



THE ART OF ANTI-SNAKE VENOM ADMINISTRATION IN SNAKEBITE GRADE III FOLLOWING VIPER SNAKEBITE IN DEVELOPING COUNTRY: A CASE REPORT

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ABSTRACT

Snakebite remains a prior Neglected Tropical Disease in the World, especially in South-East Asia. There were many diversities in the management of snake bites based on the different levels of clinician experience. Anti-snake venom remains the mainstay treatment in venomous snakebites, meanwhile, the distribution of anti-snake venom is very sparse. Snakebite is time-limited and could be a life-threatening event. This case report described a delayed anti-snake venom administration in snakebite grade III following a viper snake bite. Tight observation including clinical manifestation and laboratory tests is the foremost thing to do in managing snakebite, due to its unpredictable clinical manifestation. Anti-snake venom dosage must be decided based on the progress of clinical manifestation and laboratory results.

Keywords: *Antivenom, Case report, Hematotoxin, Snakebite, Viper snake*

INTRODUCTION

Snake bite cases remain a global public health issue with an estimated 2.7 million cases and 81.000-138.000 deaths each year attributed to snake bite.¹⁻³ Indonesia is one of the largest tropical countries and the majority of its society works in agricultural fields, which leads Indonesia to have a particularly high burden of snakebite cases. Snakebite cases are one of the neglected tropical diseases (NTD) in Indonesia because of little attention from the government and public health community despite its high incidence. Until now, there are no updated national epidemiology reports, a lack of national policy to manage and prevent snakebites.⁴

Anti-snake venom (ASV) administration is one of the main priorities in treating venomous snakebite cases.^{2,5} It is a lifesaving drug that should be universally accessible.⁵ There were many socio-cultural misbeliefs, that made patients prefer to seek help from the traditional health worker.^{6,7} They would come to the hospital if the signs and symptoms got worse, which was already late. Longer duration between the snakebite envenomation and antivenom treatment contributed to higher mortality incidence.⁷

Since years ago, clinicians have been facing difficulty in considering the dosage and kind (monovalent/polyvalent) of ASV. Inadequate dosage or giving the wrong specific kind of antivenom to a different species would lead to a fatal outcome.⁸ Different clinicians' levels of experience made the management of snakebite quite distinct between

hospitals.^{6,9} Therefore, we describe a case report of snake bite grade III with spontaneous bleeding and delayed ASV administration in a developing country with a limited source of ASV. The highlight of this case report is the art and consideration when giving ASV to snakebite cases.

CASE REPORT

A 68-year-old man was brought to the emergency room (ER) in a tertiary referral Hospital in Gresik City after getting bitten by a snake on his left hand more than 24 hours ago. He came with a chief complaint of pain and progressive swelling on his left arm. He also complained that he felt pain in his stomach, nausea vomiting more than 5 times, and headache this morning. He described the snake as a green-small-red tail snake with a triangle head. His vital signs were stable with blood pressure of 125/97 mmHg, heart rate of 101 beats per minute, respiratory rate 18 times per minute, and body temperature of 36,8°C.

On the physical examination, we found there was a diffuse pitting edema on his left upper extremity expanded to anterior truncus, hyperemia, multiple vesicles on his forearm, and ecchymosis on his flank. From laboratory results, hemoglobin levels were 21.2g/dl, MCV 62.9, white blood cells 31.600/uL, thrombocyte level 186.000/uL, urea/serum creatinine 60.1/1.1, potassium ion 5.23, international normalized ratio (INR) 1.7 seconds, activated partial prothrombin time (aPTT) 47.2 seconds, and prothrombin time (PT) 18.3 sec. Electrocardiography and chest X-ray were

Hapsari Kinanti, Agung Kusumanegara

normal. This patient had no history of chronic disease and, he is a heavy smoker. This patient was diagnosed with snake bite grade III due to green pit viper snakebite.

This patient then rehydrated in the ER with intravenous ringer lactate solution 500cc in one hour then maintenance with intravenous Futrolit 1000cc/24 hours, immobilization of his upper left extremity, injection of two vials of ASV diluted in 100cc normal saline in the first day, injection of ampicillin sulbactam 1,5 gram three times a day, injection of tranexamic acid 500mg twice a day, and symptomatic pharmacology of analgesic and proton pump inhibitor. The second day after intravenous ASV was given this patient felt better, there were no headaches, stomachache, nausea, and vomiting. The edema and ecchymosis were not expanded, and the pain was reduced. This patient achieved a total of 10 dosages of ASV, two vials on the first until the third day, 1 vial on the fourth day, and 3 vials on the fifth day. This patient showed no complications or side effects after antivenom administration.

Laboratory test evaluation was performed almost every day on this patient to observe the patient's progress (table 1). White blood cell level was significantly reduced on the second day after the broad-spectrum antibiotic was given and achieved a normal level on the fourth day. Hemoconcentration and hyperkalemia were also significantly reduced in the second day. On the fourth day after admission, his renal function test was back to normal; this patient never had oliguria. INR, APTT, and PT on the fourth day didn't achieve normal levels but there was an improvement. This patient also had a thrombotic microangiopathy on day fourth, marked with reduced thrombotic level until 75.000/uL and hemoglobin level to 10.3g/dL. His thrombotic level progressed to normal the next day so this patient didn't have to undergo platelet concentrate transfusion. This patient was then discharged on the sixth day. Further, follow-up one week after discharge this patient came with no significant clinical manifestation of envenomation and there were no disfigurements in the local site.

Table 1. Laboratory results and monitoring

Value	Day 1	Day 2	Day 4	Day 5
Hb (g/dL)	21.2	14.8	10.3	9.9
PCV (%)	62.9	43.2	32	31
WBC (10 ³ /mm ³)	31.6	20.9	8.3	8.2
PLT (10 ³ /mm ³)	186	122	75	139
BUN/SK (mg/dL)	60.1/1.2	-	18.5/1.12	-
K (mEq/L)	5.23	4.8	3.9	-
INR	1.7	-	1.16	-
APTT/PTT (seconds)	47.2/18.3	-	44.8/17.5	-



Figure 1. Patient clinical appearance when first administered to the emergency ward. Fang mark on left dorsum manus (arrow).

DISCUSSION

Snakebite remains one of the highest-priority neglected tropical diseases listed by the World Health Organization (WHO)³. Southeast Asian Nations (ASEAN) countries have the highest incidence of snake bites among other tropical countries.^{3,5,9} Snakebite epidemiology is expected to be underestimated because there were many unreported cases.^{2,8,9,10} Many cases chose to seek traditional health workers rather than go to the hospital.⁸



Hapsari Kinanti, Agung Kusumanegara

Delayed access to ASV is detrimental to patients' outcomes.^{3,5,8,10,11} Longer duration would lead to worse outcomes.¹⁰ Early intervention within 4 hours of envenomation along with higher doses of ASV offer more favorable patient outcomes. However, ASV can be given within 24 hours of envenomation and still provide beneficial effects.^{2,3} This patient had poor treatment-seeking behavior, he came to the ER more than 24 hours after the incident. There was already progressive edema in more than one extremity, systemic signs (vomiting, nausea, and headache), spontaneous subcutaneous bleeding, pre-renal acute kidney injury due to plasma leakage, and prolonged coagulopathy. This patient was managed in the hospital for 6 days. It was longer than other snake bite cases. In our experience, patients with snake bites with good health-seeking behavior only managed for two to three days in the hospital. Lack of health education, social misbelief, and unsupervised traditional medication practice were the reasons behind delayed snakebite management and leading to poor outcomes.¹¹

Based on the signs and symptoms this patient had a hematotoxin effect due to green pit viper snakebite. Hematological abnormalities are the most common effects of snake envenoming globally and contribute to morbidity and mortality.^{1,12} Venom-induced consumption coagulopathy (VICC) is the most common and most important clinical manifestation of hematological abnormalities followed by thrombotic microangiopathy (TMA). VICC could induce spontaneous hemorrhage which could be life-threatening. VICC is described as all types of coagulopathy due to snakebite toxic enzyme, worse in snake venoms that also contain metalloproteinases.^{1,12,13} VICC typically precedes the development of TMA features.¹

Viper snake species are known to be one of the main causes of haematotoxin envenoming.¹² Pit viper is the most common snake species that causes envenoming in Indonesia.⁹ The mainstay therapy for VICC was ASV administration.^{12,13} ASV is highly efficacious in binding venom and neutralizing toxic effects, known to improve recovery in viper species.^{4,8,12} ASV is not risk-free, adverse reactions can be quite common and potentially harmful.¹³ ASV administration should only be given in consideration that the benefit is more than the risk of adverse reaction.

The choice and dosage of ASV is one of the factors influencing the outcome.⁸ Indonesia only has one kind of ASV, which is Biosave. This ASV can cover 3 important species of snake in Indonesia; *Calloselasma rhodostoma*, *Bungarus fasciatus*, and *Naja sputatrix*.⁴ In this case, we believed that the species of snake that was responsible for the bite was the green pit viper based on the patient's description and geographical distribution. Pit viper has a para-specific neutralization with *Calloselasma rhodostoma*, they come from one family of venomous snakes. Because of that, giving ASV is considered to be useful in this case. Indonesia's antivenom is fully covered by national health insurance but the quantities considered are not enough and are limited only in selected urban hospitals.⁵ Great decision-making and monitoring by clinicians are needed to determine the dosage of ASV to improve patient condition.

Our hospital is one of the selected urban hospitals that could provide ASV administration. The dosage of ASV administration is still widely variable between guidelines. Proper initial dosing is critical for a poisonous snakebite's clinical course.⁷ WHO South-East Asia recommended giving an initial dosage of antivenom based on the species of the snake and the clinical severity. For green pit vipers, the recommended initial dosage is 30-50ml.⁸ In practice, the choice of initial dose of antivenom is usually empirical and based on national guidelines.⁸ Meanwhile, in Indonesia, there was no standardized guideline on ASV administration.

The ideal way to estimate the appropriate dose of antivenom is to know the amount of venom injected by the snake which is impossible.^{8,14} Another guideline recommended the usage of the traditional snakebite severity scale (TSSS) based on the severity of symptoms at presentation. However, it is very difficult to predict the expansion of localized and symptomatic symptoms. TSSS with grade 0 no ASV suggested, for grades 1 and 2 one vial of ASV is recommended, for grade 3 two vials are recommended, for grade 4 three vials are recommended. There 33.6% of patients required additional doses when given the initial dose based on TSSS.¹⁴ An additional dose of ASV should be given as many times as needed until control of envenomation is achieved.⁸

Monitoring and evaluation hold important value in managing snakebite. Snakebite treatment should



Hapsari Kinanti, Agung Kusumanegara

always be determined by the patient clinical presentation and evolution of sign and symptoms.¹⁵ Knowing the species of the snake will help the clinician predict the effect of envenomation. In this case, the predicted snake species was a haematotoxin envenoming effect. Therefore, the clinical parameters that needs to be serially monitored are evidence of bleeding (skin, mucous membrane, conjunctiva, gums, and nose), local envenoming (pain, swelling progression, and lymph nodes enlargement), and laboratory test results to monitor coagulopathy condition (reducing platelet count, prolonged PT and aPTT, INR).¹⁶ Laboratory tests should be performed every day including complete blood count, renal function test, aPTT, and PT.^{8,16} In this patient, we didn't perform all the laboratory tests every day because of financial considerations. This patient didn't show any expanded spontaneous bleeding, edema, oliguria, or other systemic signs. The clinical appearance was improved. The WHO stated that bleeding and clotting disturbance after snake envenomation usually respond satisfactorily to specific ASV.⁸ We administered 2 vials of ASV from day 1 to day 3 while monitoring the patient's clinical course and laboratory results showed progressive improvement. Therefore, we reduce the dosage of ASV administration on day four to 1 vial of ASV. But then, the laboratory result shows that the patient tends to have thrombolytic microangiopathy with normal renal function test without oliguria. We decided to give an extra dose of ASV, in the meantime, we prepared for platelet thrombin transfusion in case the thrombocyte level didn't increase. On the fifth day, this patient's thrombocyte level increased, and no decreased clinical course. Then this patient could be discharged the next day.

Even though there are already many guidelines published in the management of snakebites, the implementation is quite hard, especially in rural areas.⁴ In a rural area where there was no antivenom available, the treatment was supportive and symptomatic.⁸ Based on our experiences when facing snakebites in rural areas with indication of ASV administration, immediately give the initial dose that is available, we don't have to target the quantities of ASV given because there are many limitations in ASV availability especially in rural areas of Indonesia. If there were no ASV resources in the area then conservative management should be

done by monitoring the clinical aspect and laboratory test and supportive treatment. A case series in Nepal describes the successful conservative treatment of 15 cases of pit viper snakebite in Nepal, but the length of hospital stay is longer.¹⁷

CONCLUSION

Snakebite remains a high-priority NTD, with many unreported and late administrations of ASV that lead to worse outcomes due to sociocultural misbelieve. Increasing social awareness is important to upgrade health-seeking behavior rather than visiting traditional health workers. Giving ASV is an art, whether there are already many guidelines about antivenom administration, in clinical practice, the the most important thing in ASV administration is not the target of ASV given but always monitoring the patient's clinical condition and laboratory results.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

FUNDING

No specific funding was provided for this article

AUTHOR CONTRIBUTIONS

HK: Conceptualization, writing original draft preparation. AK: supervision and review.

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Hapsari Kinanti, Agung Kusumanegara

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