Review Article

Makshika Visha - The Concepts of Honey Bee Envenomation in Ayurveda

Shobha Bhat K*, Vishwesh BN**

Abstract

Human being is afraid of a multitude of dangers he has to encounter for his survival. These threats range from diseases of endogenous origin or exogenous factors like bites or stings of various animals. Knowingly or unknowingly, human beings are subjected to the exposure of poisons or toxins. Poisoning cases due to insect bites are very common in clinical practice. People are often bitten by mosquitoes, flies, and spiders or stung by ants, bees, yellow jackets, wasps, hornets and scorpions. Although they are not usually serious, insect bites and stings can be itchy and painful and in some cases may need an emergency medical visit.

The *damshalakshanas* of different types of *Keeta* and a wide range of drugs used to treat the same is explained in detail in Ayurveda. The main objective of the present article is to put on display the commonest clinical presentations and treatment of *Makshikavisha* stumbled upon in day to day practice.

Keywords: Apitherapy, *Keetavisha*, *Makshika*, Honey bee, Venom.

Introduction

Ayurveda has gone through several stages of development in its long history. Agadatantra is one among the eight branches of Ayurveda. This deals with the effects and treatment of poisonous substances, both animate and inanimate. Right from the beginning, poison is a subject that has fascinated human beings. Poison has been a challenge and threat to well being and even existence of life. Knowingly or unknowingly, human beings are subjected to the exposure of these poisons or toxins.

During the summer and rainy months and in warm climates year-round, people are often bitten by mosquitoes, flies, chiggers, ticks, and spiders or stung by ants, bees, yellow jackets, wasps, and hornets. Most people who are stung experience a local reaction with redness, pain, swelling and some itching only at the sting site.

It is estimated that about 1-2million people in India are severely allergic to the venom of a stinging insect. Each year 90 to 100 deaths are reported from sting reactions. More people die each year from the effects of insect venom than from snakebites.[1] Exposure to most of these organisms usually causes cutaneous affections. Insect poisoning causes injection of venom, physical trauma while burrowing the skin, sensitization reaction both local & systemic, allergic reactions which include secondary infections, contact reactions to the secretions, reaction to retained mouth parts and transmission of infectious diseases.

Acharya Charaka has classified *keeta* to be of two types-*Dooshivishaja* and *Pranahara.*[2] Sushruta has classified insects on basis of the *doshic* predominance as[3] *Vataja* (18 types), *Pittaja* or *Aagneya* (24 types), *Kaphaja* or *Soumya* (13 types), *Sannipataja* (12 types). He has again mentioned *keeta* to be of two major types based on the potency of their *visha* as *Mandavishakeeta* and *Teekshnavishakeeta.*[4] *Keeta* found in clinical practice are either of *Mandavishaja* or *Dooshivishaja* variety.

The largest phylum 'Arthropoda' consists of 3 subphyla, comprising 9 classes. Class Insecta is the largest of the arthropod classes, containing hundreds of species.

*Associate Professor, Department of Agadatantra, Faculty of Ayurveda, IMS, BHU, Varanasi 221005.
**Associate Professor, Department of Prasootitantra and Striroga, SDM College of Ayurveda, Tannerhalla, Hassan, Karnataka.
Correspondence to: Dr Shobha Bhat K, Department of Agadatantra, Faculty of Ayurveda, IMS, BHU, Varanasi 221005.
E-mail Id: drbhatshobha@gmail.com

The common biting and stinging insects are explained in Table 1.[5] The characteristics produced by their bites or stings are explained in Table 2.[6]

The differences are due to the nature of the bite or sting. Venomous insects attack as a defense mechanism, injecting painful, toxic venom through their stingers. Non-venomous insects bite and usually inject anti-coagulant saliva in order to feed on blood. Although local irritation and "allergic" reactions do occur from non-venomous bites, severe reactions such as anaphylactic shock usually only happen from venom stings.

Venomous (Stingers)	Non-venomous (Biters)
• Bees • Wasps • Hornets • Yellow jackets • Fire ants	• Mosquitoes • Fleas • Ticks • Lice • Scabies • Bed bugs

Table 1.Common biting and stinging insects

Symptoms	Venomous	Non-Venomous
Pain	Always	Uncommon
Redness	Can be intense	Mild or absent
Itching	Sometimes	Always
Swelling	Can be intense	Mild or absent
Allergic reactions	Common	Rare

Table 2.Characteristics of Bites/ Stings

Local & Systemic Reactions[7]

Venomous stings are always very painful, red, and swollen up to 12 inches around the sting site. This is called a local reaction. In sensitive individuals, a systemic or "whole body" reaction occurs, with redness, hives (itchy raised skin lumps), and swelling far away from the sting site. These systemic reactions can progress to involve the airways and circulation and may be life-threatening. Obviously it is important to know the difference between local and systemic reactions so that affective treatment can be planned.

Makshika Visha

Nirukti

The word *makshika* is also referred to as *makshi*. It is a *keetabheda*.

"*Janahaenam kopam kurvantiiti makshika*" means that which causes anger in people is termed as *makshika*. May be it causes anger because it causes injury to them by its bite.

Classification

Sushrutain Kalpasthana has classified the *makshika* to be of six types:[8]

1. Kantarika
2. Pingala
3. Krishna
4. Madhulika
5. Kashayi
6. Sthalika

Signs and Symptoms produced by *Makshikadamsha*

- Almost all the classical texts explain the signs and symptoms produced by the *makshikadamsha*. Though Charaka has not mentioned about the type of *makshika*, he mentions that their bite causes *pidakas* of blackish brown color with instant exudation. The patient suffers from burning sensation, fainting and fever. The *sthagika* variety is incurable and it causes the death of the patient.[9]

According to Acharya Sushruta, there are six types of *makshika*. Their bite causes itching, swelling, burning sensation and pain. Among them *kashayi* and *sthagika* are incurable and their bite is marked by the above said symptoms as well as blackish eruptions and other complications like pyrexia etc.[10]

Vagbhata in Ashtangasamgraha describes the same as described by Sushruta. He describes the *lakshana* of *makshikadamsha* as formation of *pitaka*, *shyavavarna* at the site of bite and increased exudation or *srava* from the bite. According to him, *makshikadamsha* usually occurs in the eyes. There is excess of swelling

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due to this, along with burning sensation & itching and among its varieties, *sthagika* is to be rejected for treatment as it is *asadhya*.[11]

Treatment of *Makshikadamsha*

The main aim of treatment is to give relief to the pain, to avoid further complications, treatment for the poison, treatment for the symptoms and psychological approach.

Acharya Sushruta has mentioned the application of paste of *Krishna valmika* (black earth or mud of ant hill) along with *gomutra* (cow's urine) in *makshikadamsha*.[12]

In Ashtangasamgraha, Vagbhata explains the use of *tagara* (Valerianawallichii), *nagara* (Zingiberofficinale Rosc), *nagakesara* (Mesuaferrea Linn) and *marica* (Piper nigrum Linn) both for *pana* and *lepana* as a remedy for *makshikavisha*.[13]

Yogaratnakara describes the yoga, which is a combination of *somavalka* (Acacia suma Buh Ham), *ashvakarna* (Dipterocarpusturbinatus Gaertn), *gojihwa* (Onosmabracteatum Wall), *hamsapadi* (Adiantumlunula tum Burm), *rajanidvaya* (Haridra-Curcuma longa Linn, Daruharidra-Berberisaristata) and *gairika*, which is to be applied in the form of *lepa* in *makshikadamsha*.[14]

According to Kriyakaumdi, a *Malayalamvishachikitsa* text, the sting must be first removed from the bite spot. Then the site must be made wet with salt-water repeatedly. The author also describes that the bite by a bee can be cured by *lepa* and *pana* of *tagara* (Valerianawallichii), *shunti* (Zingiberofficinale Rosc), *nagakesara* (Mesuaferrea Linn), *marica* (Piper nigrum Linn) and also by the application of *Saindhava* (Rock salt) mixed with ghee.[15]

Apart from these, medicines used in day to day practice include oral medications like *Dashangagutika*, *Vilwadigutika*, *Vishavilwadigutika*, *Dooshivisharigutika*, *Amritottarakashaya*, *Punarna vadikashaya*, *Guloochyadikashaya*, *Patolakaturo hinyadikashaya* etc.

External modalities include *lepa*, *seka* or *avagaha* with drugs like *Vilwadigulika* (Kaphavata), *Shigrupunarnavadi* yoga (Kapha-vata), *Haridra* (Kapha-vata), *Shatadhauta Ghrita* (Pittaghna), *Nalpamaradi* yoga (Kapha-pittaghna), *Kottamtagaradi* yoga (Tridoshagna), *Varachoorna* (Tridoshagna) depending on the dosic predominance of the presentation.

Modern Concepts of the Bee

Scientific classification	
Kingdom	Animalia
Phylum	Arthropoda
Class	Insecta
Order	Hymenoptera
Suborder	Apocrita
Family	Apidae
Subfamily	Apinae
Tribe	Apini
Genus	*Apis*
Species A. mellifera-western honeybee A. florea A. dorsata A. cerana-eastern honeybee	

Among the many species of insects, only very few have the capability of defending themselves with a sting and venom injection during stinging. All insects that can sting are members of the order Hymenoptera, which includes ants, wasps and bees. Since the sting is believed to have evolved from the egg-laying apparatus of the ancestral, hymenopteran species, only females can sting. The sting is always at or near the abdominal end, rather than the head. Therefore the pain inflicted by a honeybee, defending its colony, is not caused by a bite, as is frequently said, but by a sting.

Bees are flying insects, closely related to wasps and ants. They are about 1.5 cm long, fairly hairy and brown with abdominal bands. They are adapted for feeding on nectar, and play an important role in pollinating flowering plants, and are called pollinators. There are over 16,000 described species, and possibly around 30,000 species in total. Bees may be solitary, or may live in various sorts of communities. They are angrier on cloudy, dark rainy days in early spring of the year.

Bee Sting-Causes

Hymenoptera are social creatures that typically sting to protect their colony, nest, or hive. Most stings are incited by proximity to the colony. Noisy or vigorous activity, bright or dark colors, and perfumes also may incite stings. In addition, these insects can release defense pheromones that attract other insects and induce them to sting. These pheromones are released during stinging or when an insect is smashed.

Signs and Symptoms

At the rear end of bees, there is a sharp, pointed barbed stinger, which the bee will stick something with and release venom into its victim. The stinger can be thought of as a sort of syringe, sharp, hollow tube. When a bee stings it injects a venomous fluid under the skin. Only the honeybee leaves her stinger, with its venom sac attached in the skin of its victim. Since it takes two to three minutes for the venom sac to inject all its venom, instant removal of the stinger and sac usually reduces harmful effects.

A honeybee worker, stinging the relatively tough human skin, is unable to withdraw its sting lancets because of the fine barbs. Upon stinging someone, the bee then will immediately die, this is because when the bee pulls it stinger out to fly away, the venom sac and muscles are torn out of it, killing it. This leaves the stinger inside the victim.

When one is stung, it is shortly followed by intense pain, swelling and reddening of the site where one was stung. In the center of a bee sting, you see a small black dot, which is the stinger. Reactions vary among those who get stung. They range from mild discomfort and swelling to an allergic reaction to bee venom, and some can die from a bee sting if they remain untreated for too long. "Killer Bees" (or African Honey bees), have been known to kill an occasional person by stinging them to death. They can sting one individual over one hundred times in a matter of moments.

Reactions to Bee Sting

Local reactions involve edema at the site of the sting. This comes on over several hours and varies in size, but it can affect a hand or even an entire limb. In a dependent area, this can lead to blistering and sometimes secondary infection.

Local reactions may produce pain-immediately after sting, edema which is marked and may extend to 10 cm from site of envenomation, bleeding at site of sting, pruritus, vasodilatation producing a sensation of warmth, nausea or vomiting, distal sensation loss from stings over peripheral nerve and corneal ulceration from corneal stings.

If the reaction progresses quickly to sites other than the sting site or is followed by difficult breathing or choking at the throat, the person is experiencing a "systemic" allergic reaction (anaphylaxis) requiring emergency medical treatment.

Generalized reactions may produce urticaria, confluent red rash, shortness of breath, wheezing, edema in airway, tongue, or uvula, weakness, syncope, anxiety, confusion or chest pain.

Bee Venom

Bees produce venom as a self-defense mechanism to protect themselves and their hives. It is synthesized in the venom glands of worker and queen bees and stored in their venom sacs. During the stinging process, it is expressed through the sting apparatus. The production of potent bee venom requires good nectar, honey and pollen sources. Consequently, bees have more potent venom during the summer. Bees raised without pollen have little and less effective venom in their venom sacs.

Bee venom is a colorless liquid that dries to a powder. The crystallized venom's color ranges from white to brownish yellow.

The darker coloration is the result of contamination of the venom and oxidation of its constituents. Pure Whole Dried and Whole Dried Bee Venom are most commonly used in drug preparations.

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Class of Molecules	Component	% in Dry Venom
Enzymes	Phospholipase A2 Hyaluronidase Acid Phosphomonoesterase Lysophospholipase β-glucosidase	10-12 1.5-2.0 1.0 1.0 0.6
Other proteins and peptides	Melittin Pamine Mast Cell Degranulating Peptide (MCD) Secapin Procamine Adolapin Protease inhibitor Tertiapin	40-50 3 2 0.5 1.4 1.0 0.8 0.1
Physiologically active amines	Histamine Dopamine Noradrenaline	0.5-2.0 0.2-1.0 0.1-0.5
Amino Acids	α-aminobutyric acid β-amino acids	0.5 1
Sugars	Glucose & fructose	2
Phospholipids		5
Volatile compounds		4-8

Table 3.Composition of venom from honeybee

Physical Characteristics of Venom and its Probable Action

Honeybee venom is a clear, odorless, watery liquid. On coming into contact with mucous membranes or eyes, it causes considerable burning and irritation. Venom contains a number of very volatile compounds which are easily lost during collection.

Bee venom is cytotoxic (i.e. cell-destroying), and has contradictory effects of inhibiting the nervous system, while stimulating the heart and adrenal glands. Phospholipase A destroys cells by breaking up phospholipids, the main component of cell membranes. Lecithinase converts lecithine to lysolecithine (or phospholipase B), which breaks down the membranes of blood cells. Hyaluronidase acts as a spreading factor, by breaking down hyaluronic acid, a polysaccharide interstitial fluid in connective tissue. Mellitin, a 26 amino acid peptide, acts to destroy blood cells by breaking up their membranes. It also lowers blood pressure, causes histamine release, and is the main pain-causing component. Both mellitin and apamin cause the body to release cortisol, a natural steroid, while peptide 401 is a powerful anti-inflammatory agent. The main amino acids in bee venom are cysteine and methionine, both of which contain sulfur. Sulfur is important in inducing cortisol release from the adrenal glands.

Histamine causes itching and pain at the site of the sting. The acids present, which include formic, hydrochloric and orthophosphoric acids, are now believed to be much less important in causing pain than was previously thought.

The median lethal dose (LD_{50}) for an adult human is 2.8 mg of venom per kg of body weight. For a child weighing 10 kg, as little as 90 stings could be fatal. Therefore, quick removal of the stings is important. However, most human deaths result from one or a few bee stings due to allergic reactions, heart failure or suffocation from swelling around the neck or the mouth.

Bee venom has recently found a use in a form of complementary therapy. In bee venom therapy, bees may be induced to sting the affected area, or the venom may be applied by intramuscular injection. The venom stimulates the release of cortisol, and so is effective in the treatment of rheumatic disorders such as Multiple Sclerosis, Rheumatoid arthritis and gout. Mellitin is believed to be the main active agent. Bee venom therapy is one aspect of apitherapy-use of bee products for curing disease. Mellitin is also being

investigated as an anti-cancer agent. By modifying the mellitin molecule to prevent allergic reaction, and attaching a cancer-specific antibody (this combination of toxin and antibody is called an immunotoxin), researchers hope to produce a 'magic bullet' treatment-so called because it would only destroy cancer cells.[17]

List of Diseases Improved or Healed by Apitherapy[18]

Chronic pain, premenstrual syndrome, multiple sclerosis, arthritis-many types, epilepsy, decrease in blood viscosity and coagulability, infectious spondylitis, polyarthritis, myositis, iritis, arthritis, bursitis, some types of cancer, migraine, rhinosinusitis, polyneuritis, neuralgia, malaria, tropical ulcers, ligament injuries, sore throat, intercostal myalgia, slowly healing wounds, keratoconjunctivitis, asthma etc.

Conclusion

Bites from honey bee are commonly encountered in clinical practice. Ayurveda offers a simple and good remedy for the local symptoms produced from these bites. Thus acquaintance of the *makshikavisha* along with the signs and symptoms produced from these and their treatment is obligatory for a clinician.

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