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Review Article

Review on Control of Cowdriosis in Ruminants -

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Abstract

Heartwater is an acute, often fatal, non-contagious and tick-borne disease of domestic and wild ruminants that is transmitted by *Amblyomma* ticks. It is an important cause of death in cattle, sheep, and goats in regions where tick vectors are present. In Africa, heartwater is a major obstacle to the introduction of highly productive animals into endemic areas. The distribution of the disease follows a presence of vector *Amblyomma*, among them *Amblyomma variegatum* is the most important species which is widely distributed in the sub-Saharan Africa including Ethiopia. The control of disease involves controlling the tick vector, establishing endemic stability, performing immunization by infection and treatment, and preventing the disease by regular administration of prophylactic antibiotics. Most of these methods are subject to failure for various epidemiological reasons, and serious disease outbreaks can occur. Prophylaxis is effective, but very expensive, and the logistics are daunting when large herds of animals are involved. The development of a safe, cheap and effective vaccine is the only way for controlling of heartwater. Generally, control of cowdriosis should consider using cost-effective, environmentally safe, sustainable and integrated control methods including establishment of endemic stability.

Keywords: Amblyomma; Endemic stability; Heartwater; Tick-borne disease; Vaccine

ABBREVIATIONS

A. gemma: Amblyomma gemma; A. hebraeum: Amblyomma hebraeum; A. lepideum: Amblyomma lepideum; A.variegatum: Amblyomma variegatum; C. ruminantium: Cowdria ruminantium; E. ruminantium: Ehrlichia ruminantium; TTBD: Tick and Tick-borne disease; TBD: Tick-borne disease

INTRODUCTION

Tick-borne diseases affect most of the world's cattle population and are widely distributed throughout the world, particularly in the tropics and subtropics. The complex of vector-borne disease directly or indirectly constrains the livestock industry, which is of fundamental importance to rural people in sustaining not only their food supply, but also their daily income and other agricultural activities [1]. Ticks and Tick-Borne Diseases (TBDs) are some of the most significant and serious constraints to the improvement of livestock production in Ethiopia. TBDs and their vectors are wide spread in the country. They affect production in various ways, such as growth rate, milk production, fertility, the value of hides and mortality. In Ethiopia, several tick species are widely distributed and the domestic ruminant species dwell diverse agro-climatic zones and are raised under various production systems. This in turn results in abundance of various vector species and vector-borne diseases especially ticks and tick-borne infections like anaplasmosis, babesiosis, Cowdriosis (heartwater), and theileriosis [2].

Heartwater or cowdriosis is an infectious, non-contagious, TBD caused by a small, gram negative, pleomorphic coccus, and an obligatory intracellular rickettsial pathogen previously known as *Cowdria ruminantium* but recently reclassified as *Ehrlichiaruminantium* [3]. It is the most important tick-borne disease of exotic and cross-bred cattle and is transmitted by the ticks of the genus *Amblyomma* and affects domestic ruminants and several wild ruminants such as buffalo, giraffe, and antelope as well as some wild rodents [4]. The course of the disease varies from peracute, acute, sub-acute to mild, depending on age, immune status, breed and virulence of the strain [5]. The incubation period of the disease is influenced by the species of animal affected, immune status, breed, age, route of infection, virulence of the organism and amount of infective materials administered [5,6]. The disease is characterized by fever, nervous signs, hydropericardium, hydrothorax, lung edema and high mortality [7].

Cowdriosis is a serious constraint to livestock improvement programs throughout sub-Saharan Africa and through its occurrence on some islands in the Caribbean, poses a potential threat to ruminant species in mainland North, Central and South America. It is the second most important TBD after East Coast Fever in Africa [8]. In countries or regions where there is endemic stability, losses from heartwater are minimal until new animals are introduced. Wild ruminants may play a role as reservoirs, and the wide host- ranges of the pathogenin wildlife is important in the epidemiology and spread of the disease [9,10].In order to upgrade the livestock industry and prioritize future research on the development of improved control measures, it is essential to provide an accurate definition of the spatial distribution of the disease risk and determine the prevalence of infection in the vector population and domestic ruminant hosts [4].

Despite the fact that heartwater transmission was elucidated and causative organism described, control of disease remains a serious problem. At present, there is a lack of safe, practical and effective vaccine, and in endemic areas, the control of the disease relies mainly on chemical acaricides to prevent tick transmission and antibiotic treatment of clinical cases. The main problem encountered with the control of the disease is the lack of efficient vaccine in the field. This is thought to be related to the high genetic diversity of strains circulating in a particular area [11]. In search of better ways of control, research has been greatly hampered by the inability to cultivate the organism in vitro. In the early years, it was recognized that animal which recovered from the disease acquired immunity. Since then, numerous attempts at producing a vaccine have been made. Control of heartwater also aimed at controlling the vector. The ideal control program is likely to induce a combination of different methods: genetic resistance, strategic tick control, vaccination and treatment of early clinical cases. Vaccination is likely to be the most economical and sustainable method of controlling the diseases caused by ticks [12]. Therefore, the objectives of this paper are to review the possible control measures of heartwater in Domestic Ruminants and to highlight its epidemiology.

EPIDEMIOLOGY

There is scanty information on the epidemiology of the disease in most parts of Africa including Ethiopia, and studies into the incidence and prevalence of infection have recently been hampered by the lack of sensitive and specific diagnostic tools that are particularly suitable for use in most countries of Africa.

Distribution and transmission

The first report of heartwater as a disease entity was recorded in 1877 in South Africa [13]. From the early 20th century onwards, heartwater was reported in most other sub-Saharan African countries [14] and in several Caribbean islands [5] and a number of other *Amblyomma* species were shown to be capable of transmitting the organism. Distribution of heartwater coincides with that of the Amblyomma ticks, which require a warm humid climate and bushy grass. Nevertheless, all countries where known *Amblyomma* vectors are present are at risk of introduction of the disease, particularly where the disease is present in neighboring countries. The endemicarea includes the whole of Sub-Saharan Africa, Madagascar and, also, the Caribbean Islands, threatening the American mainland [15].

Heartwater is transmitted by many three host ticks of the Amblyomma genus that carry the agent from carrier animals to susceptible ones especially A. *variegatum,* A. *hebraeum* (in southern Africa), A. *gemma* and A. *lepideum* (in Somalia, East Africa and Sudan). The ticks may pick up the infection as larvae or nymphs by feeding on acutely ill or sub clinically infected animals and transmission of the disease can be by adult and nymph ticks in the field through transstadial transmission, i.e. from larvae to nymph, from nymph to adult and from larvae through nymph to adult (even if the nymph feeds on a non-susceptible animal) [14].

Among the several species of Amblyommacapable of transmitting *E. ruminantium*, A. *variegatum*and *A. hebraeum*are most important globally [16]. However, several other species of Amblyommahave been known to play role in a given locality. *A. variegatum* (tropical bont tick) *is* by far the most important species on most of the African continent because it is the most widespread throughout sub-Saharan Africa and it has the widest distribution in Ethiopia. It accounts for 40% of the Ethiopian tick Population [17]. The distribution of this species covers most of sub-Saharan Africa as well as surrounding islands of Madagascar, La Reunion, Mauritius, Zanzibar, the Comoros and Sao Tomé [5]

The effectiveness of *Amblyommaspp*. as vectors for heartwater in certain area depends on their distribution, activity, abundance, and their adaptation to acquire and transmit infection from local wild or domestic carriers of *E. ruminantium*. Several wild ruminants can be infected and become subclinical carriers and reservoirs. Ticks feeding on them can transmit the disease to domestic ruminants [5].

In endemic areas, there has been evidence of transmission of heartwater vertically through colostrum of carrier dams to their calves [18].Transmission can also occur by intravenous inoculation of blood, tick homogenates or cell culture material containing *E. ruminatium* [5].

Occurrence and economic importance

The occurrence of cowdriosis is corresponds to the tick population in the area, which is heavily influenced by vegetation cover, season, breed, host density, latitude, altitude, management of grass and pasture, treatment intervention, type of soil, sun light, type of host, its development stage, rainfall, temperature and humidity [19]. In the drier parts of Africa, this frequently leads to an increased incidence of heartwater after heavy rains when peak numbers of ticks occur. But in regions where the climate is temperate and the rainy season is not well defined, occurrence of heartwater is not really seasonal and this is especially true in the Caribbean islands [20].

In the sub-Saharan region, the disease is one of the major causes of stock losses, and it has been estimated that more than 150 million animals are at risk in the area [12]. Imported breeds of cattle, sheep and goats are highly susceptible, but indigenous populations in endemic areas are often resistant to infection. Therefore, heartwater is a major obstacle to the introduction of highly productive animals into endemic areas and also it is a major disease problem when local animals are moved from heartwater-free to heartwater-infected areas [13]. The effects of dipping and environmental changes influence endemic stability, which is often difficult or impossible to manipulate. Mortality rates vary between 5% and 100% depending on virulence of the strain, immune status, age, breed and species involved [21].

The economic impact of the disease is, therefore, difficult to quantify, although estimates made indicated that, the losses can be enormous [22]. Whatever the actual costs may be, it is certain that the economic importance of heartwater in Africa is comparable to that of East Coast fever, trypanosomosis, rinderpest and dermatophilosis [23]. For instance, the total economic losses directly associated with heartwater have been estimated as US$ 5.6 million per year for cattle in Zimbabwe with the greatest components of economic loss were control (acaricide - used to kill ticks) costs (76%), followed by milk loss (18%) and treatment cost (5%) [24] and US$2 million per year for cattle and goats in Guadeloupe [14].

The occurrence of heartwater was confirmed long years ago in Ethiopia where ever the vector tick occurs [25]. But the epidemiology of the disease including the infection rate in vectors and the major vector in each agro-ecology was not been elucidated. In 1992 a devastating outbreak of heartwater have occurred in some dairy farms with significant mortality (25%) at Abernosa ranch where Boran x Friesian crosses are kept and several other suspected cases were observed in sheep and cattle in various parts of the country [26].

Bovine cowdriosis is also prevalent in the Gondar University dairy farm and can be detected throughout the year, but more often in the rainy season with an annual incidence of 12.33 animals/annum (15% of the herd) succumbing to cowdriosis in one susceptible dairy herd. The total economic losses during three years study period of this area (7884.67 US $) due to the disease are associated with deaths, the cost of acaricides, management cost, antibiotics, loss of meat and milk yield [27]. The annual fatality rate in this study was 8.1% of affected animals. In a similar study conducted in Arsi, Ethiopia the mortality rate was 15.71% [28]. Heartwater was also identified among a disease posing a major threat to dairy cattle production in Jimma town with prevalence of 5.6% affecting calves (5.6%), heifers (3.7%) and lactating cows (1.9%) [29].

CONTROL OF HEARTWATER

Tick-borne diseases are less dramatic in their effect than any other infectious diseases, but their control is less likely to be subsidized, making them a serious concern for livestock owners. Their overall control aims is to minimize the adverse effects of TTBDs by using cost-effective, environmentally safe, sustainable and integrated control methods [17]. The possibility of control of heartwater as like other TBDs is usually achieved through treatment of clinical cases, the control of tick vectors at times of high infestation by strategic use of acaricides and other practices, antibiotic prophylaxis [30], vaccinations, farming with animal breeds resistant to the disease [15], and the manipulation of tick populations to allow the establishment or maintenance of conditions of endemic stability [31].

Chemotherapy

Treatment of heartwater with antibiotics is only effective if animals are treated early at the onset of clinical symptoms and showed ineffectiveness when defined nervous symptoms occurred due to the acute nature of the disease, which does not always allow timely intervention to prevent a fatal outcome. In general, antibiotics of the tetracycline group (especially oxytetracycline) are the drugs of choice for successful treatment of heartwater and will allow immunity to develop. Doxycycline and rifamycin are also very effective, and a wide variety of sulfonamides have successfully been used in heartwater treatment. Treatment for ruminalatony, a commonly observed sequel to this disease, may be indicated, and diuretics may be useful to control fluid accumulations in body cavities [15].

Prophylactic use of routine oxytetracycline injections is also possible to protect susceptible animals against heartwater when they are introduced into an endemic area, aiming to allow the natural disease challenge to stimulate immunity in the animals [32]. The success of this regimen depends upon the animals becoming naturally infected during the time that they are protected by the drug [33].

Tick control

Since the earliest times, when the tick-borne status of heartwater was realized, tick control was advocated as a means to control the disease. Even after a vaccine had been developed tick control was still propagated as a supplement or in some cases even as an alternative control measure. Through the years it has become apparent that because of the great variation in the ecological conditions in the regions where heartwater vectors occur, and even between different farms in the same area, it is not possible to advocate a single control system. To develop strategies for integrated tick control, making maximum use of naturally induced host resistance to ticks, minimal use of chemical accentuates incorporating any traditional practices or remedies that appear to be of value [34].

Two methods, namely, intensive tick control and strategic tick control, have been identified as possible ways to control heartwater [35]. Both these systems have advantages and disadvantages and it is the farmer in particular who must decide which method is the most suitable for his specific circumstances and which he can consistently follow [36].

Intensive or total tick control involves the control of all stages of ticks throughout the year (reduction in Amblyomma tick numbers) in order to limit production losses and animal deaths resulting from ticks per se to a minimum. Intensive tick control, with reference to heartwater, is usually advocated for marginal areas only where *Amblyomma*ticks are only found occasionally on animals or for farms where the ecological conditions are unsuitable for the survival of these ticks. Although, eradication of Amblyomma species is extremely difficult, regular dipping will prevent a tick population explosion in such areas especially after good rains or accidental introduction of infected ticks. Intensive tick control measures would be beneficial in controlling heartwater and preventing its outbreaks, even in endemic areas [10] and has obvious advantages in which production losses due to tick-worry or TBDs will be kept to a minimum. The main disadvantage of total tick control, apart from the considerable cost of such a method, is that it will result in the loss of immunity of the animals to TBDs owing to lack of natural challenge resulting in vulnerability of the stock to disease and heavy losses occur if control regimen breakdowns [15,37].

Strategic tick control involves minimizing numbers of ticks in such a way that it promotes a stable disease situation and at the same time limits the adverse effects of tick worry, so that natural transmission of cowdriosis occurs and high levels of immunity are maintained. It is usually recommended that animals should be dipped only if they are carrying an average more than 10 adult Amblyomma ticks each [31]. This method would make provision for natural immunization or vaccination of young animals and the maintenance of immunity. The advantages of this method includes low costs of dipping, most animals will acquire a natural immunity against heartwater which will be maintained by repeated infection, and the incidental dissemination of infected ticks by stock movement or the development of dip-resistant tick strains poses no particular risk with regard to heartwater outbreaks. The disadvantages of strategic tick control includes higher cost of vaccination and also it needs more information on the epidemiology of heartwater including infectivity of ticks (percentage of infected ticks) [10].

Tick control using acaricides: Tick control of heartwater involves application of acaricides to animals at risk of infection. The disease can be successfully controlled if all the animals on the farm can be regularly dipped in chemical acaricides throughout the year [19]. Acaricide application is still the main tick control method in Ethiopia and the majority of tick infestations on local cattle is mild and can be solved by spraying a localised part of the animal such as axilla, ventrum, abdomen or udder which is common sites for *Amblyomma*ticks [2].

A multitude of acaricide were used and the selection of them depends on the persistence of the compound on the skin and hair coat, the likely hood of residues toxic to man appearing in the milk or meats, and whether or not ticks in the area have developed resistance to the particular acaricide [24]. Major chemicals that have been used for this purpose are arsenicals, chlorinated hydrocarbons, organophosphates, carbametes, flumethrin, and amides. Mode of applications for acaricides include topical wetting (like dips, hand spray (common in Ethiopia), pour on, put on, impregnated and systemic methods. Hand dressing is another common method of applying acaricides. But adverse human health impacts of this practice may occur due to lack of protective clothing and lack of a withdrawal period for milk after treatment [38]. Dipping has also a number of limitations e.g. sunny day is not suitable as it may result in higher level of thirst. Similarly, it is most important to restrict the animals from licking their body after dipping. Otherwise, it may cause huge economic loss in terms of mortality.

The disadvantages of this method are that the acaricides need to be applied continuously and are therefore costly and time-consuming, the compounds used are potentially hazardous to human health and the environment and, particularly if treatment is sustained over prolonged periods, it may result in development of acaricides resistance in tick populations and the disruption of endemic stability. Improper application/low concentration, rain-wash, in activation due to organic contamination and frequent use of one type are all causes of acaricides resistance in ticks. Example, A.variegatum is resistant to carbamates [34].

Biological method of tick control: Under natural condition several agents may play a significant role in reducing tick number. These include non-chemical tick control such as use of predators, parasites, pasture management (pasture spelling i.e., leaving pasture unstocked to break the tick life cycle, cut and carry system and rotational grazing), use of sticky plant on grazing land, sterile male release, selection of tick resistant breed, multiple species rearing, proper hygiene conditions, burning of waste near the animal shed, filling the crevices in the walls of farm and vaccination with tick antigens. Domestic chickens of indigenous varieties are opportunistic predators of ticks and if allowed to scavenge from tethered cattle during the early morning and in the late afternoon, they could have a positive impact on the control of ticks [39]. Red and yellow billed ox peckers (*Baphagus erythrorhychus* and *Bophagus africanus*, respectively), which are virtually obligatory predators of Ixodid ticks; take large numbers of Amblyomma from both domestic and wildlife species [40].

Apart from the use of chemical compounds for tick control, certain traditional practices, such as the hand picking of ticks, burning of attached ticks with hot iron, burning of pasture/grazing land and application of plant crude extract are widely used by cattle owners in rural areas of Ethiopia even though, it has certain demerits [2]. Traditional tick control methods used in Keffa, Illubabor and Wellega Provinces in western Ethiopia includes uses of plant extracts like Latexes of *Euphorbia obovalifolia* and *Ficusbrachypoda,* juice of crushed leaves of *Phytolaca dodecandra* and *Vernoniaamygdalina,* fruit juice of *Solanum incanum,* crushed seeds of *Lepidiumsativum* mixed with fresh cattle faeces, juice of crushed leaves and bark of *Calpurneaaurea* and commercially available spice of *Capsicum* species mixed with butter, were used by peasant farmers to control ticks [41].

Vaccination

Vaccination is the most useful disease control method for introducing improved or imported animals into heartwater-endemic areas, unless all transmission can be prevented by tick control. Vaccination is probably the best and most practical way to ensure immunization of the majority of young animals without the possible adverse effects of tick worry. Moreover, where resistance of *Amblyomma* to acaricides exists, vaccination may be the only possible method of control. In the absence of periodic stimulation of the immune system resulting from the bite of infected ticks, the duration of immunity after immunization varies greatly between different domestic ruminant species and also perhaps between individuals within species depending on the time at which the animals are treated therapeutically during the reaction next to immunization [42].

Infection and treatment method of vaccination: This method of vaccination is usually practiced in South Africa for large-scale immunization in older ruminants that have lost their innate age resistance against heartwater. It was based on the fact that young animal's possess an innate resistance to heartwater and it consists of infecting animals with a vaccine that contain virulent preparation of *E. ruminantium* [43] and treating the infection as soon as the febrile reaction commences. Animals are vaccinated in small groups (less than 20) and treatment with oxytetracycline is given whenever animals temperature is elevated until it returns to normal [10].

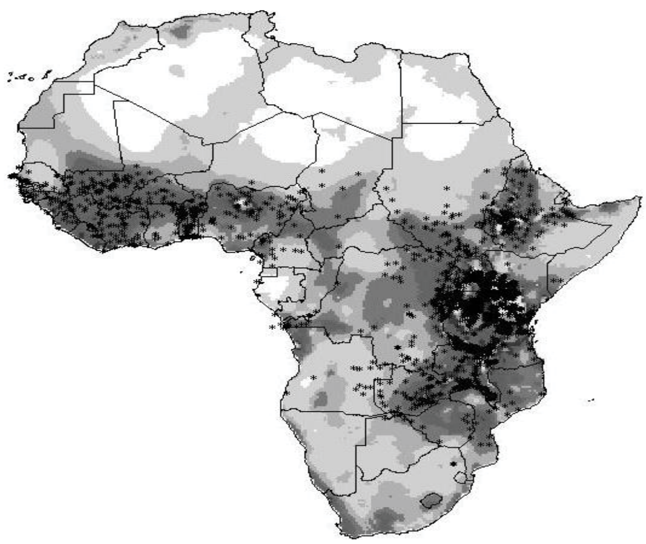

Figure 1: Distribution of vector of heartwater, A.variegatum, in Africa.

However, this method is not user-friendly as it is expensive and inconvenient because of the requirement of a cold chain for delivery, risk of transmission of blood borne pathogens and it is unreliable as breakdowns in immunity are common and deaths associated with vaccination occur. As an alternative, exposing young animals to infected ticks by introducing them into endemically stable areas during times of tick activity, rather than vaccination, is recommended to confer long term immunity [15].

Inactivated vaccines: An Inactivated heartwater vaccines consisting of culture-derived *E. ruminantium* organisms that are chemically inactivated and combined with an adjuvant have been developed [44]. In a field trial, an inactivated vaccine was used to immunize cattle, goats and sheep with significant reduction in mortality [21] and the advantage is that several field strains can be incorporated to make the vaccine more widely cross-protective. Although much safer than live vaccines, this inactivated vaccine required several doses spread over a period of weeks or months, during which the animals had to be kept tick-free [33].

Attenuated vaccines: Vaccine of this type was developed by attenuating *C. ruminantium* stock by *in-vitro* passage through endothelial cells and it could provide a cheap and effective protection of shoats against virulent challenges in endemic heartwater areas [16]. The principal advantage of using attenuated material for vaccination is that no subsequent monitoring or antibiotic treatment is required, but it doesn't protect against challenge from *E. ruminantium* isolates from geographically diverse backgrounds [45].

Recombinant vaccines: A recombinant vaccine would be the ideal solution to heartwater control, especially for export, since it would be useable anywhere in the world. This would be essential in the event of any spread of the disease outside the current endemic area. The advantage of recombinant vaccines would be the relative ease with which the evolution of vaccine genes in the wild could be followed, allowing the vaccine formulation to be changed to keep up with pathogen changes, cheaper to manufacture, and easier to store than an inactivated vaccine, and recombinant heartwater vaccine development is a very active area of research [46].

Establishment of enzootic stability: The natural method of limiting the impact of cowdriosis in domestic ruminants is by the establishment of the endemic stability using strategic tick control, is a state of equilibrium between an infectious agent, its vector and host animal population [23]. This occurs by having small number of ticks without total clearing from the resistant breeds which helps to have self-developed/acquired immunity to defend of heartwater. In endemically stable areas where tick control is not practiced, a high level of immunity in stock, particularly cattle, is seen. In these areas, intensive tick control may actually increase losses due to heartwater, while selective control, e. g. acaricidal application only when the level of infestation causes tick-worry, tends to reinforce endemic stability and herds may develop a high degree of immunity [38].

The period of natural protection is a cornerstone in the creation of enzootic stability and should be exploited to the full, especially in cattle. This periodis the non-specific, or age resistance, to heartwater which prevails in young calves and to a much lesser extent in lambs and goat kids and it can be utilized to establish the immunity against heartwater with relatively little danger of the occurrence of clinical cases. On most farms, however, immunity is obtained by means of natural tick-transmission, without the farmers actually being aware of it. This method naturally depends on the presence of infected ticks, a situation which is very difficult to assess, control or manipulate [43].

The use of resistant cattle is becoming increasingly important as the cost of acaricides is rising. The resistance of different crosses should be tested to assess their suitability for introduction in areas where heartwater are prevalent. In Ethiopia Horro-Jersey and Horro-Simmental crossbred animals have been found more tolerant of ticks than many other crosses [47].

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