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Risk factors for epilepsy in Bas-Uélé Province, Democratic Republic of the Congo: a case–control study

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SUMMARY

Background: The reason for the high prevalence of epilepsy in onchocerciasis endemic areas remains unknown. The aim of this study was to detect risk factors associated with epilepsy in a region endemic for onchocerciasis.

Methods: In June 2014, a case–control study was performed in Titule, Bas-Uélé Province in the Democratic Republic of the Congo. Individuals with unprovoked convulsive epilepsy of unknown aetiology were enrolled as cases ($n = 59$). Healthy members of families without cases of epilepsy in the same village were recruited as controls ($n = 61$). A multivariate binomial logistic regression analysis was performed to identify potential risk factors associated with epilepsy. To evaluate the potential protective effect of ivermectin treatment on the development of epilepsy, a nested age-matched case–control study was performed including only those who were eligible for ivermectin treatment in the year before they developed epilepsy.

Results: Suspected onchocerciasis skin lesions were more often present in cases than in controls: 12/41 (29%) vs. 1/56 (2%), respectively (odds ratio (OR) 20.26, 95% confidence interval (CI) 2.42–170; $p < 0.01$). Ivermectin had been taken 7 months earlier in 29/59 (49%) cases and 29/61 (48%) controls. *Onchocerca volvulus* (OV) DNA was detected by PCR in skin snips in 26/34 cases (76%) and 10/14 controls (71%) ($p = 0.7$), and there was presence of OV IgG4 antibodies in 35/48 (73%) cases and 15/18 (83%) controls ($p = 0.5$). OV DNA was not detected in the cerebrospinal fluid of cases (controls not tested). Both cases and controls reported frequent bites by blackflies (Diptera, *Simuliidae*). Bathing daily as opposed to less often (OR 16.7, 95% CI 2.2–125.8; $p < 0.01$), bathing between 11 a.m. and 4 p.m. (OR 12.7, 95% CI 1.6–103.7; $p = 0.02$), and washing clothes between 11 a.m. and 4 p.m. (OR 10.9, 95% CI 1.5–77.3; $p = 0.02$) were all independently associated with epilepsy. Blood screening by specific PCR tests for *Toxoplasma* and *Wuchereria bancrofti* was negative in all cases and controls. A *Loa loa* infestation was found in only one case and one control by PCR and Giemsa smear. Antibodies to *Taenia solium*, Toxocara, and *Trypanosoma sp* were not detected in any of the participants. In an age-matched case–control analysis, 16/18 (89%) cases had not taken ivermectin the year before they developed epilepsy, compared to 7/18 (39%) controls that same year ($p = 0.002$).

Conclusions: These data suggest that frequent activities at rivers known to be blackfly breeding sites and a historical lack of ivermectin treatment were risk factors for epilepsy in this onchocerciasis endemic area.

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1. Introduction

The prevalence of convulsive epilepsy is greater in Sub-Saharan African countries than in high-income countries, and parasitic infestations are thought to contribute to this increased burden.[1,2] A high prevalence of epilepsy has been reported in many onchocerciasis endemic areas,[3,4] and is particularly high in certain localities in South Sudan, Tanzania, and northern Uganda, where a special form of atonic epilepsy called 'nodding syndrome' (NS) has been described.[5–8] The cause of NS remains unclear,[5,9] but case–control studies have regularly found an association between onchocerciasis and NS.[5,7,10,11] In a study in Cameroon, the intensity of infestation with *Onchocerca volvulus* (OV) was found to be higher in people with epilepsy than in controls.[3]

The Democratic Republic of the Congo (DRC) is a country with large areas where onchocerciasis is still hyperendemic.[12] Between April 2014 and June 2014, several epilepsy prevalence studies were performed in villages in the Bas-Uélé Province, namely Liguga,[13] Dingila, and Titule[14] (Figure 1). Among the 12 776 people in Dingila, 373 (2.9%) individuals with epilepsy were identified. In a door-to-door survey in Titule, 68 (2.3%) of the 2908 people who participated in the survey were found to present episodes of epilepsy.[14] In Titule, epilepsy showed a marked spatial pattern, with clustering of cases occurring within and between adjacent households. The individual risk of epilepsy was found to be associated with living close to the Bima River, a fast flowing river where blackflies (Diptera: *Simuliidae*) – the vector of OV – oviposit and breed.[14] The degree of onchocerciasis endemicity in Titule was not estimated in 2014, but in 1999, during a rapid epidemiological mapping of onchocerciasis (REMO) survey, all of the 33 persons examined in the village had nodules. As a consequence, ivermectin has been distributed in Titule once a year to persons over 5 years of age, but not to pregnant or breastfeeding women, since 2000. The coverage initially was reported to be 23%, but the coverage has increased over the years to 73–81% of the eligible individuals (F. Tepage, personal communication).

During the epilepsy prevalence survey in Titule, a case–control study was also performed to investigate whether exposure to *Simulium spp* blackflies is indeed a risk factor for developing epilepsy and to determine whether treatment with ivermectin may protect against developing epilepsy.

2. Materials and methods

2.1. Setting

Titule, a locality crossed by the Bima River, has a population of 11 882 inhabitants. Our visit to Titule was announced by the local doctor and the volunteers of the 'relais communautaire'. These are villagers making up the community surveillance network, who are involved in the community-directed treatment with ivermectin campaigns (CDTI), vaccination campaigns, and mosquito net distribution; therefore they know the members of their community well. On arrival, at least 50 patients were waiting for us. During our stay in Titule at least 100 additional patients wanted to be seen by us. Two patients with epilepsy did not want to participate in the study because they did not want to undergo a lumbar puncture, a procedure included in the study protocol. No incentives were given to the patients to participate.

2.2. Design

The first 59 patients with confirmed active epilepsy after examination by one of the study doctors and who agreed to

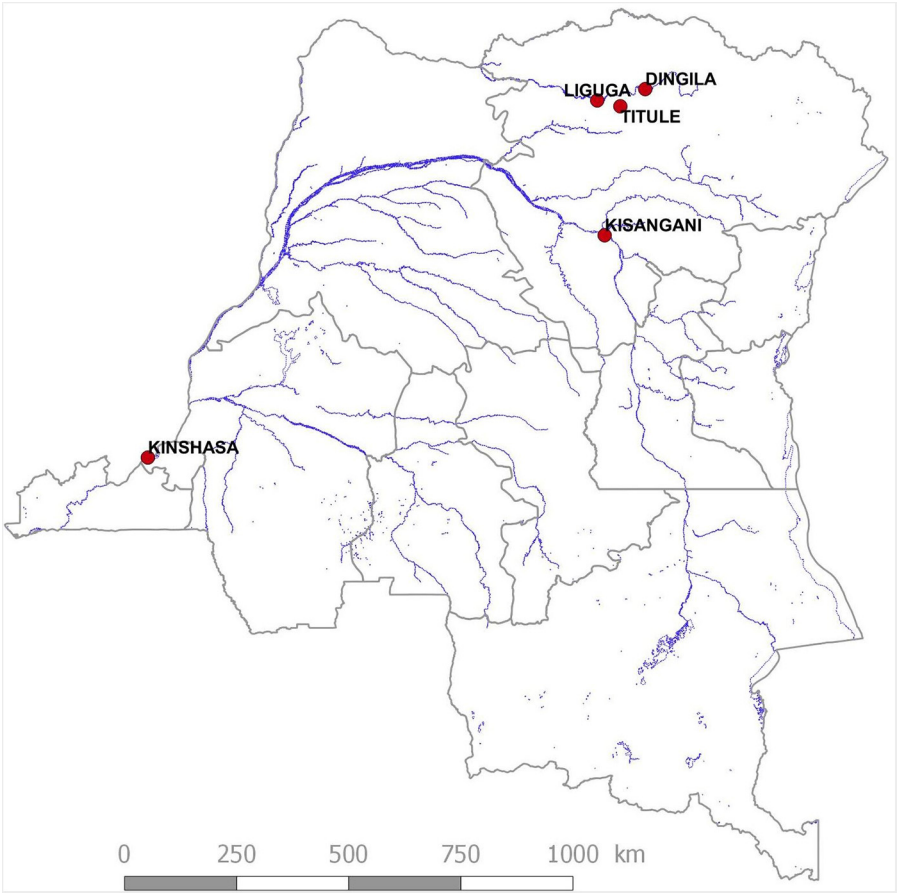

Figure 1. Location of Titule in the Bas-Uele district, Democratic Republic of the Congo.