Acta Tropica 165 (2017) 216–229

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Impact of mass chemotherapy in domestic livestock for control of zoonotic *T. b. rhodesiense* human African trypanosomiasis in Eastern Uganda

Jenna Fyfe[a], Kim Picozzi[a], Charles Waiswa[b,c], Kevin Louis Bardosh[a], Susan Christina Welburn[a,*]

[a] Edinburgh Infectious Diseases, Division of Infection and Pathway Medicine, Edinburgh Medical School: Biomedical Sciences, The University of Edinburgh, Chancellor's Building, 49 Little France Crescent, Edinburgh, EH16 4SB, UK
[b] Department of Pharmacy, Clinical and Comparative Medicine, School of Veterinary Medicine and Animal Resources, Makerere University, P.O. Box 7062, Kampala, Uganda
[c] The Coordinating Office for Control of Trypanosomiasis in Uganda (COCTU), P.O. Box 16345, Wandegeya, Plot 76/78 Buganda Road, Kampala, Uganda

ARTICLE INFO

Article history:
Received 20 November 2015
Received in revised form 17 August 2016
Accepted 24 August 2016
Available online 25 August 2016

Keywords:
Human African trypanosomiasis (HAT)
Trypanocide
Endemic
Animal reservoir
Zoonosis
Sleeping sickness
T. b. rhodesiense HAT (rHAT)
T. b. gambiense HAT (gHAT)
Animal African trypanosomiais (AAT)
Outbreak
Reservoir
T. b. rhodesiense
T. b. gambiense
Burden
Uganda
DALYs

ABSTRACT

Introduction: Human African trypanosomiasis (HAT) comprises two fatal parasitic diseases. Uganda is home to both chronic *T. b. gambiense* (gHAT) and the acute zoonotic form *T. b. rhodesiense* (rHAT) which occur in two large but discrete geographical foci. The area affected by rHAT has been rapidly expanding due to importation of *T. b. rhodesiense* infected cattle into tsetse infested but previously HAT free districts. Migration of rHAT has resulted in a considerable human health burden in these newly affected districts. Here, we examined the impact of a single, district-wide, mass chemotherapeutic livestock intervention, on *T. b. rhodesiense* prevalence in cattle and on incidence and distribution of human rHAT cases in Kamuli and Soroti districts in eastern Uganda.

Methods: A single mass intervention in domestic cattle (n = 30,900) using trypanocidal drugs was undertaken in November and December 2002 under the EU funded Farming in Tsetse Controlled Areas (FITCA) programme. The intervention targeted removal of the reservoir of infection i.e. human infective *T. b. rhodesiense* parasites in cattle, in the absence of tsetse control. Interventions were applied in high-risk sub-counties of Kamuli district (endemic for rHAT) and Soroti district (where rHAT has been recently introduced). The prevalence of *T. brucei* s.l. and the human infective subspecies, *T. b. rhodesiense* in cattle (n = 1833) was assessed before and 3 and 12 months after intervention using PCR-based methods. A combination of descriptive statistical analysis and spatial scan statistics were applied to analyse rHAT cases reported over a 5-year period (January 2000–July 2005).

Results: A single intervention was highly effective at removing human infective *T. b. rhodesiense* parasites from the cattle reservoir and contributed to a significant decrease in human rHAT cases. Intervention coverage was higher in Kamuli (81.1%) than in Soroti (47.3%) district but despite differences in coverage both districts showed a reduction in prevalence of *T. b. brucei* s.l. and *T. b. rhodesiense*.

In Kamuli, the prevalence of *T. brucei* s.l. decreased by 54%, from 6.75% to 3.11%, 3, months post-intervention, rising to 4.7% at 12 months. The prevalence of *T. b. rhodesiense* was 3% pre-intervention and no *T. b. rhodesiense* infections were detected 3 and 12, months post-treatment. In Soroti, the prevalence of *T. brucei* s.l. in cattle decreased by 38% (from 21% to 13%) 3 months after intervention decreasing to less than 10% at 12 months. The prevalence of *T. b. rhodesiense* was reduced by 50% at 12-months post-intervention (6%–3%). Most notably, was the impact of the intervention on the population dynamics between *T. b. brucei* and human infective *T. b. rhodesiense*. Before intervention in Kamuli district 56% of *T. b. brucei* s.l. circulating in cattle were *T. b. rhodesiense*; at both 3 and 12 months after intervention none of the re-infecting *T. b. brucei* s.l. were human infective, *T. rhodesiense.*

For human rHAT cases, there was a seven-fold decrease in rHAT incidence after intervention in Kamuli district (5.54 cases/1,000 head of population 2000–2002 to 0.76 cases/1,000, 2003–2005). Incidence data suggests that the intervention had minimal impact on the number of rHAT cases in Soroti overall, but showed a significant decrease in the seasonal peak of cases in the year following treatment.

* Corresponding author.
E-mail address: sue.welburn@ed.ac.uk (S.C. Welburn).

http://dx.doi.org/10.1016/j.actatropica.2016.08.022

Conclusion: A single intervention, targeted at cattle, introduced at district level, in the absence of tsetse control, was highly effective at removing human infective rHAT parasites from the cattle reservoir and contributed to a significant decrease in human rHAT cases. The differential impacts observed between the two districts are related to both the different stages of rHAT endemicity in the districts, and levels of intervention coverage achieved in the cattle population. Treatment of cattle to remove the reservoir of rHAT infection offers a promising and cost effective approach for the control of rHAT. It is important that cattle are treated before relocation to prevent possible merger of the two HAT foci, which would complicate diagnosis and treatment of both gHAT and rHAT.

1. Introduction

Human African Trypanosomiasis (HAT) or sleeping sickness is a neglected tropical disease (NTD) transmitted by tsetse flies (*Glossina* spp.). HAT comprises two distinct diseases caused by two sub-species of *T. brucei* s.l. *Trypanosoma brucei gambiense* and *T. b. rhodesiense* (Welburn et al., 2001a). *T. b. gambiense* HAT (gHAT) is a chronic disease passed between humans by human-tsetse-human contact and sustained by vertical transmission (Wastling et al., 2011; Welburn et al., 2016a). *T. b. rhodesiense* HAT (rHAT) is an acute disease with a complex zoonotic epidemiology involving tsetse transmission between a range of wildlife, livestock reservoirs and humans (Anderson et al., 2011). Both forms of HAT are fatal if untreated with death occurring 6–8 months after infection with rHAT and around three years after first indication of gHAT infection (Checchi et al., 2008) although patients have been shown to carry gHAT infections for decades (Fèvre et al., 2005; Welburn et al., 2016b).

Uganda is unique in having active foci of both forms of HAT which have co-existed in Uganda for over a century (Keorner et al., 1995; Fèvre et al., 2004) in discrete geographical foci; gHAT in the northwest and rHAT around the shores of Lake Victoria in south-eastern and central regions (Welburn et al., 2001a, 2016a).

Following a large outbreak in Tororo district in 1987 (Odiit et al., 2004) rHAT has progressively migrated around the shores of Lake Kyoga (Batchelor et al., 2009). Domestic cattle have been shown to be the major reservoir of *T. b. rhodesiense* in Uganda (Welburn et al., 2001a,b) and importation of infected cattle from districts in established rHAT has caused rHAT outbreaks in previously unaffected districts (Fèvre et al., 2001) moving rHAT towards the gHAT focus (Picozzi et al., 2005).

In 1999 rHAT first emerged in Soroti district (Fèvre et al., 2001) and was subsequently introduced into Kaberamaido and Dokolo districts (Batchelor et al., 2009) and other districts bordering Lake Kyoga (Apac and Amolatar) and to the northern district of Lira (Wardrop et al., 2012, 2013). In Soroti, rHAT spread from the point of introduction, Brooks Corner Cattle market (Fèvre et al., 2001), throughout the larger part of the district, the district reporting more than 500 cases (Batchelor et al., 2009). Cattle importation was fuelled by a number of major cattle restocking programmes that aimed to improve rural livelihoods (Selby et al., 2013). The rapid expansion of the area affected by rHAT towards the gHAT endemic focus is a major public health issue in Uganda. When the two disease overlap, diagnosis and treatment will be compromised with a significant impact on human morbidity and mortality (Welburn and Coleman, 2015).

Domestic cattle constitute the major reservoir of *T. b. rhodesiense* infection (Welburn et al., 2001a,b) in Uganda and given the predisposition of tsetse flies to feed on cattle, it was predicted that treatment of 85% of cattle with a single dose of trypanocide (a veterinary anti-parasitic treatment) would interrupt rHAT transmission to humans in Uganda (Welburn et al., 2006).

In 2000, Farming in Tsetse Controlled Areas (FITCA) a large European Union funded agricultural development project undertook a survey of rHAT and African Animal Trypanosomiasis (AAT) across 12 districts of Uganda (FITCA, 2005). Two districts, Kamuli and Soroti, which showed high rHAT incidence were selected for mass administration of a single dose of trypanocidal drug, aimed at reducing the prevalence of *T. b. rhodesiense* infection in domestic cattle. Administration of the trypanocidal treatment impacts on rHAT and all AAT parasites.

Multiple species and sub-species of trypanosomes circulate in cattle within HAT foci, including those that impact on animal health and cause AAT. While *T. congolense* and *T. vivax* are pathogenic to livestock, impacting on both animal health and productivity across much of Uganda (Okello et al., 2015); *T. b. brucei* (not infective for humans) and *T. b. rhodesiense* cause only mild illness in indigenous breeds with infection often undetected. *T. b. brucei* and *T. b. rhodesiense* are however, extremely pathogenic to exotic cattle (Wellde et al., 1989) and prevent upgrading of stock.

Kamuli district, lies within the Busoga HAT focus, and has been endemic for rHAT since at least the 1980's (Mbulamberi, 1989). In 2001, Kamuli reported over 100 HAT cases. *T. b. rhodesiense* HAT only emerged in Soroti district in December 1998. A single rHAT case was previously in Soroti in the 1960s, but the patient was considered to have been infected elsewhere, while travelling to Tanzania, passing through rHAT endemic foci (Onyango, 1967). A survey conducted in Soroti at that time failed to identify any *T. brucei* s.l., in humans or animals (Mwambu, 1969).

Here we make a comparative analysis of the impact of district level administration of a single dose of trypanocide in Kamuli, an established endemic rHAT focus and in Soroti, a newly affected focus, undertaken by FITCA in 2002. We examined the prevalence of *T. brucei* s.l. and *T. b. rhodesiense* in cattle before treatment and at 3 and 12 months after treatment. We also examined the impact of the intervention on the relationship between the human and non-human infective subspecies of *T. brucei*. To assess the impact of the intervention on the incidence of reported human sleeping sickness cases, we analysed the number, distribution and incidence of rHAT cases in the districts between January 2000 and July 2005.

2. Material and methods

2.1. FITCA intervention

Kamuli and Soroti districts lie on the southern and northern shores of Lake Kyoga respectively (Fig. 1a). An estimated 98% of the population of Kamuli and 89% of the population of Soroti are engaged in subsistence agriculture (Ugandan Bureau of Statistics, 2002). Within each district, FITCA designated 3 sub-counties as high-risk for rHAT: Pingire, Kateta and Kyere in Soroti, and Bumanya, Kitayunjwa and Namwendwa in Kamuli. High-risk areas were sub-counties where rHAT had been reported between 1996 and 2001. Medium risk areas showed AAT levels >5% (identified by microscopy) but no HAT cases. Low-risk areas had levels of