RESEARCH NOTE

AEDES AEGYPTI (L.) SURVIVAL AFTER EXPOSURE TO IVERMECTIN

James Whitehorn[1,2], Long Vo Thi[2], Le Thi Dui[2] and Cameron P Simmons[2,3]

[1]London School of Hygiene and Tropical Medicine, United Kingdom; [2]Oxford University Clinical Research Unit, Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam; [3]Centre for Tropical Medicine, CCVTM, University of Oxford, Churchill Hospital, Oxford, United Kingdom

Abstract. Ivermectin has been shown in *in vitro* studies to have insecticidal properties against *Aedes aegypti* adults. This study aimed to assess these properties *in vivo*. *Aedes aegypti* survival was not affected by acquiring a blood meal from humans both 5 hours and 24 hours after ingestion of a typical dose of ivermectin.

Keywords: *Aedes aegypti*, ivermectin, survival

INTRODUCTION

Ivermectin is a macrocyclic lactone with broad anti-parasitic activity (Campbell *et al*, 1983). It has an excellent safety profile and has been used successfully in mass drug administration programs to control the nematode *Onchocerca volvulus*, the cause of river blindness (Omura and Crump, 2004). During *in vitro* studies, ivermectin appears to have insecticidal properties against various blood-sucking insects, including *Aedes* and *Anopheles*(Tesh and Guzman, 1990; Kobylinski *et al*, 2010). In addition a study showed reduced survival of *Anopheles gambiae* mosquitoes fed on humans who had taken ivermectin (Chaccour *et al*, 2010).

The aim of the experiment was to test the hypothesis that the lifespan of *Aedes aegypti* mosquitoes is shortened after taking a blood meal on humans who have taken ivermectin.

Correspondence: James Whitehorn, Oxford University Clinical Research Unit – Vietnam, Hospital for Tropical Diseases, 764 Vo Van Kiet Street, Ward 1, District 5, Ho Chi Minh City, Vietnam.
E-mail: james.whitehorn@lshtm.ac.uk

MATERIALS AND METHODS

F3 adults bred from field-caught *Aedes aegypti* screened for arboviral pathogens were used in this experiment. Two healthy volunteers were each exposed to batches of *Aedes aegypti* females 0.5 hours before (Group 1), 5 hours after (Group 2) and 24 hours (Group 3) after taking 200 μg/kg ivermectin (Merck, Darmstadt, Germany). Each batch consisted of 30 4-6 day old mosquitoes that had been pre-starved for 24 hours prior to the exposure. Each mosquito's exposure was 5 minutes in duration.The mosquitoes that had taken a blood meal were selected and then reared in the insectary at 27±2ºC and 70% relative humidity with a 12:12 photoperiod in their separate batches. The number surviving in each batch was counted each day.

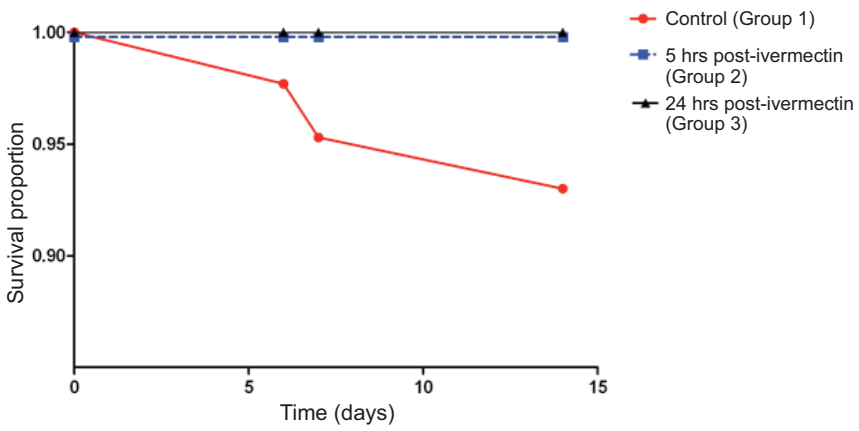

Fig 1–Survival proportions after exposure to ivermectin. The mosquitoes in each group have been counted together (Group 1 = 43 mosquitoes; Group 2 = 54 mosquitoes; Group 3 = 37 mosquitoes).

RESULTS

In Group 1, the control group, 25/25 mosquitoes survived to day 14 after feeding on subject 1 and 15/18 mosquitoes survived to day 14 after feeding on subject 2. In Group 2, 5 hours after ivermectin, 28/28 mosquitoes survived to day 14 after feeding on subject 1 and 26/26 mosquitoes survived after feeding on subject 2. In Group 3, 24 hours after ivermectin, 18/18 mosquitoes survived to day 14 after feeding on subject 1 and 19/19 mosquitoes survived to day 14 after feeding on subject 2. These data are shown in Fig 1.

DISCUSSION

This small study revealed that *Aedes aegypti* survival was not affected by acquiring a blood meal from humans who had recently ingested a typical dose of ivermectin. Despite the small number of participants, these findings contrast with studies that demonstrate a significant effect of ivermectin on the survival of various invertebrates (Chaccour *et al*, 2010; Kobylinski *et al*, 2010), and may reflect an intrinsic difference in *Aedes aegypti's* vulnerability to ivermectin compared to other invertebrates. Plasma ivermectin levels peak about 4 hours after oral administration so it might have been expected that mosquitoes that fed on the volunteers in Group 2 (5 hours after ivermectin) would have been affected (Gonzalez Canga *et al*, 2009). In fact, Lee and Eng (1994) reported that adult *Mansonia uniformis* and *Aedes togoi* fed on mice 3 days after treatment with ivermectin had a high mortality.

Crude survival observations in the artificial environment of the insectary may not reflect mosquito survival in the wild. Chaccour and colleagues (2010) noted that *Anopheles* mosquitoes exposed to ivermectin had altered coordination and an inability to fly. In the wild these features are likely to reduce the chance of survival. We did not specifically study movement behavior in the batches of *Aedes aegypti* exposed to ivermectin, but noted nothing suggestive of altered behavior.

Despite the negative findings in this small study, there is recent evidence that

ivermectin can inhibit nuclear import and thus inhibit dengue viral replication. (Wagstaff *et al*, 2012). This potential antiviral property is an area that warrants further research.

REFERENCES

Campbell WC, Fisher MH, Stapley EO, Albers-schonberg G, Jacob TA. Ivermectin: a potent new antiparasitic agent. *Science* 1983; 221: 823-8.

Chaccour C, Lines J, Whitty CJ. Effect of ivermectin on *Anopheles gambiae* mosquitoes fed on humans: the potential of oral insecticides in malaria control. *J Infect Dis* 2010; 202: 113-6.

Gonzalez Canga A, Sahagun Prieto AM, Jose Diez Liebana M, Martinez NF, Vega MS, Vieitez JJ. The pharmacokinetics and metabolism of ivermectin in domestic animal species. *Vet J* 2009; 179: 25-37.

Kobylinski KC, Deus KM, Butters MP, *et al*. The effect of oral anthelmintics on the survivorship and re-feeding frequency of anthropophilic mosquito disease vectors. *Acta Trop* 2010; 116: 119-26.

Lee HL, Eng K. Adulticidal effect of ivermectin (MK-933) against adults of *Mansonia uniformis* and *Aedes togoi*. *Mal J Med Lab Sci* 1994; 11: 46-8.

Omura S, Crump A. The life and times of ivermectin - a success story. *Nat Rev Microbiol* 2004; 2: 984-9.

Tesh RB, Guzman H. Mortality and infertility in adult mosquitoes after the ingestion of blood containing ivermectin. *Am J Trop Med Hyg* 1990; 43: 229-33.

Wagstaff KM, Sivakumaran H, Heaton SM, Harrich D, Jans DA. Ivermectin is a specific inhibitor of importin alpha/beta-mediated nuclear import able to inhibit replication of HIV-1 and dengue virus. *Biochem J* 2012; 443: 851-6.