Rural Set Up Experience of Viper Bite Treatment with Special Reference to FFP in Venom Induced Consumption Coagulopathy

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Abstract
Snake bite is one of the major public health problems in India. Venom induced consumption coagulopathy (VICC) is the commonest coagulopathy resulting from viper bites. Anti-snake venom (ASV) is the only mainstay therapy in the management of snake bite. Despite anti-venom being efficacious and bonding to multiple toxins in the venom, there are number of reasons it may not be effective. The most important being irreversible toxic effects cannot be reversed by anti-venom to toxin after damage has occurred, such as clotting factor deficiencies resulting from VICC.

This study was done to evaluate the efficacy of use of anti-snake venom and ASV with fresh frozen plasma (FFP) in haemotoxic snake bites in a tertiary care hospital. Total 500 patients admitted during period from January 2010- April 2017 with history of snake bite, vasculotoxic[278], neurotoxic[126], localtoxic[64] and nontoxic[32]. Overall outcome in term of time recovery, renal complications, and death better in ASV plus FFP group. The complications due to snake bite were minimum, if anti snake venom was administered within first 4 hours.

Introduction

Anti-snake venom is a double edged sword. It risks of anaphylactic reaction. It is also available and costly. For anti-venom to be effective against irreversible toxic effects, it must be administered early, so it can bind to toxin before they distribute their target sites and cause irreversible toxicity. Pro-coagulant toxins act in central compartment (circulation), making their onset of action relatively rapid. Once they have activated the clotting pathway and clotting factors have been consumed, this process is irreversible until further clotting factors can be re-synthesized by liver there is a period of time during which patient remains at risk of hemorrhage. For this reason, clotting factor replacement has been suggested as an adjuvant treatment for VICC. The most commonly used factor replacement is FFP as it is widely available and contains fibrinogen, factor- V, factor- VIII, factor- X. Clotting factor replacement for VICC is controversial because of the concern that it may worsen VICC by providing more clotting factors for the pro-coagulant toxins. However, it has been assumed that once anti-venom has been given and the toxins are bound, clotting factors replacement is likely to speed the rate of recovery. Full recovery of clotting function takes up to 48 hours, during which time patient potentially remains high risk of bleeding. Theoretically FFP administration should rapidly correct the coagulopathy in absence of ongoing venom induced clotting factor consumption. This has been shown for Australian elapid snake bite, but has not been investigated in viper envenoming.

Methods

The information of 500 patients’ snake bite was collected retrospectively from BKL walawalkar rural medical college and hospital Dervan, Ratnagiri, Maharashtra throughout the years: January 2010- April 2017. Detail history, clinical examinations were noted. After identification of snake and those who had ptosis and respiratory paralysis were enrolled in neurotoxic group. Those who had prolong PT(INR) and 20 min’s whole blood clotting time (WBCT) with bleeding were selected for vasculotoxic group. Those who did not have systemic manifestations but has local cellulitis were included in locally toxic group. We have studied only vasculotoxic snake bites. We have studied only vasculotoxic snake bites. This is an observational study to evaluate the efficacy of ASV versus ASV plus FFP group. Data is categorical, using statistical technique for Chi-square test and Z-test for proportion. Frequency and percentage is used for analysis.

All patients with snake bite underwent, 20min whole blood clotting time (WBCT). Blood was investigated for hemogram, fibrinogen levels, PT(INR), serum creatinine, urine. Those who had deranged PT(INR) and low fibrinogen levels and bleeding manifestations were selected for study and labeled as Venom induced consumption coagulopathy. All patients were given 10 vials of ASV(polyvalent for India). After 6 hours PT (INR) and 20 min WBCT was repeated.(PT(INR)> 2-3 min’s and bleeding patients were given FFP along with 10 vials of ASV. Dose of FFP was 10 -15 mg/kg. In this way every
Results

Total 500 patients admitted during period of January 2010- April 2017 with history of snake bite. In our observation 278 (55.60%) were vasculotoxic, 126 (25.20%) were neurotoxic, 64 (12.80%) were locally toxic, 32 (6.40%) were neurotoxic and 32 (6.40%) were toxic.

Flow-chart: Showing study procedure

6 hourly coagulation parameters and clinical bleeding was assessed and FFP was given. Maximum ASV given were 30 vials.7 Urine output was measured and creatinine was repeated every 24 hours in oliguric patients. Those who developed acute renal failure were hemodialysed according to their serum creatinine levels and fluid status. FFP was used only after 6 hrs of treatment.

Discussion

As one vial neutralizes 6 mg, this would have neutralised 144 mg of venom. The range of venom injected is 5mg-147 mg. This is sufficient to inactivate unbound venom. Therefore further administration of ASV is of no use. Fibrinogen levels were low in all envenomated patients in our study. They were given FFP. It also helps to prevent complications in elderly patients with co morbidities like DM, Hypertension, IHD and those who are on antiplatelet drugs. Isbister et al in their study demonstrated that neither earlier administration of anti-venom nor higher doses of anti-venom reduced time to recovery of Venom-induced consumption coagulopathy. However, early administration of FFP was associated with faster recovery.9

For anti-venom to be effective against irreversible side effects, it must be administered early, so it can bind with toxins before they distribute to their target sites and cause irreversible toxicity. The current evidence would suggest that FFP should be administered in patients with acute bleeding and is more likely to be effective if given more than 6 hours after the bite.3 VICC is the most common indication for anti-venom administration in patients with Russell viper bites, although there is ongoing controversy over the dose of anti-venom (initial dose of 10-20 vials) repeat anti-venom dosing and use of factor replacement.

Maduwage et al have recently shown that recovery of coagulopathy occurs over a period of 24-48 hours in patients given 10 vials of anti-venom.10 Even so full recovery of clotting function takes up to 48 hours, during which patient potentially remains at risk of bleeding. Treatment usually includes antivenom and potentially, clotting factor replacement, but evidence to support their effectiveness in resolving VICC is limited, there are no placebo-controlled trials of antivenom, and only one of fresh frozen plasma. The majority of studies of FFP in VICC have been observational in nature.11 In a study of FFP in Australian elapid envenoming causing VICC, the administration of FFP sped up the recovery of coagulopathy, except when given < 6 hrs after snake bite.12

However, the etiology of VICC is different for Russell’s viper venom, which contains metallo- protease FX and FV activators, rather than a serine protease pro-thrombin activator.13 Coagulopathy from later develops rapidly and appears to resolve irrespective of anti-venom, where as
Rusell’s viper VICC appears to be slower in onset and recovery is delayed unless anti-venom is administered. The failure of anti-venom for VICC in Australia and success of anti-venom from Echis ssp; in Africa demonstrates that studies of one snake (and therefore one pro-coagulant toxin) can’t be generalized to other snakes. Studies are required for each major group of snakes and toxin from different parts of the world, although understanding the mechanism of pro-coagulant toxin should inform empirical studies of different anti-venoms.1

**Conclusion**

Administration of anti-venom will potentially bind the active pro-coagulant toxins, allowing the clotting factors to recover. Anti-venom will effectively shorten the duration of VICC and reduces the risk of bleeding. However, while the clotting factors are re-synthesized by liver there is a period of time during which patient remains at risk of hemorrhage. For this reason, clotting factor replacement (FFP) has been suggested as an adjuvant treatment for VICC. Studies are also required for efficacious use of FFP focusing on when to use, how much to use, for how much time it has to be given.

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**References**

4. World health organization; regional office for south- east Asia; guideline for the management of the snake bite; 2016; 123-128.