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Unveiling the role of Ivermectin for effective control of Ticks! A myth

Muhammad Talha Talib[1], Naveed Aslam[2], Muhammad Bilal Arshad[3], Jawad Aslam[4], Arslan Muhammad Ali Khan[5*]

[1]Department of Clinical Sciences, University of Veterinary and Animal Sciences Lahore, Jhang Campus, Punjab, Pakistan
[2]Farm Manager & Veterinarian, Rathore Dairies, Pakistan
[3]Faculty of Veterinary Science, University of Agriculture, Faisalabad, Pakistan
[4]Department of Physiology, University of Agriculture, Faisalabad, Pakistan
[5]Department of Parasitology, University of Agriculture, Faisalabad, Pakistan
*Corresponding author: **arslanrajpootkhan374@gmail.com**

ABSTRACT

Ticks pose a serious threat to human beings as well as livestock in Pakistan. These can disseminate a variety of pathogens, including bacteria, viruses, and protozoa like rickettsia and spirochetes. Every ecological and topographical region in Pakistan is home to ticks. Pakistan has records of both cattle theileriosis and bovine babesiosis. A virus called Crimean-Congo hemorrhagic fever (CCHF) is transmitted by ticks and affects those who work with cattle, such as veterinarians, hospitals, and slaughterhouse employees. At least 40 species of ticks exist, the majority of which being *Haemaphysalis*, *Hyalomma*, and *Rhipicephalus*. In Pakistan, goats are the primary hosts of ticks throughout the summer months of June to September. Anaplasma, Babesia, and Theileria species are among the tick-borne illnesses that are more prevalent in sheep than in goats. Occasional cases of CCHF outbreaks with a 24% mortality rate have been reported in Pakistan over the past sixteen years. To stop the spread of zoonotic diseases and manage tick populations, the provinces of Sind and Punjab have launched massive tick control initiatives. These ticks can be controlled in various ways but ivermectin has significant effects and most farmers are using it to combat tick- and tick-borne diseases.

Introduction

Ticks are ectoparasites found worldwide, primarily in tropical and subtropical regions, including Pakistan, on both domestic and wild animals. Numerous bacterial, viral, protozoal, and rickettsial ailments can be spread via them [1]. Humans, animals, birds, and wild species can all contract these diseases, both directly and indirectly. CCHF (Crimean-Congo Haemorrhagic Fever) is the most common viral infection and the leading cause of illness in Pakistan [2].

Numerous investigations about the incidence of ticks on cattle have been undertaken in various parts of Pakistan. Eighteen thousand livestock animals from the three districts of the Faisalabad division, four thousand each of cattle, buffalo, sheep, and goats were checked for tick (acari) infestation. Cattle had the greatest rate of tick prevalence (28.1%), followed by sheep (19%), buffaloes (15%), and goats (12%) [3].

Many factors, including climatic conditions, the relationships and activities of various animal species, farmer's training and expertise, and livestock farm management procedures, are responsible for the disparity in tick incidence in different places. The findings clearly show that there are notable variations in tick incidence throughout various animal species. Throughout the investigation, it was discovered that buffaloes were often stall-fed with very few exceptions, flocks of small ruminants (sheep and goat) grazed together, and bovines grazed apart. This may have reduced the number of ticks from widely contaminated fields that regularly fed animals (goats and buffaloes) were exposed [4]. Further research on the genetic makeup of these animals may be necessary to investigate the possibility that genetic variations could result in varying resistance to ticks.

Economic importance of ticks:

Pakistan relies on the agricultural and livestock industry to supply a variety of excellent products including meat, milk, and wool. These products are the major income source for poor farmers all over the world. The impact of tick infestation is very harmful to animals, human beings, and the environment because these arthropods feed on blood from different parts of the animal and human body. Through their sucking and eating, ticks spread a variety of bacterial, viral, and protozoal pathogens that cause diseases that affect the production of meat, wool, and milk. On the other hand, severe tick infestation in both small and big ruminants results in skin and hide impairment, anemia, and itchiness, all of which stress out both people and animals [5].

Scientists reported that environmental changes are contributing to an increase in the prevalence of tick and tick-borne diseases (TBDs), which causes significant global losses in cattle revenue. According to estimates, tick infestations generate worldwide financial losses of 14,000–18,000 million USD while 498.7 million USD is spent annually on tick and TBD control in Pakistan's and India's cattle industries [6].

Chemical Control:

Various acaricide formulations have been used to eradicate livestock ticks. These are direct-contact, systemic poisons that can infect both domestic and wild animals. They come in a variety of forms, including wettable powder (WP) and emulsifiable concentrate (EC). Ticks' neurological systems can be damaged by insect growth regulators, or acarines, which are the most effective way to control tick populations [7].

These chemical acaricides are delivered to bovines by a variety of sprayers, such as hand sprayers that use pheromones or bucket pumps, or even by dipping the livestock animals into ponds that have been treated with acaricides. Numerous researches have documented the detrimental consequences associated with the dipping approach [8]. Before dipping animals in a treated pond, it is imperative to properly inspect any wounds on their bodies. Failure to do so can result in acaricide toxicity and a host of skin illnesses. The animals who were fatigued, thirsty, and younger than six months could not be dipped. Before using acaricides, the aquariums should be clear of organic debris, such as animal dung, to reduce the toxicity of the chemicals. Higher concentrations of acaricides can also be employed. This procedure can be completed by two attendants, and appropriate safety precautions ought to be used. It is important to provide the dipping tank or pond's proper dimensions. Pakistan does not yet have the facilities to test the dipping strategy. This costly tactic is employed in opposition to a sizable herd of cattle. Most acaricides studied on ticks are those in the following groups: clenpyrin, formamidines, chloromethiuron, and chlordimeform. Many countries, including Pakistan, have utilized ivermectin, neguvon, ecofleece, deltamethrin 2.5%, cyclomethrin, and cyclprin against tick species. These substances have shown positive outcomes and decreased tick infestations [9].

Mechanism of action

Ivermectin and similar pharmaceuticals react by blocking the helminth and insect's muscle and nervous system functioning. The medicinal

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product attaches itself to glutamate-gated chloride channels found in invertebrates' nerve and muscle cells. The arthropods particularly ticks become paralyzed and die due to the binding pushing the channels open, increasing the rate of flow of chloride ions and hyperpolarizing the cell membranes [10]. Because mammalian glutamate-gated chloride channels are limited to the brain and spinal cord, ivermectin is safe for mammals when used at the recommended therapeutic doses to treat parasite infections. Additionally, the causative ivermectin is unlikely to bind to other mammalian ligand-gated channels and typically does not cross the blood–brain barrier [11].

Other veterinary uses

The gastrointestinal tracts of small and large ruminants are frequently treated with ivermectin to control parasitic worms. Normally, these parasites enter the animal when grazing, transit through the colon, settle, and grow in the intestines. Afterward, they generate eggs, which exit the animal through its droppings and can contaminate fresh pastures. Because of a rise in anthelmintic resistance, ivermectin is only effective in killing a portion of these parasites. The reason for this resistance has been the 40 years of continuous usage of the same anthelmintic medications.

Ivermectin is frequently administered to dogs as a heartworm prophylactic. Ivermectin can cause severe poisoning in dogs that have abnormalities in the P-glycoprotein gene (the MDR1), which are frequently collie-like herding dogs [11]. Other dog breeds that are susceptible to ivermectin's toxic effects include the Australian Shepherd, Rough Collie, Smooth Collie, Shetland Sheepdog, and others. These breeds also have a high frequency of mutations in the MDR1 gene, which codes for P-glycoprotein. Ivermectin toxicity may affect kittens, according to clinical data [12]. There is a topical ivermectin 0.01% formulation available for treating cat ear mites. Ivermectin is occasionally sprayed or administered intraperitoneally to reptiles as an acaricide [13]. Although this is effective in certain situations, caution is needed because ivermectin can cause severe allergic reactions in certain reptile species. Use is especially not advised in turtles [14].

Conclusion

Researchers' interest in examining ivermectin's efficacy against ticks has grown during the last ten years. Ivermectin's acaricidal efficacy has been shown in numerous preclinical investigations, which also explain the drug's mode of action, lethal dose, and relative biosafety and biodegradability in nature. These findings suggest that ivermectin could be a viable substitute for chemical acaricides. To standardize the experimental design, define the appropriate doses to give animals, ascertain the synergistic and antagonistic effects, and investigate the toxicological profile of ivermectine in mammals, more in vivo, and clinical research is required.

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