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REVIEW ARTICLE

Breeding strategies for tick resistance in tropical cattle: a sustainable approach for tick control

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Abstract About 80 % of world cattle population is under the risk of ticks and tick borne diseases (TTBDs). Losses caused by bovine tick burdens in tropical countries have a tremendous economic impact on production systems. Chemical control of disease has been found to be ineffective and also involving large cost. To reduce our reliance on these chemical products, it is necessary to embark on programs that include habitat management, genetic selection of hosts, and development of a strain capable of inducing host resistance to ticks. Selection for disease resistance provide alternate method for sustainable control of TTBDs. Domestic livestock manifests tick-resistance by skin thickness, coat type, coat color, hair density and skin secretions etc. Zebu cattle have, on average, greater tick resistance than either European cattle or African cattle. Heritability for tick burden in cattle has been shown to range about 0.30, which is sufficient to result in the success of some programs of selection for tick resistance in cattle. To select animals at younger age, to reduce generation interval and to increase genetic gain, marker assisted selection is an important tool. There are also various MHC molecules which are associated with resistance to TTBDs.

Keywords TTBDs · Marker · Resistance · Selection · Heritability

Introduction

Ticks and tick borne diseases (TTBDs) are of global importance because of their economic and health implications in livestock, human and companion animals (Jongejan and Uilenberg 2004). TTBDs affect 80 % of the world's cattle population and are widely distributed throughout the world, particularly in the tropics and subtropics (de Castro 1997); they represent an important proportion of all animal diseases affecting the livelihood of poor farmers in tropical countries. The impact of TTBDs on the livelihood of resource poor farming communities has been ranked high (Perry et al. 2002). Cattle ticks are responsible for severe economic losses in both dairy and beef cattle enterprises in tropics (Jonsson 2006). Ticks are responsible for a variety of losses, caused by the direct effect of attachment ('tick worry'), by the injection of toxins, or through the morbidity and mortality associated with the diseases that they transmit. A systemic study for the cost of TTBDs has not been undertaken in India but roughly it has been estimated in the tune of 2000 crore rupees per annum (Minjauw and McLeod 2003). Ticks are also vectors of a variety of pathogens that are implicated in severe pathologies in many mammalian species (De La Fuente et al. 2008).

Disease control strategy includes both prevention and cure, and may include decision affecting the animal (e.g. vaccination, culling diseased animals and selection of

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resistant animals), the pathogen (chemotherapy) or the environmental (e.g. biosecurity, sanitation etc.). Chemical control has been the main strategy to overcome tick infestations, but cost associated with treatment is considerable. Price of chemical is not only the factor; there is also involvement of the most important concern, the selection of chemical resistant tick strains which evolve faster than the development of new chemicals for tick control (Kemp et al. 1999). Author of this paper conducted study to assess the resistance level in multi host tick in the three agro-climatic regions of India and found that even the multi host tick, *Hyalomma anatolicum* prevalent in the trans-gangetic region have developed at least level I resistance to commonly used acaricides (Shyma et al. 2012). A high resistance level to deltamethrin and amitraz is also recorded in the Indian isolates of *Rhipicephalus (Boophilus) microlplus* (Sharma et al. 2012; Singh et al. 2012). Against *Rhiphpicephalus (Boophilus) microplus*, vaccines have also been proposed, and in this series, in 1995 first commercial recombinant vaccine (Bm86) was released (Willadsen et al. 1995). But later it was widely recognized that it had relatively small impact on the practical control of ticks due to various scientific and commercial reasons (Willadsen 2006). Biological control of ticks also gets attention with natural predators as ants, mites, birds, parasitoid wasps, fungi etc. (Samish and Rehacek 1999; Jonsson and Piper 2007), but issues such as manufacture and stability of the living agents in the field need to be resolved before it can be applied on large scale (Willadsen 2006).

In recent centuries, domestic animals have been subjected to artificial selection, particularly for visible traits and also for easily measurable traits such as yield, weight or height. For disease traits in animals, however, studies of animal variation are less common than for easily measurable traits, so less is known about the potential to change animal susceptibility. In times when the use of drug therapy was common, cheap and acceptable, there seemed little incentive to select for disease resistance. The situation has now changed drastically due to increasing concerns over drug resistance by parasites, increasing demands for residue-free animal products, and at the same time increasing concerns for animal welfare. Hayward (1981) stated that the best solution to high acaricides prices and resistance to drugs might be the identification of naturally resistant breeds and the encouragement of their use. Natural disease resistance refers to the inherent capacity of an animal to resist disease when exposed to pathogens, without prior exposure or immunization (Adams and Templeton 1998). Utech et al. (1978) defined tick resistance as the ability of cattle to limit the number of ticks that survive to maturity. Selection for disease resistance has been applied successfully in poultry, and opportunities are also being applied increasingly in pigs and sheep in some countries. The present article reviews information on genetics and breeding strategies for prevention of parasitic diseases, with the major emphasis on ticks.

Expression of host: resistance to ticks

The first account of host immunity to ticks appears to be that written by Nuttall (1911), which refers to the phenomenon of natural immunity in humans. From the 1930s onwards, investigations into host resistance to ticks began to appear, and since then innumerable studies on the immunological aspects of the host-tick relationship has been carried out. Domestic livestock manifests tick-resistance by various ways; better familiarity of indigenous cattle of the infected zone in grazing area or by morphological differences in the host altering the chance of attachment to the ticks (Meltzer 1996). Skin thickness also appears to play an important role on host resistance to ticks (Foster et al. 2007). Although contradictory results were reported on this issue, the coat type, hair density and skin secretions may have some roles. Contemporary group comparison reveals lighter colored animals are more resistant than dark colored ones (Gasparin et al. 2007). Utech et al. (1978) and Silva et al. (2010) observed that females, pregnant cows and younger animals are more resistant when compare to their respective counterparts.

There is uniform agreement that Zebu cattle (*Bos indicus*) have, on average, greater tick resistance than either European cattle (*Bos taurus*) or African cattle (Utech et al. 1978; Madalena et al. 1990; Frisch and O'Neill 1998; Mwangi et al. 1998; Wambura et al. 1998; da Silva et al. 2007). Immunological mediators induced by tick antigens introduced into host skin contribute to the itching sensation which stimulates grooming. However, dislodging of ticks in the case of two–three host ticks by grooming may simply be a response to the irritation of ticks walking on the skin while seeking their predilection sites before attachment (Mooring et al. 1995).

Gene and markers associated with tick resistance

Integrating current breeding programmes with selection for tick resistance idea seems to be promising but as seen earlier there is either low or no correlation between tick counts and various productive and reproductive traits. Moreover, under extensive farming conditions, it is not feasible economically to record tick counts. Prevailing scenario compelled people to look for the development of genetic markers. Several efforts have been made in an attempt to isolate and validate markers for selection of resistant genotypes. Marker assisted selection could be used to pre-select young animals, shorten generation interval and increase genetic gain (Beckmann and Soller 1987; Martinez et al. 2006). These molecular markers have the capacity to allow prediction of breeding value for traits that had previously been difficult to measure and hence were not included in the selection criterion (Beckmann and Soller 1987). Understanding the biological and physiological mechanisms of these resistance genes could help to develop new and more effective acaricides and vaccine. First such effort was made by Francis and Ashton (1967) who found an association between the distribution of biochemical polymorphic amylase genes and tick burden which reached significance in drought master but not in *B. taurus* cattle. Recently, acute-phase proteins (haptoglobin, serum amyloid A, alpha-1 acid glycoprotein and transferrin) were re-evaluated by comparing the response of Holstein (*B. taurus*) and Nellore (*B. indicus*) animals under natural infestation (Carvalho et al. 2008). Differences in serum concentration of some proteins (e.g. haptoglobulin and transferrin) were confirmed and these could potentially be used as biomarkers to monitor the level of tick infestation. Regitano et al. (2008), reported that in naturally infected crossbred *B. taurus* X *B. indicus* and also in pure *B. indicus*, genotypes for a microsatellite marker close to the interleukin-4 locus were associated with tick numbers.

Association between, bovine major histocompatibility complex (MHC) (BoLA) class II alleles and tick resistance have been reported (Acosta-Rodríguez et al. 2005). Martinez et al. (2006) found an association between BoLA alleles and low tick number for alleles DRB 3.2 *18, *20 and *27 and suggested that BoLA–DRB 3.2 alleles could be used to help in the selection of animals resistant to tick infestation. Unfortunately valid comparisons among these studies are complicated by differences in the microsatellites used and differences in nomenclature regarding the alleles as well as differences in the genetic base of the cattle used and the species of tick studied. Consequently there remains no firm evidence of a role for any specific allele or haplotype of any of the genes in the MHC. More recently, in a linkage analysis, quantitative trait loci (QTL) were detected when a crossbred population (F2 Holstein × Gir) was scanned using 180 microsatellites covering all autosomal chromosomes (Gasparin et al. 2007; Regitano et al. 2008; Machado et al. 2010a). Different QTL were found to have significant effects on tick burden in different seasons, perhaps indicating the environmental influence on tick counts. However, the QTL span large chromosomal fragments and it is difficult to clearly identify any gene as a potential candidate conferring tick resistance or tick susceptibility.

Barendse (2007) has identified a number of SNPs which acts as genetic marker and allows a rapid and precise test for genetic variation for the trait, which would allow many cattle to be tested over a short period of time in a cost effective manner, to establish the characteristics. The majority of markers however explained a small proportion (>1 %) of the phenotypic variation of the trait (transformed tick counts). This suggested that if SNP were to be used in selection programs, it would have to be as a panel of markers rather than a single marker with a high predictive value. For tick resistance QTL on BTA3 and BTA10 were recently confirmed and fine-mapped (Porto Neto et al. 2011). Both initial QTL on BTA3 and 10 were confirmed in dairy and Brahman cattle and the QTL intervals were reduced and candidate genes identified.

Breeding and selection for host resistance

Economization of tick control can be effectively done by selection of animals for increased host resistance. Genetic improvement program aimed at improvement in tick resistance should make use of the selection of animals that can transmit resistance to their offspring, thus reducing the susceptibility of a population in a given enzootic area. This would bring about a decline in the region's parasite load, which would in turn contribute to reducing the need for chemical control methods.

Real hurdle in selection for increased host resistance is to explore the presence of genetic resistance to ticks in a given population. One of the simplest ways to achieve this is to find the breed of animal that is naturally resistant. However, if the resistant trait is associated with production and reproduction traits, multiple objective of any breeding programme can be achieved without much additional investment. Earlier studies at Belmont (Frisch 1981; Burrow et al. 1991) showed that in population susceptible to ticks and worms, selection for high growth in presence of these parasites, increases resistance (reduce ticks and worms load). Many workers (Davis 1993; Prayaga et al. 2009) indicated that there is low and non significant genetic correlation between tick count and various productive, adaptive and pubertal traits. Prayaga and Henshall (2005) suggested that selection for growth under tropical condition is unlikely to improve tick resistance at genetic level. Prayaga et al. (2009) however concluded that the overall favorable association, or indeed lack of association, of adaptive traits to tropical conditions, such as heat tolerance and parasite resistance, with productive and reproductive measures means that selection for female reproductive performance will not compromise tropical adaptation.

Despite the complexity of tick host interaction, there is genetic component of variation in host resistance to ticks. Resistance to ticks is a heritable character and several workers have estimated the heritability for resistance to ticks (Table 1). Cattle have been selected for tick resistance and significant progress has been made with the development of breeds of cattle that are resistant to ticks, and at the same time, show good productivity. Heritability of tick resistance varies from very low to high (Alencar et al. 2005). This broad variation is attributed to both evaluation methods (artificial and natural challenge) and additive genetic variation for resistance, which is intrinsic to each studied population. Further, differences in heritability also reflect the extent of natural parasite challenge under extensive conditions, enabling the expression of variation in tick resistance across various studies. Utech et al. (1978) concluded that resistance in Brahman cattle appeared to be a dominant trait when interbreeds are observed. Over years of selection, resistance has been increased from 89.2 to 99 % in an Australian, Illawarra Shorthorn herd. Concurrently, in this herd the resistance of the progeny increased from 93.7 to 97.7 %, demonstrating that the selection and breeding of cows and bulls resulted in genetic improvement in the resistance of the progeny (Utech and Wharton 1982). Tick resistant breeds of cattle have now been developed in an effort to find animals that are productive (particularly for milk) under tick challenge and in a tropical environment. The development of these breeds started with the parallel development of cows with acceptable levels of milk production and bulls with high tick resistance and from there excellent dairy breeds, such as the Australian Friesian Sahiwal, have been created. Mackinnon (1990) also showed that tick resistance can be readily changed by selection in tropical beef breeds. Despite the progress made in Australia, in selection for tick resistance where they are concerned with only one tick species, there is less enthusiasm from other part of the world, especially in Asia and Africa.

Selection will be most efficient in improving productivity if a multi-trait index is developed incorporating breeding values for both production and resistance traits. The rate of genetic improvement in any single trait is reduced by selection for additional traits, unless those traits are positively genetically correlated. Milk yield did not decrease under intense selection for tick resistance, suggesting that both traits can be improved simultaneously. Evidences are there to prove that growth and reproductive potentials are not related to tick resistance. Across breeds, reproductive and growth rates were unrelated to tick count, demonstrating that it is possible to develop breeds with both high tick resistance and high production potentials.

Major genes

The zebu breeds, resistance to *R.* (*Boophilus*) *microplus* is clearly polygenic. While polygenic resistance will respond readily to selection in breeds of moderate to high resistance. It is impractical to select for, or to introgress polygenic resistance into, lowly resistant breeds. For lowly resistant breeds to make the transition for a state where they suffer high mortality when ticks are uncontrolled to a state of stable coexistence with ticks, there has to be a quantum leap in their resistance. This can be achieved by exploiting major resistance genes. Belmont Adaptaur (Kerr et al. 1994; Frisch 1994), the breed is remnant of the original highly tick-susceptible Herefords and Shorthorns used for beef production in Northern Australia before the introduction of Brahmans. Herefords and Shorthorns were reciprocally crossed at the National Cattle Breed Station, "Belmont" and the resulting HS line (now called the Adaptaur) was maintained thereafter in the presence of continual tick challenge and with minimal intervention to control parasites. Research for major genes for tick resistance was initiated and achieved great success in short period of time. In the presence of ticks, carriers of the gene acquire resistance early in life and at a relatively low tick challenge. The resistance is stable, inheritable and lasts the lifetime of the animal. A significant proportion of animals homozygous for the anti-tick gene acquire total or near-total resistance to ticks (Frisch 1994). It is not known if the

Table 1 Heritability (h^2) estimates for resistance to common ticks in cattle

Reference	Location	Breed	Challenge	h^2 (SE)
Fraga et al. (2003)	Brazil	Caracu	Natural	0.22
Henshall (2004)	Australia	HS	Natural	0.44
Prayaga and Henshall (2005)	Australia	Cross bred	Natural	0.13 (0.03)
Peixoto et al. (2008)	Brazil	Holstein X Gir	Artificial	0.21 (0.12)
Prayaga et al. (2009)	Australia	Brahaman	Natural	0.15 (0.10)
Budeli et al. (2009)	–	Bonsmara	Natural	0.17
Turner et al. (2010)	Australia	*B. taurus* a number of breeds	Natural	0.37
Machado et al. (2010b)	–	Gir X Holstein (F2)	Artificial	0.21

h^2 heritability, *SE* standard error, *F2* second filial generation, *HS* Hereford–Shorthorn (*B. taurus*) cross anti-tick gene affects resistance to other tick species, but the possibility need to be investigated.

Conclusions

Over-reliance on acaricides for the control of ticks creates more problems than it solves. Improvement of the efficiency of the anti-tick vaccine appears technically possible and recent report suggests the possibility of development of cross-protective tick vaccine. This would further reduce, but is unlikely to eliminate, the use of acaricides, particularly where production is based on breeds with low tick resistance. There have been various attempts at controlling ticks and tick borne disease in tropical livestock. Breeding for genetic resistance is one of the promising ways to control the ticks. High host resistance is the most important method for controlling ticks, but no breed is totally resistant. Total resistance is the ultimate goal, is technically possible to achieve, and is permanent. For breeds with moderate to high resistance, selections based on an index that combines breeding values for resistance and production traits will achieve the desired result. Progress could be enhanced through introgression of resistance genes to breeds of low resistance. The quest for knowledge of the genetic basis for tick resistance in cattle is strongly warranted, given that 70 % of global beef production and significant dairy production occurs in tropical and subtropical zones where ticks are highly prevalent and have a major impact on welfare, production efficiency, amount of product, and product quality.

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