. There are very few studies on snake bite envenoming in Bulgaria. The aim of the study was to find the incidence of the acute accidental intoxication (AAI) caused by snake venom in adult individuals in a large region of Bulgaria between 2004 and 2012 and characterises it by number, type, main clinical features, course and socio-demographic parameters of the victims so that preventive measures can be taken, wherever necessary. Materials and Methods: We studied retrospectively all 68 cases of AAI caused by snake venom in adult individuals (> 18 years old) hospitalized in the Clinic of Toxicology in St. George University Hospital, Plovdiv over the period from 2004 to 2012 by 23 quantitative and qualitative parameters. Results: We found that the average annual incidence of snake venom AAI in adult population in the region of Plovdiv was relatively low for the specified period (9.5 per 100000 residents); the snake venom AAI increases or decreases every other year, with no clearly delineated trend for now. The prevalence of envenomation by poisons of biological origin increased from 2.3% in 1990–1998 to 9.5-10.33% between 2007 and 2012. The main sociodemographic characteristics of snake bite victims are similar to those in other Balkan and Central European countries. The clinical response to poisons of biological origin is generally identical with the response to the viper (Vipera ammodytes) - mild to medium intensity with predominantly local toxic syndrome. Conclusions: The algorithm of Clinical Pathway 293 (CP) is effective and conducive to the reduction of duration of the morbid condition. There are, however, still aspects of it that can be optimised.

Key words: acute accidental envenomation, viper Vipera ammodytes, medical assistance

REZIOME

Введение: Отравления биологическими ядами широко распространены в тропических и субтропических зонах, где биологическое разнообразие видов и их эволюция предполагает селекцию сильно токсических видов. Циклическая или прерывистая тенденция к потеплению в Болгарии дает возможность изменения в биологическом ответе на виды рептилий и насекомых, обитающих умеренную климатическую зону посредством возможной миграции биологических видов в субтропическую к умеренной зоне из-за новых климатических условий. Исследования змеиных отравлений в Болгарии исключительно недостаточны. Цель: Установить и характеризовать острую инъекционную интоксикацию змеиным ядом у взрослых в Болгарии за период 2004 – 2012 г. по числу, виду, основной клинической характеристике, тенденции и социодемографическим показателям пострадавших с целью организации превентивной тактики и мероприятий при необходимости. Материал и методы: Исследованы все 68 зарегистрированных случаев лиц за 18 лет с острой интоксикацией змеинным ядом, госпитализированных в Клинике токсикологии, Университетская больница им. „Св. Георгия”, г. Пловдив. Результаты: Установлено, что острую интоксикацию змеиным ядом показывает сравнительно низкий средний уровень годовой заболеваемости 9.5/100 000 ж.; динамика „нарастание/снижение” в год - без явно очерченной тенденции на настоящем этапе. Наблюдается известное нарастание отравлений биологическими ядами: 1990–1998 г. до 2.3%, 2007–2012 г. до 9.5-10.33%. Основные социодемографические характеристики пострадавших отравлений змеиным ядом схожи с характеристиками в других балканских и среднеевропейских странах. Клинический ответ на впрыснутый биологический яд преимущественно отвечает на яд гадюки - Vipera ammodytes – легкая до средней степени с выраженным локально-токсическим синдромом.

Выводы: Алгоритм КП 293 эффективен и работает для снижения продолжительности болезненного процесса, однако, не надо забывать, что в целях его оптимизации, имеются возможности.

Ключевые слова: остroe инъекционное отравление, гадюка Vipera ammodytes, медицинская помощь
INTRODUCTION

Envenomation by poisons of biological origin is very common globally in the tropical and subtropical areas in which highly poisonous species can easily evolve because of the great biological diversity of the species in these regions.

A change in the climate has been recently apparent. The weather warming trend in Bulgaria, whether cyclic or permanent, enables the reptiles and insects inhabiting the temperate climatic zone to change their biological response. A hypothesis of a possible migration of biological species from the subtropical zone to the temperate zone due to the new climatic conditions can lend support to this change. There is every likelihood that the herpetology applicable to the Central Southern region of Bulgaria has now changed and needs to be more extensively studied. Unfortunately, the studies on snake bite envenomation in Bulgaria are exceptionally few.

AIM

We aimed at finding and characterizing the snake venom-induced acute accidental intoxication (AAI) in adult individuals in the Plovdiv region for the period from 2004 to 2012 by number, type, main clinical features, course and socio-demographic parameters of the victims so that the proper preventive measures can be taken, wherever necessary.

MATERIALS AND METHODS

We included in the study all 68 cases of adult individuals (more than 18 years old) that suffered acute intoxications caused by snake venom and were hospitalized for treatment in the Clinic of Toxicology in St. George University Hospital, Plovdiv between 2004 and 2012.

A total of 23 quantitative and qualitative features were investigated. These include number and dynamics of envenomation, sex, age, place of residence, habitat, month of occurrence, time of the envenomation, time of hospital admission, bite site, local features - pain, edema, degree of the edema, puncture hole and characterization, erythema, necrosis, lymphadenitis, general toxic syndrome, therapeutic sequence, duration of illness and outcome.

The study is retrospective and is extensive investigation of the cases registered in the largest Bulgarian University Hospital, St. George Hospital, Plovdiv. Descriptive statistics, graphical and alternative analysis were used in the statistical analysis of the results.

RESULTS

DYNAMICS AND SOCIODEMOGRAPHIC CHARACTERISTICS

Between 2004 and 2012, a total of 68 cases of reptile bites with varying degrees of toxic viperine syndrome manifestation were registered for medical assistance in the Plovdiv region. As evident in Fig. 1, the number of envenomation cases varied during the studied period with a tendency of increase every other year.

The average incidence for the period from 2004 to 2012 is 9.65/100 000 inhabitants (based on the average annual number of inhabitants older than 18 years as quoted by the archive and yearbook of the Regional Health Center)

Age and sex

The mean age of the victims was 50.50 ± 18.9 years. The men were 32 (47.1%) and the women - 36 (52.9%). The mean age of men was 44.34 ± 3.63 years (mean ± SEM), and the mean age of women was 55.97 ± 2.61 years, and the difference is not statistically significant (p >0.05). The age range of the victims was 17 to 81 years for both men and women.

Place of residence

By place of residence the victims were distributed as follows – residents of Plovdiv - 25 (36.8%), residents of another town in the region - 17 (25.0 %) and residents in a village - 26 (38.2 %).

Month

Acute envenomation cases were registered at intervals of 9/12 months, from March to October inclusive – 1 in March (1.5 %), 4 in April (5.9%), 10 in May (14.9%), 27 in June (39.7%), 13 in July (19.1%), 8 in August (11.8%), 2 in September (2.9%) and 3 in October (4.4%). The greatest number of toxic accidents occurred during the summer months, especially in July with usually warm weather, but it also coincided with a period of intensive biological activity of the viper (Vipera ammodytes).

Time of bite occurrence

Bites and toxic reactions were registered in the daytime, from 6:00 a.m. to 8:00 p.m., with isolated cases registered in the early and the late hours of the day. The greatest number of bites occurred at 10:00 a.m. - 7 (10.4%), 12:00 - 7 (10.4%), 2:00 p.m. - 7 (10.4%) and 5:00 p.m. - 9 (13.4%). It is noteworthy that during the dark part of the day, between 9:00 p.m. and 11:00 p.m., there were 6 (9%) toxic bites with no peculiar features in the clinical course.
CLINICAL MANIFESTATIONS

Bite site - the lower limbs were affected in 37 (54.4%) victims and the upper limbs - in 31 (45.6%) victims. The bites in the right limbs predominated - 44 (64.7%) cases of right limbs affected versus 24 (45.6%) people bitten in the left limbs, most probably because of the predominance of people using their right hands for agricultural work (t = 2.33; p < 0.05). No other location of the bites was registered.

The local toxic syndrome is manifested by edema, erythema, pain, regional lymphadenitis and local necrosis (Table 1).

Local edema: it occurred in 56.1% of the cases; reaching an area as big as 1% of the body surface (the area of the palm), it is one of the most prominent signs of intoxication. About 10.3% of the hospitalized patients had no edema, either because they were admitted to hospital very soon after the accident or because they sustained only a “dry bite”. The pronounced form of toxic edema was rare (1.5%).

Local inflammatory erythema: it was found in 63.6% of the victims, 36.4% of the patients having no local erythema.

The envenomation was accompanied by mild subjective pain in 87.5% of the victims, and 7.8% of the hospitalized patients defined the pain as “severe”.

Regional lymphadenitis was found in 17.6% of the victims, and local necrosis was detected only in 1 patient (1.5%).

Visible double puncture marks on the skin were found in 82.4% of the patients, while in the remaining 17.6% of the patients the bite site was not conclusively established .

The general toxic manifestations were rare and mild in intensity. There were no significant abnormalities in the laboratory tests performed in accordance with requirement in the Clinical Pathway 293.

Secondary infection was prevented with antibiotics and it did not develop actively, and accordingly was not registered.

MEDICAL HELP

Hospitalization

Analysing the time of hospital admission, we found that there were significant delays of treatment from 30 to 630 minutes after the actual time of sustaining the bite. The average time of providing medical aid in a hospital, which in most cases was the first medical aid, was 136.12±13.68 minutes, which is more than 2 hours after the actual accident!

About 28% of the victims were hospitalized within two hours, and 66% were hospitalized by the third hour. One fifth (21%) of the patients, however, received medical aid relatively late, as late as 5-6 hours after the bite had occurred.

Treatment

All patients received treatment in accordance with the algorithm of CP 293, including injection of
antiserum to snake venom, Bul Bio 100 AE, for intramuscular administration; only one patient was given a double dose of it, because of the more severe clinical manifestations of envenomation in him - a combination of manifested local and general clinical syndromes.

**Duration of hospital stay**

Most of the patients were treated for 2 days - 48 (73.5%). Three patients (4%) were treated for 4 and 5 days, and two of the patients (3%) had an overnight stay after which they left the hospital at their own will. Most patients, however, wanted to be discharged earlier than recommended due to their good general status and the local toxic process well under control.

**Outcome**

Most of the patients, 65 (94%), were discharged healthy or in an improved condition, and 3 patients (6%) left hospital at their own will with pronounced local toxic manifestations. None of the patients had a fatal outcome.

**DISCUSSION**

Acute exogenous poisonings caused by snake venom in the countries of the temperate zone in Europe do not present a major toxicological problem, and yet they keep stirring up a natural biological and medical interest. The climate changes that are quite apparent lately, whether they are permanent or cyclical, may bring about a change in the biodiversity of reptiles and insects when these species start searching for food and suitable habitats.

Studying the epidemiology and the clinical characteristics of a series of cases of accidental snake venom poisoning can help prepare an adequate medical response to any new cases; moreover, in most of the cases it is impossible to identify correctly what kind of snake is responsible for the envenomation relying only on the morphological characteristics.

The clinical studies of M. Dobrev (1931), Iv. Buresh (1934), N. Karalambev (1938), K. Sultanov, L. Tsvetkov, M. Popov (1963) and Al. Monov (1967) and the biological data provided by prominent Bulgarian herpetologists are well-known in the Bulgarian medical literature of the 20th century. In the last two years, other Bulgarian scientists working in the field of toxicology have published interesting reports.

Bulgaria is well known in Europe with its rich herpetofauna (snakes including) because of its favourable geographical location and climate diversity. There are 17 species of snakes in Bulgaria. Only 6 of them are poisonous - the viper, the adder, the meadow viper, the asp viper, the European cat snake and the Montpellier snake. Their biological characteristics have been extensively studied and their range of habitation is known. There are, however, very few medically significant reports of acute envenomation caused by these species of snakes.

In the past 8-9 years, however, the proportion of AAI in the Plovdiv region caused by biological poison has increased from 2.3% in 1990-1998, to 9.5 - 10.33% during the period from 2007 to 2011. In our study, we found that the average number of cases of envenomation in adults per year is 7 per year, in contrast to the small number of envenomation (3-4 cases per year) reported in a recent study by Hungarian researchers. Our results are similar to those of Polish researchers (5-6 bites per year) reported for the period from 1999 to 2003 in Silesia, Poland.

Figure 1 clearly shows that AAI increases in the specified period every other year without setting any clear trend for now. Since AAI is dependent on the size and type of snake population and on behaviour of the susceptible population, we cannot provide currently any scientifically substantiated answer that can reasonably account for the observed fluctuation in the number of cases of envenomation. Anthropogenic interference cannot explain this finding as it did in the 90s of the last century when an intensive hunt for snakes took place because of the high price set for snake venom at the time. There have been no significant ecological processes in the Plovdiv region, such as floods, big fires, toxicological disasters, that may have disrupted the ecological balance in the region.

Our findings are consistent with those reported by Croatian researchers in a study of 542 snake-bite envenomation cases over a period of 21 years by age range, predominance of adult population, place of residence, lesion area and a causing snake (viper). But the average incidence of venomous snakebite in southern Croatia, as reported in the study, is twice as low (5.2/100 000) as the one we found in our study even with the inclusion in the study of cases of envenomation in children.

Unlike the findings in our study, researchers found a significant difference in the prevalence of male victims in Bosnia and Herzegovina between 1997 and 2002 and in the northern Dalmatia.
region of the Republic of Croatia.12

Most of the studies conducted by authors in the Balkans have reported of a characteristic clinical response to the snake venom of two snakes indigenous for the region, the viper (Vipera ammodytes) and the adder (Vipera berus), and especially its Bosnian subspecies - Vipera berus bosniensis, by area of habitation. These studies also report a combination of local toxic and general toxic manifestations, with prevalence of the local, mild-to-severe and severe cases of envenomation which are relatively rare, just as rare as the fatal outcome of the snakebites.10,12,13

In contrast to the studies of other Balkan regions, a prevalent manifestation of a mild clinical form of intoxication was found in our study, manifested by the local toxic features of edema, erythema, pain, haemorrhage, lymphangitis and regional lymphadenitis. Local necrosis was identified only in one patient who sustained a snakebite administering a large amount of venom and who was provided a late medical aid. The general toxic manifestations were mild and transient, probably due to the timely medical aid. Hospital stay was short - 2 days for 73.5% of the patients.

Medical aid, both as outpatients and as inpatients, is provided relatively early for most of the victims.

It is noteworthy that the treatment was carried out in accordance with the algorithm of CP 293, with administration of antiserum early in the course of treatment, even during the outpatient stage and before hospitalization, and in some cases the bite was ignored, especially if it happened to be a dry bite; the administration of antiserum in cases with relative indications is similar to the condition described by Luksić B et al. involving medical assistance in the Republic of Croatia, for a more remote period of time; it differs considerably in frequency and range from the report from the region of Prague, the Czech Republic at the end of the 20th century, when antiserum was administered only in extremely severe cases of systemic and local toxic manifestations.14

We found no cases of allergic manifestations resulting from the injecting of the snake venom antiserum. Most patients were not monitored for signs of serum sickness since they were left the hospital at their own will.

CONCLUSIONS

The acute accidental intoxications caused by snake venom in adults in the Plovdiv region for the period from 2004 to 2012 have a relatively low average incidence (9.5/100000 inhabitants); it increases and decreases every other year with no clearly delineated trend for now. The proportion of envenomation with poisons of biological origin increased from 2.3% in 1990-1998 to 9.5-10.33% in the period between 2007 and 2011.

The main sociodemographic characteristics of the snake venom poisoning victims are similar to those in other Balkan and Central European countries.

The clinical response to the injected poison of biological origin predominantly corresponds to that of the viper (Vipera ammodytes) – from light to mild-to-severe clinical degree with a clearly manifested local toxic syndrome.

Medical treatment is provided mostly in time. Administration of the specific antiserum of Bul Bio 100 AE is widely practiced at both the outpatient stage and during hospital treatment. It can be assumed that this practice is of great importance for the milder course of intoxication, if there are no adverse side effects, in spite of the fact that it makes the treatment rather expensive. The algorithm of Clinical Pathway 293 (CP) is effective in reducing the duration of the morbid condition. But it can be still further optimized.

REFERENCES