



COAGULATION PROFILE IN SNAKE BITE ENVENOMATION

General Medicine

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KEYWORDS

INTRODUCTION

Snakes reside in most habitat ranging from warm seas to deserts and are still the common cause of medical emergencies encountered in day-to-day practice. Russell's viper, kraits and cobras are among the most important biting snake species in India¹. WHO has stated that India had 1.2 million snakebite deaths, representing an average of 58,000 per year and Andhra Pradesh being one of the 8 states which have suffered 70 percent of deaths during the period 2001-2014. Snake bite envenomation manifests as acute renal failure^{2,3}, neurologic abnormalities⁴ requiring mechanical ventilation and Disseminated Intravascular Coagulation (DIC)⁵. DIC can result in life threatening complications if the treatment is delayed and that includes hemorrhage, infarction and death.

AIMS AND OBJECTIVES

The aim is to assess the changes in coagulation profile, the clinical severity associated with it and the time taken for reversal of changes in coagulation profile.

MATERIALS AND METHODS

INCLUSION CRITERIA:

Individuals alleged history of snake bite with definite evidence in the form of local cellulitis, regional lymphadenitis and/ or presence of prolonged clotting time is considered for the study.

EXCLUSION CRITERIA:

individual with local swelling due to tourniquet application and native treatment

METHODOLOGY:

The study conducted in King George Hospital, Visakhapatnam between the period July 2019 to February 2020 comprised of Individuals who are admitted in the hospital following snake bite and have undergone laboratory investigations which included Complete blood picture, urine deposits, plasma glucose, blood urea nitrogen, serum creatinine and coagulation studies. Blood samples are collected at the time of admission prior to any medical intervention.

RESULTS

64 individuals with alleged snakebite in the defined time period have features suggestive of hemostatic abnormality. Of these 64 individuals, 48 are selected at random for the study. The average age of the patients in our study ranges from 7 to 65 years. The study population is divided into three categories depending on clinical features and clotting time. 11 individuals belong to grade I, 25 individuals belong to grade II, and the rest belong to grade III. The average duration of hospital stay of the alleged snakebite individuals is 6 days, ranging from 3 to 31 days.

Clotting Time: Of the 48 individuals' 76 percent of individuals had prolonged clotting time at the time of admission. In other 3 individuals (6.2%) the test turned out to be prolonged in a period of 4 to 12 hrs. Thus, in total 82% of patients have prolonged clotting time.

Bleeding Time: The test is analyzed in 40 individuals and it is found out to be normal despite few cases having systemic manifestations in the form of hematuria, hematemesis and hemoptysis. The average bleeding time is found to be 2 to 6 minutes.

Platelet Count: It is found to be reduced in all cases belonging to

grade II and III. The average platelet count being 97,486 cells/cu.mm and thus 100% reduction is noted. The average count in grade I is 2.3 lakhs.

Prothrombin Time: The test is done in 10 out of 11 cases in grade I and it is found out to be normal in all except one patient. This patient who belongs to grade I with prolonged PT had abnormal coagulation profile over a period of six hours and another two patients who had similar clinical condition showed a normal prothrombin time. 21 out of 25 individuals and 10 out of 12 cases of grade II & III respectively are tested and all of these individuals' reports showed prolongation of prothrombin time denoting a 100% positivity.

Activated Partial Thromboplastin Time: The test is done in 10 out of 11 individuals in grade I and is normal except for one individual who developed abnormal profile over due course of time. 20 individuals of grade II and 10 individuals of grade III severity have prolonged values. Thus, the test is 100% positive in group II & III individuals.

Thrombin Time: 8 individuals of grade I envenomation are tested and are found out to be normal despite few cases having prolonged PT and aPTT levels. 20 individuals of grade II and 10 individuals of grade III are tested and showed 100% prolongation as seen in case with PT and aPTT levels. The test results are back to normal range by 48 hours.

Fibrin Degradation Products: 6 individuals of grade I are tested and all of them showed no evidence of fibrinolysis. 16 individuals of grade II are tested and 64.9% showed positive results in a dilution of 0.5mg and 35.1% in a dilution of 1 to 2. Thus the test is 100% positive. The test is done in 5 individuals of grade III severity, 8% showed positive result in dilution of 0.5 to 1 and the next 20% in 1 to 2mg and thus it is 100% positive.

Fibrinogen: Plasma fibrinogen is estimated in all patients. The average values are 245.5mg, 166.7mg and 143.9mg in grade I, II and III individuals respectively. Thus there is 100% reduction in fibrinogen levels in grade II and III individuals.

Systemic Bleeding: a total of 12 individuals had systemic bleeding with a distribution of 58.3% gum bleeding, 33.33% of hematuria, 25% of hemoptysis, 8.3% of hematemesis and 8.3% of epistaxis.

Analysis of the time interval between snake bite and onset of coagulation abnormality:

The time of onset of abnormal coagulation was analyzed based on two set of findings. The first was based on the number of patients who had prolonged clotting time at the time of admission. 77% of patients had abnormal clotting time at the time of admission. The average time period between the bite and hospital admission was 7.15 hours ranging from 2 hours to 12 hours.

The second group analyzed has a set of three patients who have normal clotting time at the time of admission which become abnormal over a period of time. Two of them developed it in a period of six hours and the third patient by 12 hours. Thus it is concluded that the onset of abnormal coagulation occurred as early as 2 hours and as late as 12 hours, with majority developing it at an average time of seven hours.

All the patients who had prolonged clotting time at the time of admission also had a prolonged Prothrombin Time, Thrombin Time

and Fibrin Degradation Products. One patient who has initial normal clotting time and later developing abnormal coagulation has prolonged PT and aPTT at the initial period itself.

Correlation of clinical severity with quantitative coagulation tests:

Three quantitative tests FDP, platelet count and fibrinogen are analyzed in relation to clinical severity and Fibrinogen alone is found to be decreasing with severity of envenomation.

Time taken for return of coagulation profile to normal:

Clotting time is analyzed in grade II and III individuals and the average time taken for normalization of clotting time is 7.9 and 18 hours, ranging from 2 to 21 hours and 4 to 24 hours respectively. The time taken for the return of PT, aPTT, TT, FDP, Fibrinogen and platelet count to normal following ASV therapy is studied in four patients who have normal clotting time at admission but had prolonged values when managed in peripheral hospitals. PT, aPTT, TT, Fibrinogen, FDP and Platelet counts are abnormal in two patients in whom test is done at 48 hours. In two other patients in whom test is done on 3rd and 5th day, only FDP, Fibrinogen and Platelet are abnormal. Thus the average time taken for normalization of PT, aPTT, TT is found to be 48 hours and while that for Platelet count, FDP and Fibrinogen to normal is longer.

DISCUSSION

Reid et al^{6,7} reported 100% prolongation of clotting time in cases of definite envenomation. Mohapatra et al⁸ reported prolonged clotting time in 95% of the individuals and 6% of these developed abnormality 6 to 12 hours after admission, which emphasizes the fact that local cellulitis and lymphadenitis is an important clue for viper bite. When Clotting time is considered along with local features the specificity is significantly increased in this study. None of the individuals with systemic bleed has an abnormal bleeding time inferring that platelet abnormality maybe a contributory factor but not the major cause of bleeding as suggested by the findings in this study. Studies conducted by Reid et al^{6,7} and Mohapatra et al⁸ reported a reduction in platelet count of 95% and 93% respectively and Saini et al⁹ reported a reduction of 10% but there was no significant correlation with severity as evidenced in this study that the individuals even with mucosal bleeds has moderately reduced platelet count and a normal bleeding time. TT, PT, aPTT are prolonged in all cases of the study conducted by Mohapatra et al and PT, aPTT are found to be prolonged in the study conducted by Reid et al suggesting that both the intrinsic and extrinsic pathway is activated by venom. Reid et al^{6,7} and Mohapatra et al⁸ stated that DIC is the primary mechanism where as Saini et al⁹ stated Fibrinolysis as the primary mechanism. Primary Fibrinolysis is a relatively rare condition, diagnosed by the presence of normal platelet count, early lysis of formed clots, marked elevation of FDP and negative test for fibrin monomers and these findings are not seen in this study.

In this study 33.3% individuals with systemic bleeding have hematuria, 58.3% have gum bleeding and the rest have hemoptysis or hematemesis. Other common forms cited in literature are hemoptysis by Reid et al^{6,7} and hematuria by Virmani et al¹⁰.

Reid et al^{6,7} reported that the clotting time returned to normal in 9 hours with specific antiserum and 24 hours with polyvalent serum. In the present study fixed adequate doses of polyvalent serum alone is used and the average time for normalization of clotting time is 7.9 hours in grade II and 18 hours in grade III individuals. The time taken for TT, aPTT and PT to return to normal is 48 hours, findings which are similar to the study conducted by Mohapatra et al⁸. Reid et al^{6,7} in his study has proved that the coagulation profile will return normal rapidly with the treatment, regardless of the time elapsed before starting the treatment. Dwivedi et al¹¹ in the lancet publication stated that the ASV can be effective even if given late and therefore there is no time limit for starting ASV therapy.

CONCLUSION

1. In the diagnosis of hemotoxic envenomation, the presence of local signs plus a prolonged clotting time has a sensitivity of 100%.
2. Disseminated Intravascular Coagulation appeared to be the primary mechanism responsible for coagulation abnormality.
3. Snake venom acts on both intrinsic and extrinsic pathways of coagulation as all cases showed prolongation of both PT and aPTT.
4. Fibrinolysis is an important component of coagulation abnormality in snake bite as evidenced by reduced Fibrinogen and FDP.

5. Among the quantitative coagulation tests only Fibrinogen level correlated with the severity of envenomation compared to FDP and Platelet Count.
6. The time interval between the bite and initiation of treatment is found to be related to the time taken for normalization of the coagulation abnormality or to the development of complications in this study.

SUMMARY

The temporal pattern of coagulation abnormalities and their response to treatment is analyzed. The severity of the bite is most important factor in deciding the outcome and DIC is responsible for the majority of coagulation abnormalities. The findings suggest that early adequate doses of ASV and anticipation of the complications of DIC are the most significant aspects of management. Monitoring the coagulation status with the help of the tests quoted in this study may increase our ability to diagnose coagulation abnormalities at an early stage, and thus may improve the management of snake bitten individuals.

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