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SNAKEBITE POISONING: Advances in treatment, Vaccination, and Management Strategies

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Abstract: *So, roughly 15% of the 3000 snake species discovered globally are thought to be harmful to humans. The eastern and western diamondback rattlesnakes cause the most fatalities. Snake poisoning deaths are more common in youngsters, the elderly, and those to whom antivenom is not supplied or is administered late or in insufficient quantities. Snake poisoning kills mostly young individuals between the ages of 17 and 27. Snakebites envenoming is mostly an occupational condition that can result in death or severe disability. The treatment is based on both the patient's history and a syndromic approach. The treatment should be provided rapidly and affordably to all citizens of the particular country. Snakes have both dry and moist bites. Dry bites do not produce envenoming symptoms. In such a situation, many people noticed it as a miraculous solution that suggested the bite from the offending snake species was quite innocuous. The diagnosis for such bites is also not noted in the literature, which may cause difficulty while treating the sufferer with antivenom. Because humans are too huge to be considered food for even the largest dangerous snakes, snakes may not always deliver venom when they bite, instead saving this metabolically costly weapon for predation. These dry bites appear as bites from non-venomous snakes, which exhibit comparable symptoms. To aid with this, a greater awareness of both the snake-related and human-related aspects involved in both wet and dry snakebites is essential. Snake venom poisoning is a complex medical emergency that not only involves the site of bite but also multiple organ failure; hence, contacting a physician who is qualified in the diagnosis and treatment of venomous snake bites is vital.*

Keywords: *antivenom, clinical management, diagnosis, polyvalent, monovalent, 3Rs*

I. INTRODUCTION

Every year, people die as an outcome of a neglected disease that causes a significant cost of mortality, ultimately surpassing 1,25,000 deaths per year globally. Whereas the number of people suffering permanent sequelae may be around 400,000 and disability adjusted life years might add up to over 6 million. Carpet vipers, Russell's vipers, Malayan and Lance-head pit vipers, rattle snakes, puff adders, cobras, mambas, krait, and Taipan belong to the most important species participating worldwide. These snakes' venom contain hemotoxins, neurotoxins, which are, cytotoxins, and mytotoxins. Swelling, vomiting, necrosis of the affected body part, rhabdomyolysis, local bleeding, systemic hemorrhage, coagulation issues, anemia, shock, and paralysis are the clinical signs of a snake bite. Death occurs when it is left untreated or poorly managed. Despite the enormous burden of envenomation by snakebite on victims, it is still neglected because the therapy isn't mentioned in the literature, and little attempt has been made to develop better treatments and diagnostics.

The most popular treatment for snake envenomation is antivenom with other auxiliary methods of therapy. Monovalent antivenom can be used when the species of the offending snake is known, however polyvalent antivenom can be used when the snake species is unknown. In fact, several methods for determining the species of the biting snake. Snake identification is most frequently performed with a description of the snake if observed, a physical examination of the snake if killed and provided by patients, or through identification of typical clinical symptoms. However, the ability of polyvalent antivenom to neutralize a variety of venom may be at the expense of decreased efficiency because the relative proportion of antibodies in a polyvalent antivenom that targets toxins of a specific snake venom is usually not equal to the proportion of antibodies in a monovalent antivenom targeting the same venom poison. As a result, the polyvalent antivenom needs to be a higher dose than the monovalent antivenom. It is crucial to keep in mind that raising the dosage of this antivenom can increase the cost of medication as well as the probability of developing antivenom-related adverse responses. Based on the studies, polyvalent antivenom is being used in many regions due to the shortage of monovalent antivenom or the difficulty in choosing which monovalent antivenom to administer without knowing the snake species

II. REVIEW OF LITERATURE

- 1) As previously mentioned, a basic diagnosis of snakebite envenoming requires a detailed patient history, targeted examination, and appropriate laboratory testing. Snakebite diagnosis varies by place and continent. Because species vary by continent, corresponding to their symptoms. Australians utilize diagnostic algorithms to help physicians recognize the species of serpent. Based on this, the victim is directed to have treatment and testing. The snake venom detection kit (SVDK) is an extensively used immunoassay kit. Additionally, monovalent antivenoms are utilized. Further, there are five various kinds of terrestrial monovalent and polyvalent antivenom which are effective against five specific snake groups. On the other hand, envenomation for snakebite is performed differently in Asia. Since venomous snakes range greatly both within and across species. In Southeast Asia, syndromic diagnostic methods as well as algorithms are available. To the benefit of clinical practice, systemic signs of poisoning are also recognized. The National Snakebite Management Guidelines serve as the basis for some of the inquiries. The National Snakebite Management Guidelines act as the basis for some of the inquiries. In India, one may discover both monovalent and polyvalent antivenoms. Although they lack any native snake species that are different from those found in the US and other countries, Canadians use algorithms. whereas, US clinicians perform a comparison investigation in which they detect snakes utilizing the information provided and treat snakebite envenomation using polyvalent antivenom. Additionally, it has been recorded that "the risk of acute kidney injury, acute renal failure, and the overall severity of poisoning in the snakebite victim rises if treatment is prolonged." Additionally, it indicates that those who experienced acute renal failure required more antivenom and spent more time in the hospital than those who did not. Treatment delays frequently have an adverse effect on the patient's outcome. The diagnostics include a range of techniques, including forensic genetics, enzymatic activity testing, and immunoassay (ELISA). Different techniques are used in each nation to diagnose snake envenomation^[1].
- 2) A key stage in the clinical presentation of envenomation is the positive identification of snakes. Here, symptoms such nausea, vomiting, diarrhea, clammy skin, etc. are the main focus. In 1954, Wyeth, Polyvalent (ACP), and antivenom (Crotalidae) became available in the US to treat snakebite. A brand-new antivenom called Crotalidae Polyvalent Immune Fab (Ovine) (FabAV) has just been released. The signs and symptoms of intoxication should vary depending on the kind of snake. Therefore, the course of treatment for snakebite toxicity varies. Opioid analgesics should be avoided if the snakebite has been recognized and is known to include neurotoxic components. 4-6 vials of FabAV should be administered within an hour if compartment pressure is increased, as compartment syndrome is typically encountered in rattlesnake bites. To release the venom components and lower the compartment pressure, more antivenoms are added. In certain regions of the United States, fasciotomy is utilized; however, it does not stop the progression of envenomation or treat coagulopathy or further antivenom^[2].
- 3) Conventional antivenom, which is based on animal polyclonal antibodies and aids in therapy, is administered in addition to medical and surgical care. Although antivenoms save many lives, they also have certain drawbacks, such as their limited potency. Human monoclonal antivenom, a recent addition to the antivenom family, has a stronger neutralizing effect and is less immunogenic. Different snakes and species may experience unusual presentation, long-term consequences, and chronic problems. Following the recommended clinical manifestation protocols following discharge is crucial. It aids in the advancement of new diagnostics and technologies that are safe and effective for small molecule therapeutics and monoclonal antibody-based treatments^[3].
- 4) The pathophysiological profile of snake venom makes it simple to assess how well other harmful actions are neutralized. The 3Rs (Replacement, Reduction, and Refinement) idea is developed to satisfy this requirement. Antivenomics, the study of antivenoms' immunological response against venom, was created and is assessed using mass spectrometry. Before embracing the new antivenom, thorough preclinical testing should be conducted^[4].
- 5) A study carried out at Kottayam Medical College, which has a population of roughly 6 million, looked at the clinical features, demographic information, degree of envenomation, risk of complications, and factors influencing the outcome and subsequent treatment of patients who were admitted to the emergency room with snakebite between May 2005 and December 2006. Complications and envenomation symptoms were documented. Polyvalent snakebite antivenom (SAV) was the antivenom employed in the treatment. In order to identify the variables influencing problems and results in connection to the scheduling of SAV, treated patients were examined. Complications are less likely to occur when SAV is administered early. Adverse outcomes can be predicted by the presence of severe coagulopathy and leucocytosis^[5].
- 6) By 2030, the World Health Organization aims to reduce the rate of snake envenomation globally. Several online databases were searched, Express was contacted, and the bibliography was checked in order to create a summary of the systematic reviews (SR). Screening, evaluation of quality, and data excretion were completed. The need to fund high-quality SRs, evidence gaps, and core outcomes sets that can shape guidelines recommendations and funding priorities for conducting future trials were all

- identified by the study of these articles. Many species have different venom compositions, which means that specific randomized controlled trials and SRs on various SAV and their dosage regimens must be conducted in a region, country, or state^[6].
- 7) Modern biotechnologies would be applied in the development of the new therapeutic agents with the combination of different neutralizing capacities and pharmacokinetic profiles. Monoclonal antibodies and its fragments stand out as the most used types of versatile molecular scaffolds that possess these attributes^[7].
 - 8) Since snakebite causes death and illness, the venom of several snake species identified in the Cukurova area of Turkey produced significant systemic and local tissue damage. According to a study, patients with lethal injuries in that area received effective therapy with low-dose antivenom^[8].
 - 9) The mortality of the snakebite is considered to be one-tenth that of malaria and it is said no equivalent global snakebite control program exists. There is an urgent need to gain knowledge of the epidemiology of snakebite envenomation around the world^[9].
 - 10) There is a lack of evidence to base clinical management of neurotoxic snakebite envenoming, mainly in making a right choice of initial antivenom dosage. In the early trial it was noticed that antivenom dosage used for neurotoxic snakebite envenoming was poorly effective. Development of new and more effective antivenoms was the better option to save the lives of the rest of the neurotoxic snakebite envenoming patients^[10].

III. GROUP DISCUSSION

Because of the unknown species and degree of toxicity, it is challenging to determine the precise course of treatment for snakebite poisoning, and the clinical care of snake envenomation is somewhat drawn out. Medication will be delayed in cases of late-night snakebite or when the victim is unable to identify the snake, among many other situations. Accordingly, the WHO guidelines for antivenom place a lot of emphasis on the development and quality of antivenom, and a number of groups are interested in implementing the 3Rs (Replacement, Reduction, and Refinement) concept. This will replace a lot of immunochemical methods and in vitro functional methods that would correlate with in vivo toxic activities, like clotting tests and neuromuscular preparation, among others. Less damage to the animals employed to test the antivenom's accuracy and to review and assess the trial designs. Following treatment, it is essential to conduct a follow-up because, after receiving treatment, victims are sometimes neglected. The goal of the evaluation and care that follows should be to prepare the muscles and joints of that specific snakebite area. Counseling sessions should be held in order to help those victims prevent future mental stress and trauma.

IV. CONCLUSION

Since there are limited chances that the person will be puzzled and startled in that specific situation, it is not impossible to obtain the snake and then cure them based on the snake, as was previously described. Although polyvalent antivenoms are the most common, they might not work in all situations. The development of novel techniques for detecting the clinical signs of snake envenomation is crucial for increased safety, effectiveness, and affordability. New therapeutic compounds with various neutralizing powers could be developed with the aid of biotechnological techniques. This makes it possible to create novel antivenom varieties that are safe, guaranteed to be of high quality, and reasonably priced. Assays, which are preclinical studies designed to determine venom activities that are crucial to the pathophysiology of various envenomings, must be carried out to determine cardiovascular and renal toxicity.

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