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In Vivo Study of Efficacy of *Arka* (*Calotropis procera*, Ait.) *Moola Swaras* as First Aid Measure in Snake Venom Poisoning.

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Abstract-

Snakebites are a major health threat in India. About 2 million people are bitten by snakes annually of which 15,000 to 30,000 cases prove fatal. Snake bite cases are more common in the states of Maharashtra, west Bengal, Uttar Pradesh, Assam & Kerala. Currently the only scientifically validated treatment for snake venom envenomation is serotherapy i.e. Poly Valent Anti Snake Venom Serum (PVASVS). It is available at Government Hospitals. Average time for reaching there is 3 hrs. There is need of first aid treatment. It should be easily available, easy to carry and should not require trained person for administration. *Arkamool swaras* can be given in the above condition. As common Cobra and Russell's viper are very common types of snakebites in India, study has been done on both. In Common Cobra group when *Arkamool swaras* was administered, appearance of convulsions was prolonged by 19 min, appearance of tremors was prolonged by 6 min, appearance of paralysis was prolonged by 11 min and duration of survival was prolonged by 22 min. In Russell's viper venom group, when *Arkamool swaras* was administered, duration of survival was prolonged by 40 min. This study confirmed the *Vishaghna* property of *Arkamool swaras* and thus it is proved that *Arkamool swaras* is efficient as a first aid measure in snake venom poisoning.

Keywords: Snakebite, *Arkamool Swaras*, Snake Venom Poisoning, Poly Valent Anti Snake Venom.

Introduction

Snakebite cases are more common in rural area, mountainous region which are covered by the dense evergreen forests. In India majority of population is crowded in rural area. Currently the only scientifically validated treatment for snake venom envenomation is serotherapy i.e. Poly-Valent Anti-Snake Venom Serum (PVASVS) which is available at Government Hospital.

In rural areas, when a snake bites a person it takes about 3 hours to start serotherapy as there are no proper transportation facilities in distant areas. The average fatal period of poisoning by Common Cobra bite is 2-3 hours, Krait bite is 6-12 hours, Viper bite 24 hours. Hence we require a first aid measure before serotherapy, which will increase the survival period and decrease mortality.

In snakebite cases available first aid measures are, physical/external i.e. pressure bandage, application of tourniquet, incision and suction, hence the effectiveness is limited. So we require a first aid measure for snake bite that will be a) Nontoxic b) easily available c) easy to prepare d) easy to administer e) should prolong the appearance of symptoms or prolong the survival period.

Snakes are classified into neurotoxic, vasculotoxic and myotoxic. Myotoxic snakes are sea snakes. Sea snake bite is less common. Out of neurotoxic snakes, Common Cobra snakebite poisoning is more common. And in Vasculotoxic snakes, Russell's viper snakebite poisoning is more common.

Symptoms of Common Cobra Bite

Local Features: Indistinct fang marks, burning pain, swelling, discoloration of skin.

Systemic Features:

Pre - Paralytic stage**:** Vomiting, headache, loss of consciousness.

Paralytic stage: Ptosis, opthalmoplegia, tremors, drowsiness, dysarthria, dysphagia, convulsions, bulbar paralysis, respiratory failure.

Symptoms appearing after 30 minutes: Patients feel drowsy, slightly intoxicated, weakness of legs, nausea, vomiting, and weakness of muscles increase paralysis of lower limbs, paralysis then spreads to the trunk and affects head, eye lids hang down (Ptosis).

After 30 minutes - 1 hour: Excessive salivation and vomiting, paralysis and swelling of tongue and larynx, difficulty in speech and swallowing, extra-ocular muscle weakness, ptosis.

After 2 hours: Complete paralysis, respiration slowed, heart rate increased, unable to speak though the patient is conscious, coma, convulsions may be present or may not.

Symptoms of Russell's viper Bite:

Local Features: Rapid swelling with discoloration, blister formation over bitten limb, swelling over trunk, frank bleeding from bite site, severe pain.

Systemic Features:

Generalized bleeding tendency (epistaxis, haematuria, haemoptysis, malena), renal failure, respiratory depression increased, blurring of vision, headache, dizziness, weakness.

Selection of Drug:

'*Arkamool swaras'* mentioned in '*Bhaishajya Ratnavali Vishachikitsa Adhyaya 72/49'* in snake venom poisoning was selected. Route of administration of '*Arkamool swaras'* is oral. Hence this study was undertaken to see the efficacy of *Arkamool swarasa* as a first aid measure in

Common Cobra venom and Russell's viper venom poisoning.

Aims and Objectives

1. To study *in vivo* efficacy of '*Arkamool swarasa'* in Common Cobra venom poisoning as a first aid measure.
2. To study *in vivo* efficacy of *Arkamool swarasa'* in Russell's viper venom poisoning as a first aid measure.
3. To study whether there is any *in vivo* adverse drug reaction between *Arkamool swarasa'* and PVASVS.

Materials and Methods

1. Collection of Raw Material: Raw sample of dry *Arkamool* was taken. Authentication of *Arka* was done in Botanical Survey of India, Pune.
2. Standardization of Drug: To ensure the quality of drug it is necessary to standardize that drug before using it in experiment. This study was done in the Laboratory of Post Graduate Studies and Research Centre of Tilak Ayurved Mahavidyalaya, Pune. Physico-chemical analysis like color, odor, foreign matter, total ash, acid insoluble ash, alcohol soluble extractive, water soluble extractive were carried out.
3. Preparation of *Arkamool Swaras*: *Swaras* was prepared according to *Sharangdhar Samhita*. *Swaras* was made by decoction method.
4. Collection of Venom: Dried lyophilized form of 110 mg of Common Cobra venom and 90 mg of Russell's viper venom was collected from Snake farm, Haffkine Institute for Training Research and Testing, Mumbai.
5. Collection of PVASVS: PVASVS was procured from Haffkine Institute for Training Research and Testing, Mumbai.

Animal Experiment

Animal experiment for efficacy of *Arkamool swaras* as a first aid measure on Common Cobra venom and Russell's viper venom was carried out in National Toxicology Centre (NTC), Pune.

Method

a. Drug Samples of *Arkamool swaras* were freshly prepared from dry drug for each group and then administered.
b. Doses were given to the animals according to their body weight.
c. After dosing all animals were observed for 24 hours for toxic signs and up to 7 days for mortality.

Protocol Used:

Animal species **:** Albino Mice
Source **:** NTC, Pune
Average Weight **:** 22 gm.
Number **:** 3 in each group
Age **:** 6 - 8 weeks
Sex **:** Female
Number of Groups **:** 8

Groups for study:

Group I (Control Group): Common Cobra venom.
Group II: Common Cobra venom + *Arkamool swaras*
Group III (Control Group): Russell's viper venom
Group IV: Russell's viper venom + *Arkamool swaras*
Group V (Standard Group): Common Cobra venom + PVASVS
Group VI: Common Cobra venom + *Arkamool swaras* + PVASVS
Group VII (Standard Group): Russell's

viper venom + PVASVS
Group VIII: Russell's viper venom + *Arkamool swaras* + PVASVS

Dose:

Dose calculation for Mice: Conversion factor from man to mice was 0.0026 so according to this, venom dose, drug (*Arkamool Swarasa*) dose and PVASVS dose was calculated.

Dose calculation of Venom: Human fatal dose of Common Cobra is 12 mg. According to conversion factor, fatal dose of Common Cobra venom in mice is 31.2µgm. Initially, total fatal dose was taken but, no death occurred in Albino mice. So after pilot study, the dose of Common Cobra venom was taken as 60 µgm. and dose of Russell's viper venom was 750µgm.

Dose of *Arkamool Swaras*: According to conversion factor mice dose of *Arkamool swaras* was 0.104 ml.

Dose of PVASVS for Common Cobra Group: 0.1 ml

Dose of PVASVS for Russell's Viper Group: 0.125 ml

Route of Administration:

1. Snake venom – intramuscular (IM).
2. *Arkamool swaras* – oral and
3. PVASVS – intravenous (IV).

Procedure

In all groups, weight of each animal was recorded. Venom dose was given by IM route, followed by trial drug dose (orally) after a span of 5 minutes, and then PVASVS was given after 5 min by IV route according to the groups.

After dosing, the animals were observed for tremors, paralysis, convulsions and death, round the clock for 7 days. The time according to signs was noted.

Comparative observations were tabulated.

Results

A) Common Cobra groups: (Graphs 1-4)

Observations in minutes	**Group I**	**Group II**
Appearance of tremors	36	+6
Paralysis	43	+11
Convulsions	48	+19
Death	59	+22

Group V

One mouse died after 197 minute, this may be due to serum sickness reaction of PVASVS. Remaining two mice survived well.

Group VI

All three mice survived well without showing any signs.

B) Russell's viper groups: (Graph 5)

Group III

Death of mice occurred on 121 minutes after given Russell's viper venom.

Group IV

Death was prolonged by 40 minutes.

Group VII

One mouse died after 55 min. This may be due to serum sickness reaction of PVASVS. Remaining 2 mice survived well.

Group VIII

All three mice survived completely without showing any signs.

Significant Results

Bhaishajya Ratnavali states that this remedy is effective in all types of snake venom poisoning.

The results of survival period in Russell's viper venom group were proved to be statistically significant. P value is 0.07(one tail). (Table 5)

The results of survival period in Common Cobra venom group was proved to be statistically significant. P value is 0.009(one tail). (Tables 1 to 4)

Impact Statement:

From the observation and analysis of the data, it is observed that *Arkamool swaras* is efficient against Common Cobra venom and Russell's viper venom as a first aid measure because.

- It delays the duration of appearance of symptoms.
- It increases the duration of survival period.
- It does not interact with PVASVS.

Discussion

As revealed in literature review very few '*in vivo*' studies have been published for antiophidian drugs. Usual method for antiophidian drugs seems to be '*in vitro*' study or '*pre incubation*'study. The' *in vitro*' study may not be applicable to a living organism, pharmacodynamics may change in different animals& for snake venom '*in vitro*' studies the assumption can be stated as "The drug interacts chemically with the venom compounds & neutralize them or binds with the components making them pharmacodynamically inactive." Preoccupation study also assumes the first part of the above assumption namely chemical neutralization of venom components.

Any drug which acts by any other mode of action i.e. other than chemical neutralization cannot be studied by these methods. This is particularly true of drugs acting on nervous system which primarily act by blocking of receptor sites or competitive inhibition. Both these methods give results which seldom stand true in clinical situations. Thus '*in vivo*' study becomes of paramount importance in proving the efficacy of antiophidian drugs.

It was very difficult to observe and distinguish the pre-paralytic and paralytic signs of the Common Cobra venom. It was impossible to record the pre-paralytic signs. Paralytic signs e.g. tremors, paralysis, convulsion in Common Cobra venom i.e. control group I were observed. As Russell's viper venom is haemotoxic, external bleeding from mouth, nose, ear and necrosis at the bite site are the common symptoms in humans. But these symptoms were not observed in Russell's viper venom group i.e. control group II.

Conclusion

The present study confirms the *'Vishaghna'* property i.e. Antiophidian property of the *Arkamool swaras.*

Arkamool swaras is useful as a first aid measure in snake venom because, it delays the onset of symptoms in both venoms, it increases the survival period, and it does not interact with PVASVS.

Thus, the above study shows that *Arkamool swaras* is efficient as a first aid measure in Common Cobra and Russell's viper snake venom poisoning.

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OBSERVATIONS:

Table 1: Appearance of Tremors in minutes

Test	Common Cobra Control Group Gr. I	*Arkamool Swaras* Gr. II
Mean	36	42.66666667
Standard Error	3.785938897	1.763834207
Standard Deviation	6.557438524	3.055050463
Range	13	6
Minimum	29	40
Maximum	42	46
Sum	108	128
Count	3	3

Appearances of tremors were prolonged by 6 min in Group II.

Table 2: Appearance of Paralysis in minutes

Test	Common Cobra Control Group Gr. I	*Arkamool Swaras* Gr. II
Mean	43	54.66666667
Standard Error	5.859465277	3.711842909
Standard Deviation	10.14889157	6.429100507
Range	20	12
Minimum	32	50
Maximum	52	62
Sum	129	164
Count	3	3

Appearance of paralysis was prolonged by 11 min in Group II.

Table 3: Appearance of Convulsion in Minutes

Test	Common Cobra Control Group Gr. I	*Arkamool Swaras* Gr. II
Mean	48	67
Standard Error	5.291502622	5.567764363
Standard Deviation	9.16515139	9.643650761
Range	18	18
Minimum	38	60
Maximum	56	78
Sum	144	201
Count	3	3

Appearance of convulsion was prolonged by 19 min in Group II

Table 4: Duration of Survival Period in Minutes

Test	Common Cobra Control Group Gr. I	*Arkamool Swaras* Gr. II
Mean	59.33333333	81.33333333
Standard Error	3.282952601	4.666666667
Standard Deviation	5.686240703	8.082903769
Range	11	16
Minimum	53	74
Maximum	64	90
Sum	178	244
Count	3	3

Duration of survival was prolonged by 22 min in Group II.

Table 5: Duration of Survival Period in Minutes

Test	Russel's Viper Control Group Gr. III	*Arkamool Swaras* Gr. IV
Mean	121.3333333	161.6666667
Standard Error	0.666666667	22.73274682
Standard Deviation	1.154700538	39.37427248
Range	2	71
Minimum	120	136
Maximum	122	207
Sum	364	485
Count	3	3

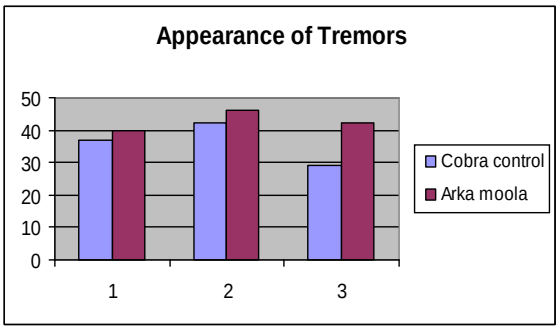
Duration of survival was prolonged by 40 min in Group IV.

GRAPHS OF OBSERVATIONS

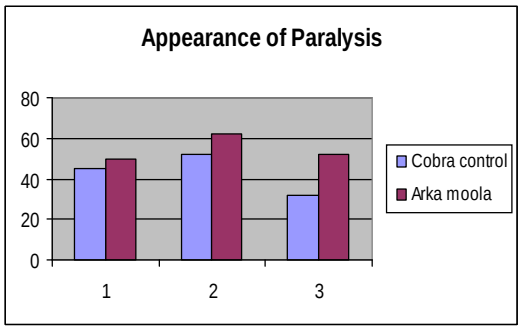
X Axis – Mice in that group

Y Axis – Appearance of signs in minutes

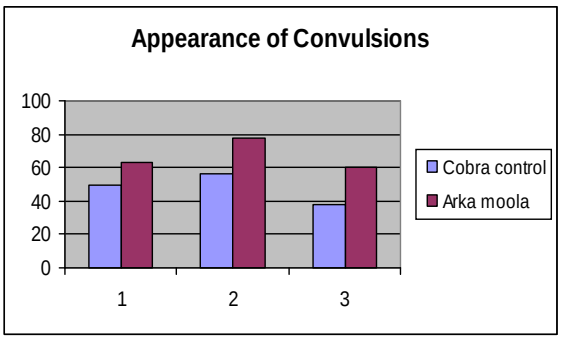
GRAPH 1



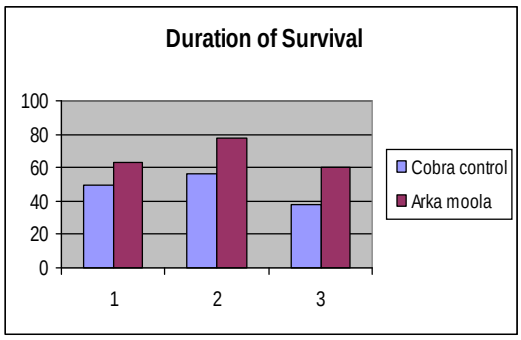
GRAPH 2



GRAPH 3



GRAPH 4



GRAPH 5