High-Dose Anti-Snake Venom Versus Low-Dose Anti-Snake Venom in The Treatment of Poisonous Snake Bites — A Critical Study

V Paul*, S Pratibha**, KA Prahlad***, Jerry Earali***, S Francis***, Francy Lewis***

Abstract
Objectives: To assess the optimum dose of anti-snake venom to treat snake bites cases effectively. This is particularly relevant in the present scenario when the cost of anti-snake venom (Serum Institute of India) has gone up to nearly Rs. 400 per vial and the cross-section of people usually affected belong to the poor socioeconomic class.

Methodology: One hundred snake bite cases with envenomation, irrespective of whether they were bitten by viper, cobra or krait, brought within 24 hours of the bite to Jubilee Mission Hospital, Trichur, Kerala State during the 15 months from August 2001 to October 2002 were randomized into two groups of 50 cases each, irrespective of the severity of the cases. One group received a fixed dose regime of six vials of anti-snake venom and the other 12 vials of the same.

Results: In the low-dose group there were five deaths giving a mortality rate of 10%, nine (18%) required dialysis and three (6%) required ventilatory support. In the high-dose group there were seven deaths giving a mortality rate of 14%, 13 (26%) required dialysis and three (6%) required ventilatory support. The average hospital stay for the low-dose group was 8.42 days while that of the high-dose group was 9.02 days.

Conclusion: While there was no additional advantage in following a high-dose regime for snake bite cases, there was considerable financial gain by following the low-dose regime. Most of the parameters showed a beneficial trend for the low-dose group though the differences were not statistically significant.

INTRODUCTION

Though the use of anti-snake venom (ASV) has been in existence for many years, there is no universally accepted standard regarding the optimum dose of ASV, its frequency of administration and duration of therapy. SR Vijeth et al have found in their trial that the mean effective dose of ASV required in a snake bite case with envenomation is about 180 ml (18 vials). Tariang et al have reported that the mean dose ASV required to manage a case with envenomation effectively is 4.7 vials. During the last 37 years of our experience in managing snake bite cases there were 3 occasions when we could not administer ASV because of allergy to the drug. Two of these cases were cobra bites and one was that of a viper bite. To our relief and surprise, we could manage these cases successfully with conservative measures i.e. with ventilatory support in the former and dialysis in the latter. Of course, all of them required intensive supportive treatment to maintain their vital functions. This experience prompted us to conduct this trial using two fixed dose regimes; one with six vials of ASV, (The Low-Dose Group (LDG) and the other with 12 vials, the High-Dose Group (HDG).

Patient’s and relative’s consent was obtained for this trial. The Ethical Committee of the hospital had given its clearance after evaluating a pilot study where low-dose ASV was found to be effective and safe.

MATERIAL AND METHODS

One hundred patients of snake bite with evidence of envenomation brought within 24 hours of the bite to Jubilee Mission Hospital, Thrissur, Kerala State, South India during the period from August 2001 to October 2002 were included in the study, irrespective of whether the bite was from a viper, cobra, or krait. By and large viper bite causes...
haemotoxicity, cobra bite produces neurotoxicity and krait bite causes a combination of both. Haemotoxicity was said to be present if the patient’s bleeding time was more than 8 minutes, prothrombin time more than 16 seconds or the clotting time more than 30 minutes or if there was abnormal lysis of the clot. The usual presenting neurotoxic features were respiratory distress due to weakness of the respiratory muscles, dysarthria, dysphonia, blurring of vision or diplopia.

Patients were excluded from the study if they presented more than 24 hours after the bite or if they gave history of any bleeding diathesis or any other previous neurological abnormality. Patients who had manifested allergy to the ASV were also excluded from the study. Patients who were eligible were allotted at random either to the HDG who were given 12 vials of ASV or to the LDG who were given six vials of ASV. The polyvalent ASV made by the Serum Institute of India was used in the study. Both the patient and the investigator were blinded as to which group the patient belonged. The patients in the HDG were given ASV after a sensitivity test, 2 vials of ASV diluted in 100ml of dextrose or saline over 2 hours followed by 10 vials of ASV diluted with 500ml of dextrose or saline given over 4 hours. All patients were given IM tetanus toxoid and IV hydrocortisone 100 mg. Whenever required, blood transfusion was given to the haemotoxic cases. Snakes were identified either by direct examination of the snakes when brought by the patients or on the basis of the signs, symptoms, and results of the investigations. The end point of the study was normalisation of haematological or neurological parameters or death.

Statistical Analysis

Comparison between LDG and HDG is done using chi-Square test. P < 0.05 is considered significant. The results of clotting time, platelet count and prothrombin time are expressed as mean ± SD for each group. Comparison between both the groups is done using T test for unpaired data. P < 0.05 is considered significant.

RESULTS

Table 1 gives the details of the age and sex distribution of the cases, time delay after the bite before hospitalisation, the details of the snakes brought to the hospital for identification, the details of the site of bite and the investigation results. Among the 100 cases accepted for the trial, 75 were males and 25 females. There were none below the age of 10 as children bitten by snakes were admitted in the paediatric wards. In the HDG. There were seven deaths giving a mortality rate of 14% while in the LDG there were five deaths giving a mortality rate of 10%. While in the HDG 13 patients (26%) required dialysis and three cases (6%) required ventilatory support, in the LDG nine (18%) required dialysis and three (6%) required ventilatory support. The average hospital stay for the HDG was 9.02 days while that of the LDG was 8.42 days. Of the 12 cases who died, the cause of death in 10 cases was refractory shock while one in the HDG who had dialysis died of GI bleed due to DIC. One in the LDG who had dialysis died of acute respiratory distress syndrome. Of the

<table>
<thead>
<tr>
<th>Variable</th>
<th>High-dose 12 Vial</th>
<th>Low-dose 6 Vials</th>
<th>Statistical significance</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>7 (14%)</td>
<td>5 (10%)</td>
<td>Not significant</td>
<td>&gt; 0.05</td>
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<tr>
<td>Cause of Death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refractory shock</td>
<td>6</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GI Bleed due to DIC</td>
<td>1</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute respiratory distress syndrome</td>
<td>—</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients requiring Dialysis</td>
<td>13 (26%)</td>
<td>9 (18%)</td>
<td>Not significant</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Hospital stay in days</td>
<td>9.02</td>
<td>8.42</td>
<td>Not significant</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>
22 cases who underwent dialysis, two died and one from the HDG became a chronic renal failure case. The cases who were taken for dialysis had an average hospital stay of 15.3 days and the average number of hemodialysis required for each patient was 5.5. When hypotension was present it was indicative of serious prognosis both in the neurotoxic as well as in the hemotoxic cases. Development of parotid swelling was also found to be a bad prognostic sign.

There was no significant statistical difference in the average clotting time and platelet count between the two groups. But in the case of prothrombin time the difference between the two groups was statistically significant in favour of the HDG though it did not ultimately reflect in the morbidity or mortality of the patients. There was no statistically significant difference between the two groups with regard to the mortality rate, number of patients requiring dialysis and the number of days spent in the hospital.

**DISCUSSION**

With our experience in treating over 10,000 cases of snake bites during the last 37 years, we would like to put forward certain postulations which may explain the unexpected results we have got in this study, contrary to the beliefs held by a large majority of the workers in this field. We admit that these postulations have as yet no scientific basis and have to be proved or disproved by future research work.

The postulations are:-

1. When a person is bitten by a snake, the major part of the toxin gets fixed to the tissues and only a relatively small part remains in the circulation by the time the patient is brought to the hospital.
2. Though it is useful and essential to neutralize the circulating toxin, it is more important to treat the systems involved effectively and aggressively. Besides the initial supportive measures to sustain the vital functions and maintain the hemodynamic integrity, dialysis for the renal failure cases and ventilatory support for the neurotoxic cases may be required.
3. Repeated high doses of ASV to restore the clotting time to normal within the shortest time, do not seem to be necessary to reduce the ultimate morbidity and mortality. A smaller dose sufficient to bring down the clotting time and make the clotting time graph take a downward trend seems to be sufficient to manage the case effectively and safely. The body’s detoxifying system will bring down the clotting time eventually though it may take a slightly longer time. This delay does not seem to affect the morbidity and mortality as shown by the results of this trial. Administration of a bottle of fresh blood is often helpful in bringing down the clotting time further, without any additional dose of ASV.

In this trial, the mortality rate and the percentage of cases requiring dialysis is more in the HDG. One of the possible explanations is that the ASV made from equine protein may be causing subclinical toxic effects in a patient who has already multi-organ involvement, and this may tilt the balance adversely against the patient. Tariang et al reported in their series, that the neurotoxic envenomation requires higher dose of ASV. Our experience is contrary to this. We have found that haemotoxic viper envenomation requires a higher dose of ASV than the neurotoxic envenomation. We hope that the future workers in this field will try and evolve an economically viable test to estimate the exact amount of circulating venom at different stages after the bite, so that the exact amount of antivenom to neutralise the toxin can be accurately determined.

The economic significance of the result of this study is considerable for the developing countries in Asia and elsewhere where the major cross-section of patients afflicted falls within the lower income group. The difference in the dosage of ASV between the HDG and LDG is six vials (polyvalent ASV made by the Serum Institute of India) the cost of which would be about Rs. 2400. We feel that there is scope for further trials using a still smaller dose of ASV.

In conclusion, we wish to say that this study has confirmed that a smaller fixed dose of ASV is sufficient to manage snake bite cases with evenomation effectively yet economically.

**Acknowledgements**

We acknowledge the help provided by all the doctors of the medical unit and the nurses of the Medical ICU and the Lab Technicians for conducting this study. We are grateful to Rev. Fr. Francis Alappat, the Director of Jubilee Mission Hospital and the hospital administration for permitting us to conduct this study. Our thanks to Prof. TB Ramkumar and Prof. Krishnakumar, Dept of Statistics, St. Thomas College, Trichur for their help in the statistical analysis of this study.

**References**


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**NOTICE**

**To all State Chapter / City Branches**

A meeting of the Chairpersons and Secretaries of all State Chapters and City Branches will be held on **19th January, 2004 at 5.00 pm in Hall D** - International Convention Centre, Shilparaman, Hyderabad. All Chairpersons and Secretaries are requested to attend the meeting.

Secretaries of all State Chapters and City Branches are requested to fill the form given below and mail it to the Dr. Sandhya A Kamath, Hon. General Secretary, Association of Physicians of India, Laud Mansion, 3rd Floor, 21 Maharshi Karve Road, Opp. Charni Road Station (East), Mumbai - 400 004.

All the State Chapters / City Chapters of API furnish the following information by **15 January, 2004**.

1. Name of the Chapter/Branch __________________________________________
2. Membership Strength __________________________ Type: full/Associate________________
3. Registration with competent authorities - Yes / No
4. Constitution - Adopted / Not Adopted
5. Bank Account __________________________
6. P.A.N. Number __________________________
7. Audit of the Account __________________________
8. Name of Office Bearers -
   Chairman :
   Secretary :
9. Detailed Correspondence Address with Tel./Fax./Mobile/E-mail
   __________________________________________________________
10. Any other relevant information

**Secretary Branch**

You are requested to send the above form to
Dr. Sandhya Kamath, Hon. General Secretary,
Association of Physicians of India,
Laud Mansion, 3rd Floor, 21 Maharshi Karve Road,
Opp. Charni Road Station (East), Mumbai - 400 004.
Tel.: 2382 9348, Fax : 022-2389 5297
E-mail : api_ho@vsnl.com

Sd/-
Dr. Sandhya A Kamath
Hon. General Secretary