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A REVIEW OF TRYPANOSOMOSIS-INDUCED REPRODUCTIVE DYSFUNCTIONS IN MALE ANIMALS

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ABSTRACT

Trypanosomosis has been recognized as one of the major limitations to livestock production in the African continent. In addition to its clinical manifestations such as weight loss, lethargy, weakness and dullness, reproductive organs are also affected which has led to reduction of fertility in infected farm animals. This paper highlighted the major dimensions of reproductive dysfunctions induced by African animal trypanosomosis in male animals with emphasis on ruminants and simultaneously discussed how the pathogenesis lead to the observed reproductive disorders with the aim of identifying areas of ambiguity where further research need to be focused. Testicular degeneration, reduced libido, orchitis and poor semen characteristics have been established in infected males. Studies of receptors of these reproductive hormones under trypanosomosis infection are very rare in literature and hence, the involvement of endocrine glands most especially the anterior pituitary and hypothalamus remains inexplicit enough. A sequential investigation of the relationship between the concurrent pathological changes in reproductive and endocrine organs, reproductive hormones and their respective receptors as well as the reproductive performance of animals suffering from trypanosomosis are suggested. This will improve our knowledge on the pathogenesis of trypanosomosis as it affects reproduction while promoting development and implementation of strategies to contain the disease in food animals.

Keywords: Trypanosomosis, testis, pituitary, hypothalamus, sperm, infertility.

INTRODUCTION

Trypanosomosis is an infectious disease caused by pathogenic blood parasites known as trypanosomes (*Trypanosoma spp)* and transmitted through tsetse flies (*Glossina spp*). The disease is unique to Africa, affecting both human (human African trypanosomosis or sleeping sickness) and animals (animal African trypanosomosis or Nagana). It occurs in 37 sub-Saharan countries, covering more than 9 million square kilometres; an area that corresponds approximately to one third of Africa total land mass (Maudlin, 2006). Trypanosomosis threatens an estimated 60

million people and 50 million heads of cattle. In a situation where the disease is tolerable, up to 50% cases of mortality and morbidity is recorded in farm animals. Presently, an estimate of direct loss in meat and milk yield as well as cost of control amounts to a sum of $600 million to $1.2 billion annually on the global scale (FAO, 1994). Therefore, trypanosomosis is recognized as one of the major factors limiting livestock production in Africa especially in the sub-Saharan region (Swallow, 2000). Debatably, in the context of the economic implications, it is the most important diseases affecting animals in Africa (Maudlin, 2006) and a potential hindrance to food security in Nigeria (Samdi *et al.,* 2010). Reproductive organs are reportedly affected under trypanosomosis infection in both male and female animals. Sterility, menstrual disorder, and still birth have been reported in human during trypanosomosis infection (Maudlin, 2006). It causes abortion, premature birth and prenatal losses as well as cystic ovaries in female animals (Faye *et al.,* 2004, Silva *et al.,* 2013) with associated vertical transmission through the placenta (Batista *et al.,* 2012). In trypanosomosis-infected male, studies had indicated adverse effect of the disease on almost all fertility indices. Despite these findings, more studies are required in the area of reproduction to know the extent of involvement of the reproductive system and the mechanism involved in the effects as well as reproductive hormones and their respective receptors under trypanosomosis infection.

Many studies on trypanosomosis have focused on female animals at the expense of male, whereas subfertility in male has a greater impact on the overall fertility in the herd because of reduced number of bull-to-cow ratio which may be up to 1:60 or 1:25 under synchronized and non-synchronised practice respectively (Healy *et al*., 1993). This remains a common practice to reduce associated problems of bull overlap (more than one bull breeding cow on oestrus), risk of injury while competing for oestrus cow and pressure on social dominance couple with extra cost of purchasing and maintaining more bulls. Therefore, it is the purpose of this review to highlight the major findings in trypanosomosis studies as regards reproductive dysfunctions induced by the disease in male farm animals paying particular attention to ruminants. Furthermore, I also examine the pathogenesis and the possible mechanisms that culminate in the observed reproductive dysfunctions. Moreover, it is envisaged this will stimulate more research on trypanosomosis vis-à-vis its effects on reproduction. Undoubtedly, such endeavours will enrich our understanding and subsequently facilitate further development of strategies to control the disease as it affects reproduction in farm animals.

Endocrine involvement

The roles played by endocrine glands especially the hypothalamus and anterior pituitary in reproductive process are well documented (Senger, 2005). The gonadotrophin releasing hormone (GnRH) produced from the hypothalamus induces release of gonadotropins, follicle stimulating hormone (FSH) and luteinising hormone (LH) from the anterior pituitary. FSH and LH

are required for spermatogenesis and sperm maturation, while development of male secondary characteristics and libido depends on the testosterone. In other words, GnRH, LH and FSH directly or indirectly affect the level of testosterone produced by the interstitial cells, which reportedly has been shown to be a good marker for semen quality and production (Khisk, 2008). Several studies have reported involvement of central nervous system under trypanosomosis infection and impairment of the hypothalamic-pituitary-gonadal axis (Batista *et al.,* 2007, Abebe *et al.*, 1993).

African animal trypanosomosis caused local inflammation of the pituitary and the gonads, associated with increase in the level of cytokines such as tissue necrotic factor α (TNF- α) and interleukins 6 (IL-6) (Reincke *et al.,* 1998). It also leads to reduction in the size of the anterior pituitary and the tuberal region of the hypothalamus with extensive tissue damage (Adenowo *et al.,* 2005), that may subsequently reduce the amount of GnRH released from the hypothalamus (NgWena *et al.* 1997). Studies on hormonal assay under trypanosomosis infection revealed decline in the level of LH and testosterone in goats (Waindi *et al.,* 1986), rams (Mutayoba *et al.,* 1994) and bulls (Boly *et al.*, 1994). The reduction in LH was attributed to low level of GnRH produced by the hypothalamus while the decline in plasma testosterone was caused by reduced sensitivity of Leydig cells to an already low circulating LH in trypanosomosis-infected ram (Mutayoba *et al.,* 1994). Moreover, the inefficiency of the gonads may also be due to impairment in the hypothalamic-pituitary-gonadal axis (Petzke *et al.,* 1996) or hypo-thalamo-pituitary-adrenal axis (Reincke *et al.,* 1998); a special portal that links the hypothalamus, pituitary and the gonads (Noakes *et al.,* 2009). Sheep infected with *T. brucei* developed acute coagulative necrosis and leucocytes infiltration of the anterior pituitary as well as localisation of trypanosomes in the pituitary tissue (Ikede and Losos, 1975).

The mechanism of these endocrine lesions has been postulated on the ability of the trypanosomes to localise in the organs thereby causing severe damage. Darsaud *et al.,* (2003) suggested neurological phase in the human animal trypanosomosis because they isolated trypanosomes and observed inflammatory cells in the choroids plexus of an experimental rat model. The earlier study of Ikede and Losos (1975) was the first to isolate trypanosomes in sheep pituitary tissues after experimental infection with *T. brucei*. This is understandable for *Trypanosoma brucei* infection but could not be substantiated for others such as *T. congolense* and *T. vivax* that are known to be intravascular and non-tissue invasive. In addition, body cells essentially depend on oxygen for survival. The oxygen is delivered to cells through the blood. Therefore, tissue hypoxia (Logan- Henfrey *et al.*, 1992) and formation of reactive oxygen species sequel to anaemia may also be a contributing mechanism. Anaemia is a persistent feature of trypanosomosis (Anosa, 1988).

Libido

Libido is a critical aspect of male sexual function because it indicates the ability of the male to detect and subsequently service the female animal on oestrus (Farin *et al.,* 1989). Even in flock where artificial insemination is practiced, a male with good libido is still desirable because semen collection via artificial vagina in bull with good libido tends to be easier as the animal is more responsive to a dummy or a live teaser than a bull with poor libido. Sekoni *et al*. (2004) established a reduction in libido in bull, due to trypanosomosis infection. The same was also reported for West African dwarf buck experimentally challenged with *Trypanosoma congolense* (Raheem *et al.,* 2009). The mechanism of causing decline in libido has been premised on decline in plasma testosterone (Adamu *et al*., 2006) which has been reported in several studies stated earlier. Testosterone plays an important role in optimal functioning of the testis and initiation of sex drive (Senger, 2005). Testosterone concentration is an indicator of the level of libido expressed by the bull (Nix *et al.,* 1998). Therefore, when its testicular production is impaired, the clinical manifestation is reduced libido.

Testicular lesions

The mammalian testis fulfils a dual role of exocrine and endocrine organ by producing spermatozoa and testosterone respectively (Senger, 2005). The essence of testicular descent in mammals is to facilitate reduction in the testicular temperature 4-7^{o}C below the body temperature (Chemineau *et al.,* 1991), a temperature that is mostly conducive for spermatogenesis and steroidogenesis. In trypanosomosis, hyperthermia is a common attribute (Radostits *et al.,* 2007) and this has led to testicular degeneration. Ikede (1979) reported orchitis in experimental *T. brucei*-infected ram. In a similar study, *T. congolense* in Sabi ram produced seminiferous tubular atrophy and mononuclear infiltration of the testis and lesion in the epithelium of the corpus epididymis (Aire *et al.,* 2001). *T. congolense* infection in goat caused testicular necrosis and infiltration of mononuclear cells (Raheem 2008). Degeneration of germ cells and sertoli cells were also encountered in boar (Omeke and Igboeli, 2000) and dromedary bull (Al-Qarawi *et al.,* 2004). Dargantes *et al*., (2005) reported testicular enlargement in goat sequel to experimental infection with *T. evansi.* The report of Anosa and Kaneko (1984) gave a detailed histopathological lesion of the testes under trypanosomosis infection in mice. The study revealed individual percentage of different cells constituting the interstitium while indicating the reduction in size and cluster formed by mitochondria of the Leydig cells. In addition, the parasites (*T. Brucei*) were actually localized within seminiferous tubules (Anosa and Kaneko, 1984).

Semen characteristics

Characteristics of semen considered relevant for fertility study are sperm concentration, sperm motility, spermatozoa live/dead ratio and sperm morphological abnormalities (Senger, 2005).

Reduction in sperm count, motility and live/dead ratio as well as increased in sperm abnormalities, have been reported in male farm animals infected with trypanosomosis. Poor semen characteristics are reported in trypanosomosis-infected bull (Sekoni *et al.,* 2004), goat (Raheem *et al.,* 2009) and sheep (Akpavie *et al.,* 1987).

In these studies, semen characteristics were compromised beyond acceptable range of values for infected farm animals, and eventually leading to infertility. The deterioration in semen qualities in trypanosomosis infection is due to testicular degeneration, the pathogenesis of which involves thrombosis of testicular vessels leading to ischaemic necrosis (Anosa and Isoun, 1980), thermal degeneration of the testes especially experienced at the peak of hyperthermia (Radostits *et al.,* 2007) and anoxia (Logan-Henfrey *et al.,* 1992) as well as other earlier stated testicular lesions that may eventually lead to disruption in spermatogenesis.

The process of regeneration of the degenerated testicle, even after termination of the infection through chemotherapy or natural recovery is always a protracted process (Akpavie *et al.,* 1987; Leigh and Fayemi, 2010). Genomic studies have evolved to understand the pharmacokinetics of some therapeutic agents used for treatment of trypanosomosis (Alsford *et al.,* 2012). It is anticipated that similar studies will also focus on the possible implication of these drugs on reproduction. The finding of Fayemi (2006) relating infertility of trypanosome-infected goat to high level of sperm antibodies calls for further investigation.

CONCLUSION

The practical implications of poor semen qualities, testicular lesions, reduction in libido and decrease in gonadotropins in trypanosomosis-infected male animals are *impotentia coeundi* (failure of normal service) and *impotentia generandi* (failure of fertilization). Apart from the economic loss due to mortality of trypanosome-infected animals, there is a greater loss associated with infertility of morbid and recovered male animals that cannot be economically quantified. It is certain that more studies are required for better understanding of the effect of trypanosomosis on reproduction. A sequential investigation of the relationship between the concurrent pathological changes in reproductive and endocrine organs, reproductive hormones and their respective receptors as well as the reproductive performance of animals suffering from trypanosomosis are suggested. This will improve our knowledge on the pathogenesis of trypanosomosis as it affects reproduction while promoting development and implementation of strategies to contain the disease in food animals especially in ruminant.

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