Update on onchocerciasis-associated epilepsy in Cameroon

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What was known before 2017

- Surveys in the Mbam valley (1991-1993)
- Onchocerciasis survey alone Epilepsy census alone Oncho & Epil survey
- Prevalence of epilepsy1 = low< 1%</td>2 = moderate1 2.5%3 = high2.5 6%4 = very high> 6%



What was known before 2017

Analyses at **community level**

TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (2002) 96, 537-541

Relationship between onchocerciasis and epilepsy: a matched case-control study in the Mbam Valley, Republic of Cameroon

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Fig. 1. Relationship between the prevalence of epilepsy (%), and the level of endemicity for onchocerciasis, as assessed by the community microfilarial load (CMFL), in 14 villages of the Mbam Valley (Cameroon). mf, Onchocerca volvulus microfilariae.

Fig. 2. Relationship between the prevalence of epilepsy (%), and the distance to the Mbam River, for the 23 villages of the Mbam Valley (Cameroon) where an exhaustive census of the epileptic individuals has been conducted.

12

14

Case-control study (72 PWE and 72 matched controls)

| | No (%) mf+ | Mean (Arith) mf/snip | Mean (Geo) mf/snip | Median mf/snip |
|----------|------------|-------------------------|-----------------------|-------------------|
| PWE | 71 (98,6) | 288 | 148 | 216 |
| Controls | 68 (94,4) | 141 | 45 | 63 |

What was known before 2017

Meta-analyses

At community level (2009)

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PLOS REGLECTED

Epilepsy in Onchocerciasis Endemic Areas: Systematic Review and Meta-analysis of Population-Based Surveys

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At individual level (2013)

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PLOS REGLECTED TROPICAL DISEASES

Case-control Studies on the Relationship between Onchocerciasis and Epilepsy: Systematic Review and Meta-analysis

Christoph Kaiser¹*, Sébastien D. S. Pion², Michel Boussinesq²



What was known before 2017

Demographic impact (Kamgno et al., *Epilepsia* 2003) 128 PWE and 128 matched controls 10-year follow-up

Excess mortality



Impact on nuptiality and fecundity

Many Nakalanga cases (Boussinesq et al., unpublished)



Studies in 2017 (1) Incidence study

- In 1991-1993, skin O. volvulus mf densities had been measured in thousands of people aged ≥ 5 years in the Mbam valley
- In 2017, 7 villages with various initial infection intensity (CMFL) were revisited to collect information on the vital status (live v. dead) and the occurrence of epilepsy for all 858 individuals who had been examined in 1991-1993 at the age of 5–10 years
- The classical 5-item questionnaire developed in Limoges was used to identify suspected cases of epilepsy
- A multi-variate analysis was conducted to assess the association between the occurrence of a suspected epilepsy and four factors (gender, age, CMFL and individual mf density in 1991-1993)
- Information could be obtained from the subjects themselves or from their family for 731 individuals (85.2%)

Studies in 2017 (1) Incidence study

- 60 cases of suspected epilepsy occurred between the initial and 2017 surveys and the incidence rate was 3.1 / 1,000 (60/19.075 PY)
- Initial individual mf density was very significantly associated with the occurrence of epilepsy

| Factor | Categories | Incidence rate ratio | 95% CI | р |
|-------------------|------------|----------------------|-------------|-------|
| Age (ref: 5 y.o.) | 6 | 0.55 | 0.33-0.91 | 0.019 |
| | 7 | 0.71 | 0.46-1.11 | 0.132 |
| | 8 | 0.66 | 0.28-1.56 | 0.343 |
| | 9 | 0.45 | 0.22-0.91 | 0.027 |
| | 10 | 0.43 | 0.14-1.35 | 0.149 |
| Sex (ref: female) | male | 1.15 | 0.74-1.90 | 0.535 |
| CMFL (ref: low) | medium | 0.81 | 0.36-1.84 | 0.618 |
| | high | 1.33 | 1.04-1.69 | 0.021 |
| individual | 1-12.5 | 8.56 | 1.30-56.96 | 0.026 |
| mf density | 13-64.5 | 11.83 | 4.51-31.04 | 0.001 |
| (ref: 0 mf/snip) | ≥65 | 26.31 | 4.01-172.40 | 0.001 |

Studies in 2017 (2) Prevalence study

- A census of PWE using key informants was conducted in 21 villages in 1991-1993. Three of them were selected to measure the prevalence of epilepsy in 2017, using a door-to-door strategy
- In Bilomo, door-to-door surveys were conducted both in 1998 and 2017
- In 2017, the prevalence had not decreased significantly in three of the four villages, where it remained still very high

| Village | Prevalence in 1991-1993 or 1998 (%) | Prevalence in 2017 (%) | р |
|----------|--|---------------------------|-------|
| Bayomen | 13.6 | 2.5 | 0.001 |
| Ngongol | 8.7 | 6.6 | 0.335 |
| Nyamongo | 6.4 | 5.4 | 0.418 |
| Bilomo | 4.9 | 4.6 | |

Studies in 2017

(2) Prevalence study

- A very marked shift towards higher ages in the population of PWE between the early 1990s and 2017
- Probably due to the community-directed treatment with ivermectin which started in 1998



Studies in 2017 Conclusions

- The first longitudinal study on the relationship between oncho and epilepsy was conducted in the Mbam valley, Cameroon
- the O. volvulus microfilarial density in childhood in the early 1990s constituted a major risk to develop an epilepsy later on
- This might suggest that the association between the two conditions is due to a direct effect of the parasite, and not (only?) to autoimmunity phenomena, as suggested recently
- The age shift in the population of PWE suggest that MDA with ivermectin, by decreasing the *O. volvulus* mf densities, led to a decrease in the incidence of epilepsy
- Typical cases of nodding syndrome were identified for the first time in Cameroon and are being further investigated

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