Original Research Article

To study the efficacy of *Panchsheerisha Agada* as a first aid measure in snake venom poisoning

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Abstract

Background: Use of Albizzia lebbeck (Shirish) plant has been mentioned in literature of Ayurvedic Samhita's. It is also known commonly as Shirish, continues to be a plant useful in snake bite in India. Medicinal uses of this plant including antitoxic have been mentioned in literature, but scientific evidence is lacking. **Objective:** The objective was to study the efficacy of Panchsheerisha Agada in Common Cobra and Russell's viper venom poisoning as a first aid measure. As well as to study whether there is any adverse reaction between Panchsheerisha Agada and Poly Valent Anti Snake Venom Serum (PVASVS). **Material and Method:** In this vivo study Common Cobra snake venom, Russell's Viper snake venom, experimental drug- Panchsheerisha Agada and PVASVS are given separately, simulating actual situation of snake bite. **Observation and Discussion:** In the eight groups of 6 animal in each group symptoms like- Tremors, Paralysis, Convulsions and Survival period with Common Cobra venom and Muscle weakness, Survival period with Russell's Viper venom is observed with PanchsheerishaAgada and PVASVS. **Result:** Survival period in Common Cobra venom + Panchsheerisha Agada as well as Russell's Viper venom + Panchsheerisha Agada is statistically significant. **Conclusion:** Panchsheerisha Agada can be use as first aid measure in snake venom poisoning.
Keywords: Albizzia lebbeck, Shirish, Panchsheerisha Agada, PVASVS, Common Cobra snake venom, Russell's Viper snake venom, Albino mice.

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INTRODUCTION

Snake bite is a major health threat in India. About 2 million people are bitten by snake annually, of which 15,000 to 30,000 cases prove fatal. Snake bite cases are more common in rular area, mountainous region which are covered by the dense evergreen forests. In India majority of population is crowded in Rular area. If patient need any medical or any other treatment, they have to go higher medical centre. But each and every patient doesn't go to higher centre directly. In between they take primary treatment at Rular Hospital and Primary Health Centre. Primary Health Centres are also away from periphery. People of periphery don't have their own vehicles. They have to arrange some vehicles to come at Rular Hospital and Primary Health Centre. These all travelling process is time consuming. Currently the only scientifically valid treatment for snake venom envenomation is serotherapy i.e. Poly Valent Anti Snake Venom Serum (PVASVS). It is available at Rular Hospital, Primary Health Centre and Government Hospital. When a snake bites the patient, it takes time to raise alarm. First aid help arrives within average 10 min. then the arrange van, Bullock-cart or any other vehicle to reach to PHC, RH. This travelling will take average 2-2.5 hrs. When patient reaches to PHC or RH it may not be OPD timing, doctors may not be available at that time. After arrival of doctors they start serotherapy. Average time to start serotherapy is 30 min. so that average time laps will be 3- 3.5 hrs. Average fatal period of Common Cobra is 2-3 hrs, Krait 6-12 hrs, Viper is 24 hrs. Usually irreversible damage takes place within 3 hours. After irreversible damage by venom poisoning, serotherapy will not be able to rescue the patient, delay in

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treatment may turn to be fatal. Serotherapy still presents some drawbacks. Those are limited or no access of antivenin in Hospital. Before administration of PVASVS, its sensitivity test should be done, so it required trained person for administration. Irreversible changes may occur due to delay in getting PVASVS. Adverse reaction of PVASVS may turn as a fatal, so emergency medical facility should be available at that time. There is limited effectiveness of serotherapy against venom components and rapid local tissue damage is not reversed. Hence, we required the primary substitution or first aid measure before serotherapy, which will increase the survival period and decrease the mortality and morbidity. In snake bite cases available first aid measures are physical and external i.e. pressure bandage, application of tourniquet, incision and suction, hence their effectiveness is limited. So we required a first aid measure for snake bite, which will be safe i.e. non-toxic. Its rout of administration should be oral, because nasal or collyrium application will required trained person and it will be time consuming. A first aid measure should be easily available, easy to prepare, easy to administer. It should prolongs the appearance of symptoms or prolong the survival time, so that patient can get serotherapy before irreversible changes should happen. The most important factor in first aid measure is that it should not interact with PVASVS, as almost all snakebite patients will eventually receive PVASVS 850 species from 138 families of plants are mentioned as antiphidian. 96 Ayurvedic formulations are considered as effective in snake venom. Only a few species have been scientifically investigated. Most of the experimental studies were done by in- vitro or pre-incubation assay method. Neutralizing actions of extractives of plants, upon venom are more notable in vitro but not confirmed in vivo study. In pre-incubation assay venom and plant extractives are collectively given for in vivo study snake venom, experimental drug and PVASVS are given separately, simulating actual situation of snake bite. I have selected in vivo study for screening of plants species as a first aid measure. Snakes are classified into neurotoxic, vasculotoxic and myotoxic. Myotoxic snakes are sea-snakes, theseare less common. Out of neurotoxic and vasculotoxic Common Cobra and Russell's Viper poisoning is more common. So the efficacy of the drug on Common Cobra venom and Russell's viper venom poisoning needs to be investigated. I have selected "*Panchsheerisha Agada "* mentioned in *Charaka Samhita* as a first aid measure in snake venom poisoning. The homogenous mixture of equivalent quantity of *Shirish*'s fruit, root, bark, flowers and leaves with the *goghruta* is known as a "*Panchsheerisha Agada "* . It neutralizes all types of poisons. *Shirish* is told as 'Agrya' in all *vishaghna dravyas* and "*Panchsheerisha Agada "* contains all parts of *Shirish*. That's why its potency is more than any single part of *Shirish* and it may be more effective against poison. So I have select the drug "*Panchsheerisha Agada "*against Snake Venom poisoning as first aid measure. "*Panchsheerisha Agada "* is primary route of administration is oral and it is non-toxic formulation. The type of venom to which it is effective is not mentioned, so we can test its efficacy in both types of snakes. It is easily available, easy to carry, does not require trained person for administration. It contains *panchanga* of *Shirish* which is an 'Agrya' meaning the drug is most effective for *vishaghna karya,* i.e. it is most anti poisonous plant. In this *yoga Goghruta* will probably act as vehicle for *Shirish* to act at appropriate site. As compare to PVASVS it is cheap and can easily be made available. It will reduce the fatality and morbidity as it will not interact with PVASVS. Therefore I planned to study the efficacy of "*Panchsheerisha Agada "* as a first aid measure in snake venom poisoning in standard experimental models in Albino Mice of strain Swiss albino.

AIMS AND OBJECTIVE

1. To study the efficacy of *Panchsheerisha Agada* in Common Cobra venom poisoning as a first aid measure.
2. To study the efficacy of *Panchsheerisha Agada* in Russell's Viper venom poisoning as a first aid measure.
3. To study whether there is any adverse reaction between *Panchsheerisha Agada* and Poly Valent Anti Snake Venom Serum (PVASVS)

MATERIALS AND METHODS

Material

Animals

Healthy adult Albino Mice of strain Swiss albino of either sex weighing 20 g were used in this study. They were caged in polyvinylwire mesh cages in the animal house of National Toxicology Centre (NTC) Pune. They were maintained under standard laboratory conditions (12 h light and dark cycle and temperature of 20°C - 24°C and humidity (40% - 60%)with access to food supplied by Nav Maharashtra Chakan oil mills Ltd. Pune and water *ad libitum*. Animals were acclimatized to laboratory conditions before the test for7 days. (and fasting overnight before the test)

Drug Collection of plant material

Fresh flower, leaves, bark, fruit, root of *Albizzia lebbeck* were collected from Jawaharalal Nehru Botanical Garden Kothrud Pune.

Preparation of drug

All parts of *Albizzia lebbeck* were dried in shadow (*Chayashuska*) for two to three days and finely powdered. A fine, light brownish green coloured powder of *Panchsheerisha* was obtained.

Authentication and Standardization

Authentication of *Shirish* was done at Botanical Survey of India, Pune. Standardization and phytochemical analysis of *Panchsheerisha* powder was obtained from Indian Drug Research Association Laboratory, Pune. Goghruta for experimentation as first aid measure in Snake Venom Poisoning is of AGMARK standards.

Drugs and chemicals

- Dried lyophilized form of 100 mg of Common Cobra Venom
- Dried lyophilized form of 100 mg of Russell's Viper venom and
- Poly Valent Anti Snake Venom Serum (PVASVS)

Were collected from Haffkine Institute for Training Research and Testing, Mumbai.

Ethical clearance

Ethical clearance was obtained from Institutional Animal Ethics Committee of institute where the research was conducted**.**

METHODS

Experimental Study Dose calculation for mice

Conversion factor from man to mice was 0.0026. So, according to this venom dose, drug (*Panchsheerisha Agada*) dose, and PVASVS dose was calculated.

Dose calculation of venom

Human fatal dose for Common Cobra is 12 mg. According to conversion factor mice fatal dose for Common Cobra venom is 0.0312 mg i.e. 31.2 ugm. Fatal period of Common Cobra was short duration, so 80% of total fatal dose was taken to observe the effect of venom for a longer time

80% dose of Common Cobra venom was 24.96 ugm. #25 ugm

Human fatal dose for Russell's Viper is 20 mg. According to conversion factor mice fatal dose for Russell's Viper venom is 0.0520 mg i.e. 52ugm. Russell's Viper Fatal period was sufficient enough to observe effect of venom, so 100% fatal dose was taken

100% dose of Russell's Viper venom was 52 ugm.

Dilution criteria for venom

Dried lyophilized form of Venom was diluted to get appropriate fatal dose to inject mice. In a vial of 100 mg Cobra venom 10 ml distilled water was added, from that 1 ml was removed and added to 100 ml distilled water containing glass bottle. Then it was sealed with rubber cork. From this dilution 0.25 ml was taken out injected to mice.

100 mg in 10 ml	So 1 ml = 10 mg
10 mg in 100 ml	So 1ml = 0.1 mg = 100 ugm
	0.5 ml = 50 ugm
	0.25 ml = 25 ugm

In a vial of 50 mg Russell's Viper venom 5 ml distilled water was added, from that 1 ml was removed and added to 50 ml distilled water containing glass bottle. Then it was sealed with rubber cork. From this dilution 0.25 ml was taken out injected to mice.

50 g in 5 ml	So 1 ml = 10 mg
10 g in 50 ml	So 1ml = 0.2 mg = 200 ugm
	0.5ml = 100 ugm
	0.25 ml = 50 ugm

Dose calculation of *Panchsheerisha Agada*

Dose of churna in *Sharangadhar Samhita* was given as 1 *Karsha* i.e. 10 gm. But for today's time period it is too high. So ideal dose of churna was taken as 1 gm. Human dose of *Panchsheerisha Agada* was 1 gm.

According to conversion factor mice dose was0.0026 gm i.e. 2.6 mg.

Dose of *Panchsheerisha Agada* in mice was 86.66 mg/kg.

To give appropriate oral dose we have to make 8.66 mg /ml strength of solutions. For that purpose 130 mg of *Panchsheerisha Agada* was made. Then 15 ml Corn oil was added to it. This mixture was stirred for 15 min and good suspension was made. Out of this 0.3 ml was given for oral dose.

Dose calculation of PVASVS:

1 ml of reconstitute PVASVS neutralizes 0.6 mg of Common Cobra venom. For animal experiment 25 ugm Common Cobra venom is required. So required dose of PVASVS was 0.0416 ml

Dose of PVASVS for Common Cobra group = 0.04 ml

1 ml of reconstitute PVASVS neutralizes 0.6 mg of Russell's Vipervenom. For animal experiment 52 ugm Russell's Viper venom is required. So required dose of PVASVS was 0.086 ml

Dose of PVASVS for Russell's Viper group = 0.08 ml

Animal Experiment

The animals were divided into eight groups of 6 animals each.

Group I received only Common Cobra venom and served as **control group.**

Group II received Common Cobra venom + *Panchsheerisha Agada*

Groups III received Common Cobra venom + *Panchsheerisha Agada*+PVASVS

Groups IV received Russell's Viper venom and served as **control group.**

Groups V received Russell's Viper venom +*Panchsheerisha Agada*

Groups VI received Russell's Viper venom + *Panchsheerisha Agada*+PVASVS
Groups VII received Common Cobra venom + PVASVS and served as **standard group.**
Groups VIII received Russell's Viper venom + PVASVS and served as **standard group.**

1. Samples were converted into suspension by through mixing with corn oil.
2. Samples were freshly prepared for each group and then administered
3. Snake venom was given by Intramuscular route, *Panchsheerisha Agada* was given by Oral route and PVASVS was given by Intravenous route.
4. Dose given to animals according to their body weight.
5. After dosing all animals were observed for 24 hours for toxic signs and symptoms and mortality up to 7 days.

Procedure

1. First of all preliminary toxicity study was done.
2. In each group, mice were gone weighted first. Venom was given intramuscular route. After 5 min. drug was given orally. After 10 min. from venom administration PVASVS was given intravenous.
3. After dosing, animals were observed for 24 hrs up to 7 days.
4. Comparative observation were noted.

OBSERVATION

Table 1

	Observation	Common Cobra venom	Common Cobra venom + *Panchsheerisha Agada*
Observation 1	appearance of tremors	59.8	75
Observation 2	appearance of paralysis	76.4	108.5
Observation 3	Appearanceofconvulsions	90.6	124.833
Observation 4	Survival period	98.4	130.8

	Observation	Russell's Viper venom	Russell's Viper venom + *Panchsheerisha Agada*
Observation 5	Survival period	131.75	1076.5

DISCUSSION

It was very difficult to observe and distinguish the pre-paralytic and paralytic signs of the venom injected mice. Perhaps trained veterinary doctors may record the accurate observation. Various sophisticated instruments are required for recording observations. We observed tremors, paralysis, convulsions etc. in Cobra venom injected mice, but external bleeding, necrosis at injected site in Viper venom was not seen. For experimental observation in these eight groups it can be stated that, progressive symptoms of Common Cobra venom were: Tremors, Paralysis, Convulsions and Death.
Russells Viper venom were: Muscle weakness, Death
Two 't'tailed test applied for these observations

Tremors:

Mean of appearance of tremors in Common Cobra Venom Control group = 59.8
Mean of appearance of tremors in Common Cobra Venom + *Panchsheerisha Agada* = 75
Difference Between two means = 75 – 59.8 = 15.2

Paralysis:

Mean of appearance of paralysis in Common Cobra Venom Control group = 76.4
Mean of appearance of paralysis in Common Cobra Venom + *Panchsheerisha Agada* = 108.5
Difference Between two means = 108.5 – 76.4 = 32.1

Convulsions:

Mean of appearance of convulsions in Common Cobra Venom Control group = 90.6
Mean of appearance of convulsions in Common Cobra Venom + *Panchsheerisha Agada* = 124.833
Difference Between two means = 123.8 – 90.6 = 34.2

Survival period:

Mean of Survival period in Common Cobra Venom Control group = 98.4
Mean of Survival period in Common Cobra Venom + *Panchsheerisha Agada*= 130.8
Difference Between two means = 130.8 – 98.4 32.4

Survival period:

Mean of Survival period in Russell's Viper venom Control group = 131.75
Mean of Survival period in Russell's Viper venom + *Panchsheerisha Agada* = 1086.5
Difference Between two means = 1086.5 – 131.75 = 954.75

Statistical Analysis

't' test applied to prove these statistically.
For Common Cobra Venom

- Duration of tremors
  'P' one tail = 0.0192
  'P' two tail = 0.03857
- Duration of paralysis
  'P' one tail = 0.0192
  'P' two tail = 0.03857
- Duration of convulsions
  'P' one tail = 0.0264
  'P' two tail = 0.05
- Survival period

'P' one tail =0.487
'P' two tail = 0.975

It means that duration of symptoms and survival period in Common Cobra venom + *Panchsheerisha Agada* is statistically significant For Russell's Viper venom Survival period

'P' one tail =0.0048
'P' two tail = 0.00978

It means that survival period in Russell's Viper venom + *Panchsheerisha Agada* is statistically significant

Out of these 8 groups mentioned, 4 groups namely

Groups III Common Cobra venom + *Panchsheerisha Agada* +PVASVS

Groups VI Russell's Viper venom + *Panchsheerisha Agada* +PVASVS

Groups VII Common Cobra venom + PVASVS

Groups VIII Russell's Viper venom + PVASVS

were given ASV and hence all the animals included in these groups were expected to survive. As per expectation all the animals from all these groups were survived.

CONCLUSION

1. *Panchsheerisha Agada* increases the duration of appearance of symptoms.
2. *Panchsheerisha Agada* increases the duration of survival period
3. It is not interact with PVASVS

Thus it proves the efficacy of *Panchsheerisha Agada* as first aid measure in snake venom poisoning.

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