JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Untreated villages and factors associated with the absence of Community-Directed Treatment with Ivermectin (CDTI) in DRC

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Abstract

Introduction: The African Programme for Onchocerciasis Control (APOC), the main objective of which was the Community-Directed Treatment with Ivermectin (CDTI), was closed by the end of 2015. The purpose of this study was to describe untreated villages in DRC and to assess the factors associated with the absence of CDTI in endemic villages, between 2001 and 2014.

Methodology: This retrospective study was descriptive. Several annual technical reports of the National Onchocerciasis Task Force (NOTF) and national technical reports of CDTI projects were analysed; 21 projects implemented to control the disease were considered, representing the coverage of 42,778 endemic villages. Data were collected over a 3 month-period, between October and December 2016.

Results: Only 15,700 endemic villages were not treated through an annual CDT with Mectizan, i.e. 36.7%. The population at risk totalled 29,712,381 individuals and 7,681,995 of them were not treated, i.e. 25.9%. Eight projects recorded high proportions of untreated villages, i.e. 7,100 endemic entities (16.6%). Factors independently associated with non-treatment were the fear of serious side effects (adjusted OR: 10.6; 95% CI: 4.5-27.7), supply impaired by insecurity (adjusted OR: 15.9; 95% CI: 6.7-41.4) and geographical inaccessibility (adjusted OR: 19; 95% CI: 6.9-63.9).

Conclusion: After 15 CDTI-cycles in DRC, the mean geographical coverage and therapeutic coverage rates reached 63.3% and 74.1%, respectively. The 2025 target of onchocerciasis eradication, as advocated by APOC, will not be reached. Untreated areas are partly responsible for such results. Many weaknesses persist in the National Program for Onchocerciasis Control (NPOC) and new strategies of disease control should be investigated.

Key words: Onchocerciasis; untreated villages; ivermectin; factors associated; absence; Democratic Republic of Congo.

J Infect Dev Ctries 2018; 12(9):771-779. doi:10.3855/jidc.9881

(Received 26 October 2017 – Accepted 25 July 2018)

Introduction

Commonly known as 'river blindness' due to the geolocation of its vector, onchocerciasis is caused by a parasite named *Onchocerca volvulus* [1]. Human beings acquire the infection through the bites of black flies, i.e. *Simulium damnosum* species complex, which carry infective larvae of *Onchocerca volvulus* [2]. They are the definitive host of the parasite whereas *simuliid* vectors feed on a range of animals. Human blood index is a key indicator of the potential for human onchocerciasis transmission [3]. The skin is the main organ affected , even though infection with *Onchocerca volvulus* can cause serious eye problems, and even blindness. Its pathogeny is closely related to the immune reaction caused by dead or young immature microfilariae in skin and eyes. Murdoch referred to it as a chronic systemic disease [4].

Onchocerciasis - the world's second leading infectious cause of blindness - is present in 36 countries of Africa, the Arabian Peninsula and the Americas [5]. As a public health problem the disease is most closely associated with Africa, where it represents a serious obstacle to socio-economic development [5]. Out of some 120 million people world-wide who are at risk of contracting onchocerciasis, 96% are located in Africa [5]. A total of 18 million people are infected with the disease, of whom 99% live in Africa and at least one million are either blind or severely visually disabled. An estimated 40,000 people develop blindness as a result of the infection every year. [6,7]. Onchocerciasis compared to trachoma which is also one of the neglected tropical infectious diseases and the leading cause of preventable blindness, affects 21.4 million people of whom about 2.2 million are visually impaired

and 1.2 million are blind [8,9]. Currently, it is responsible, for more than 3% of the world's blindness, however, that figure keeps changing due to the socioeconomic development effect and current control programs for this disease. At a recent WHO meeting it was estimated that trachoma is endemic in 55 countries, mainly in Africa and Asia. [8,9].

In the Democratic Republic of the Congo (DRC), onchocerciasis is a major public health problem; it is endemic in all of the 26 provinces [10]. It is estimated that more than 26 million people representing 40% of the whole population are at risk of infection [11]. About 65,000 persons, representing one person in a thousand, develops blindness as a complication. The first onchocerciasis control programme was implemented 43 years ago. The African Programme for Onchocerciasis Control (APOC) started in 1995; its primary objective was to implement a programme for an effective and self-sustainable Community-Directed Treatment with Ivermectin (CDTI) in endemic villages falling in the geographical scope of the Programme and, if possible, in selected and isolated foci, to eradicate the vector by using environmentally safe methods. Ivermectin is a microfilaricid with no direct action on *Onchocerca volvulus* adult stages [12]. The main aspects of APOC focused on the following issues: disease mapping, CDTI, co-implementation of sanitary operations, increased treatments of *lymphatic filariasis*, control of onchocerciasis and assessment of the impact of onchocerciasis treatment on eradication [13,14]. It is estimated that nearly two billion treatments will be needed between 2016 and 2025 to eradicate onchocerciasis [15]. The WHO target for control of *lymphatic filariasis* was set for 2020, whereas 2025 is the target for onchocerciasis eradication [16]. In DRC, APOC started one project in 2001, came up with 21 projects in 2012, and 22 from 2014 until the end of its activities in 2015 [10,17].

The success of APOC in Mali and Senegal, illustrated by a decreased prevalence in onchocerciasis by 2001, led to a paradigm shift, i.e. moving from onchocerciasis control to its eradication with the help of CDTI [18]. This objective is achievable if ivermectin is delivered annually to all people aged 5 years or older, excepting pregnant and breast-feeding women (first week after childbirth), for at least 15 years [5,19]. The CDTI is delivered only once a year and it is likely that onchocerciasis could be eradicated if an 80% therapeutic coverage rate and a complete geographical coverage are ensured during at least 15 years, with no interruption, as demonstrated by previous studies [3,16,20]. However, a 2015-study identified untreated areas in DRC, impairing the achievement of the APOC target mentioned above. Targets for individual or therapeutic and geographical coverages were not met due to the co-endemicity of loiasis in numerous villages but also due to political conflicts [10,21]. In 2015, before APOC ceased its activities, the following results were reported in DRC: ivermectin had been delivered to 28,251,053 persons, among whom 26,049,139 needed a treatment against onchocerciasis, corresponding to a national coverage of 63% [22].

Despite 15 years of activities, the therapeutic coverage was below 80% and conditions of eradication were related to different factors dependent of the context. For example, a study performed in DRC concluded that CDTI-related challenges were serious side effects linked to the use of ivermectin in hyper-endemic villages, and villages where onchocerciasis and loiasis were co-endemic [10]. All villages not covered by CDTI were significant obstacles to the new APOC objective, i.e. the reduction of onchocerciasis infection leading to its eradication by 2025 [23].

The purpose of this study was to describe untreated villages in DRC and to assess the factors associated with the absence of CDTI in endemic villages, between 2001 and 2014.

Methodology

Study area

DRC is the second largest country in Africa, right behind Algeria. It is a central African country covering an area of 2,345,410 km^2. Between the years 2000 and 2016, its population increased from 65 to 80 million (79,795,627) people, as per to DRC National Institute of Statistics [24]. DRC is characterised by a wide linguistic and cultural diversity. Indeed, more than 400 tribes exist and are grouped in four main ethnic groups, i.e. Bantus (majority), Nilotics, Sudanese and Pygmies. The country is a highly decentralised unitary state. According to the last territorial reform, it includes 26 provinces, with 96 cities, 337 urban districts, 267 rural districts and 5,397 groupings subdivided into villages. From a health point of view, DRC has516 health zones (HZ) and 8,504 health areas (HA); each HA includes several villages [25].

The health zone (HZ) is the basic operational level for organising, planning and developing sanitary activities. It is a well delimited geographical entity (maximum diameter of 150 km) included within the limits of a territory or administrative municipality; its population reaches at least 100,000 inhabitants and gathers homogeneous communities from a sociocultural point of view. Health services exist at two

interrelated levels, i.e. first line health centres and the second-level General Reference Hospital, but under the supervision of a HZ management team. A HZ is subdivided into several health areas (HA); an HA is a well delimited geographical entity gathering several villages in rural areas/several streets in urban environments, and established according to socio-demographic affinities. There are approximately 10,000 inhabitants in each HA, covered by a Health Centre, depending on the context (rural vs. urban) [11].

In 1996, with the support of WHO/APOC, DRC Ministry of Health created the National Onchocerciasis Control Programme (NPO). Later on, a National Onchocerciasis Task Force (NOTF) using the CDTI approach was set up. The provinces had a relative autonomy in the management of CDTI projects and storage facilities; provincial warehouses allowed storing ivermectin for the projects. The first CDTI project was launched in 2001 in Kasai areas, followed by Uele in 2002. In 2003, seven new projects were implemented, i.e. Bandundu, Tshopo, Bas-Congo/Kinshasa, Sankuru, Katanga-Nord, Katanga-Sud and Lualaba. In 2004, the following six projects were added: Tshuapa, Ubangi-Nord, Ubangi-Sud, Mongala, Rutshuru Goma and Equateur Kiri. However, between 2004 and 2005, and in addition to new projects launched during 2014, the Uele, Tshopo, and Bas-Congo/Kinshasa projects were suspended temporarily because of ivermectin-associated deaths in onchocerciasis and loiasis co-endemic areas. Therefore, the combined use of loiasis mapping using 'Rapid Assessment Procedure for Loiasis' (RAPLOA) and onchocerciasis mapping with Rapid Epidemiological Assessment (REA) allowed for identifying onchocerciasis treatment areas; areas of onchocerciasis and loiasis co-endemicity were then excluded from the CDTI. In 2005, populations from Bandundu, Kasai and Sankuru projects only were treated with ivermectin. In 2006, the following projects set up ivermectin treatment: Bandundu, Bas-Congo/Kinshasa, Equateur-Kiri, Kasai, Katanga-Nord and -Sud, Lualaba, Mongala, Rutshuru-Goma, Sankuru, Tshopo, Tshuapa, Ubangi-Nord and –Sud, and Uele. In 2007, the Kasongo project was started. In 2008, four new projects, i.e. Butembo Beni, Lubutu, Masisi-Walikale and Ituri-Nord were launched. The last project, Ituri-Sud, finally started in 2012. If we consider the 2001-2014 period, this brings us to a total of 21 CDTI projects in DRC, which mainly relied on APOC objectives [10,22]. Several awareness-raising and mobilisation activities were implemented among communities, on one hand for their participation and their ownership of the CDTI project, and on the other hand, for an advocacy with several international organisations to seek for financial support [10].

Study design

Our study focused retrospectively on the 21 projects implemented between 2001 and 2014 that covered 42,778 villages endemic with onchocerciasis which participated in the Community-Directed Treatment (CDT) with Mectizan. Data were collected between October and December 2016.

Data sources

Two sets of data sources were analysed. Data on ivermectin delivery were collected from the National Onchocerciasis Task Force (NOTF). The global number of projects was considered. For each project, the following information was taken into account: CDTI-duration (in years), geographical coverage, therapeutic coverage, total population, number of persons treated, number of persons absent and refusals, as well as tablets delivered or not used. The second data source consisted of the national technical reports of CDTI projects, published annually between 2001 and 2014. These reports also allowed for analysing the involvement of local communities at the village level, participation of stakeholders, as well as treatments and side effects. All necessary information and data were collected from a literature review.

Variables of interest and statistical analyses

Dependent variable: the untreated village was a geographical unit identified as disease-endemic, untreated, but circled by villages covered by CDTI. The village was seen as the operational and functional CDTI-unit.

Independent variables: the number of persons absent, people who refused to join a CDTI project, as well as tablets delivered or not used. Non-involvement of populations (at the village level), stakeholders, treatments and serious side effects, mortalities, insecurity due to the presence of armed groups and geographical inaccessibility were also tested as independent variables.

Data collection and analysis

Investigators, all trained beforehand, collected data from NOTF annual technical reports, and stakeholder reports.

Statistical analysis

Projects, health villages, and annual proportions of untreated villages were compiled in an Excel™ file. Statistical analyses were performed with STATA 12.0 software (Statacorp, Texas, USA) and EPI-INFO 2.5.3 software (Centers for Disease Control and Prevention). Geographical coverage was considered as the reference indicator and represented by the ratio of N treated villages to the total N endemic villages (in which CDTI was supposed to be implemented). A logistic regression allowed for exploring the factors potentially associated with non-treatment of villages. An exploratory approach was performed. The variables included in the models were selected via a step-by-step decreasing procedure based on likelihood ratios; independent variables with non-significant regression coefficients ($P > 0.05$) were removed from the regression model. The maintained adjustment variables were: type and duration of the projects and the geographical location of the projects.

Odds ratios (ORs) and their 95% confidence intervals (CI) are presented for the final model. The Hosmer and Lemeshow goodness-of-fit test was applied in this study. Results were considered as significant if the *P*-value was less than 0.05.

Results

Over the 21 projects implemented to ensure the coverage of 42,778 onchocerciasis-endemic villages, beneficiaries of 15 cycles-CDTI, 15,700 entities were not treated, i.e. 36.7%. Eight projects (Butembo-Beni, Ituri-Nord, Ituri-Sud, Kasongo, Masisi-Walikale, Rutshuru-Goma, Tshuapa, and Ubangi-Sud) recorded high proportions of untreated villages, i.e. 7,100 endemic entities (16.6%). The Ituri-Sud project accounted for the majority of untreated villages (80.3%), i.e. 1,322 villages out of 1,646; 62.5% of villages (860 out of 1,376) were not treated in the Masisi Walikale project. Two projects, Butembo-Beni and Rushuru-Goma, similarly recorded a 60%-therapeutic coverage rate, with 968 out of 1,613 villages and 382 out of 636 villages, respectively. The mean national therapeutic coverage rate during APOC activities reached 74.1% whilst geographical coverage was 63.3% (Table 1).

After performing the univariate analysis, the following factors were identified as being independently associated with non-treatment: fear of serious side effects and mortality, insecurity (impairing supply) and geographical inaccessibility. Proportions of untreated and treated villages were significantly

Table 1. Proportions of villages non-treated for onchocerciasis, between 2001 and 2014, as recorded by projects implemented in the Democratic Republic of Congo (DRC).

Projects	Number of endemic villages	Number of untreated villages	Proportion of untreated villages (%)	Total Population at risk	Number of untreated persons	Proportion of untreated persons (%)
Bandundu ****	3,606	516	14.3	1,269,781	101,579	8.0
Bas-Congo Kin*	3,061	606	19.8	745,223	167,554	22.5
Butembo-Beni	1,613	968	60.0	1,100,556	460,334	41.8
Equateur-Kiri*	1,621	716	44.2	1,132,013	560,350	49.5
Ituri-Nord	1,620	863	53.3	1,002,562	234,366	23.4
Ituri-Sud***	1,646	1,322	80.3	1,139,457	714,984	62.7
Kasai**	9,911	2,052	20.7	10,767,690	800,912	7.4
Kasongo*	2,082	1,045	50.2	1,195,785	300,284	25.1
Katanga-Nord	641	263	41.0	526,909	210,033	39.9
Katanga-Sud	1,061	438	41.3	779,262	121,835	15.6
Lualaba	382	134	35.1	205,976	32,297	15.7
Lubutu*	671	328	48.9	328,864	165,814	50.4
Masisi Walikale*	1,376	860	62.5	905,907	466,192	51.5
Mongala*	1,280	521	40.7	1,208,165	491,723	40.7
Rutshuru-Goma	636	382	60.0	610,173	266,104	43.6
Sankuru* and ****	1,359	162	11.9	939,301	111,777	11.9
Tshopo*	2,629	1,262	48.0	1,034,260	490,445	47.4
Tshuapa*	1,950	989	50.7	1,095,512	455,425	41.6
Ubangi-Nord*	1,097	360	32.8	759,742	209,195	27.5
Ubangi-Sud*	1,281	671	52.4	1,324,433	794,003	60.0
Uélé*	3,255	1,243	38.2	1,640,808	526,789	32.1
Total	**42,778**	**15,700**	**36.7**	**29,712,381**	**7,681,995**	**25.9**

*: Projects for which the occurrence of serious adverse reactions was the cause of treatment refusal; **: Breaking of ivermectin supply was the cause of refusal or absence of treatment; ***: Project that started integrating onchocerciasis control; only 30% of the communities have started; ****: Projects that did not register high proportions of untreated villages.

Table 2. Factors explaining the lack of treatment for onchocerciasis in the Democratic Republic of the Congo, between 2001 and 2014 – univariate analysis.

Factors	Proportion of untreated villages (%)	*P*
Community ownership		**0.997**
Yes	36.8	
No	36.7	
Serious side effects		**< 0.001**
Yes	48.1	
No	8.3	
Death		**0.001**
Yes	41.5	
No	28.1	
Expired tablets		**0.933**
Yes	36.5	
No	35.5	
Insecurity hindering supply		**< 0.001**
Yes	58.2	
No	8.2	
Geographical inaccessibility		**< 0.001**
Yes	49.5	
No	4.9	

different reaching 48.1% and 8.3%, respectively ($P \leq 0.001$). The fear of serious side effects significantly increased the proportion of untreated villages by a factor of 10. Insecurity significantly hindered ivermectin supply to villages and its further door-to-door delivery, which resulted in the non-treatment of some villages (58.2% *vs* 8.2%; $P \leq 0.001$) (Table 2); adjusted for type and duration of the projects, the geographical location of the projects; the odds of missing treatment for insecure village was 16 times higher than for secure villages. Lack of supplies increased the proportion of untreated villages by a factor of 19 (Table 3).

The proportion of untreated villages progressively decreased from 90.7% in 2001 to 1.7% in 2014, based on projects durability. Proportions reached 35.9% in 2007, 45.5% in 2008, 14% in 2009 and 5.8% in 2010 (Figure 1). Previously treated villages (except in 2014), were located in the northern half of the country, i.e. former provinces of Equateur, western and northern

Figure 1. Trend in the proportions of untreated villages between 2001 and 2014 (NPOC/DRC).

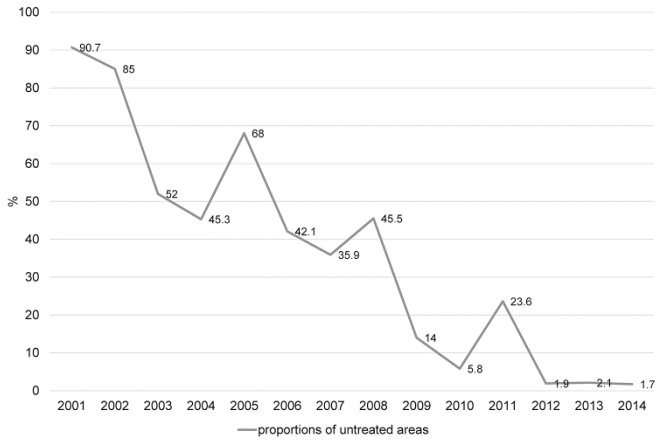

Table 3. Factors explaining the lack of treatment for onchocerciasis in the Democratic Republic of the Congo, between 2001 and 2014 – multivariable analysis.

Factors	Adjusted Odds Ratio (95% CI)	*P*
Serious side effects		**< 0.001**
Yes	10.6 (4.5-27.7)	
No	1	
Insecurity hindering supply		**< 0.001**
Yes	15.9 (6.7-41.4)	
No	1	
Geographical inaccessibility		**< 0.001**
Yes	19 (6.9-63.9)	
No		

Kivu. Onchocerciasis-loiasis co-endemicity could be the reason for non-treatment. In the Kasai project, weakness of reporting could partly be responsible for non-treatment as well.

Discussion

The existence of untreated villages reveals that treatment cycles were not regularly applied, and not all eligible individuals were treated nationwide. Our results showed that 15,700 endemic villages initially included in the CDTI plan were not treated, representing 36.7% and 8 projects out of 21 (Butembo-Beni, Ituri-Nord, Ituri-Sud, Kasongo, Masisi-Walikale, Rutshuru-Goma, Tshuapa and Ubangi-Sud) recorded high proportions of untreated villages. The non-treatment may jeopardise the disease control due to the persistence of microfilariae and their subsequent availability for black flies upon blood feeding. In our opinion, control of onchocerciasis in DRC seems more necessary than ever, especially since it would lead to substantial health and economic benefits and would reduce the need for workforce and outpatient services. To achieve such objectives, the support and collaboration of community, national and international decision makers are unavoidable, in order to support control strategies, as suggested by Kim and collaborators [26].

Our results highlight mean therapeutic and geographical coverage rates below 75%. However, previous studies demonstrated the need to ensure an 80% therapeutic coverage and a 100% geographical coverage to eradicate onchocerciasis in a (hyper-) endemic countryduring at least 15 cycles without interruption [3,16,20]. Therefore, our results highlight the insufficient therapeutic and geographical coverages in DRC, to achieve the 2025 WHO target of onchocerciasis eradication. Previous studies have demonstrated that controlling onchocerciasis was possible. In the case of DRC, we think onchocerciasis eradication is possible by means of CDTI application following several mathematical models suggested by WHO. To our opinion, such models should be adjusted and adapted to the geographical and therapeutic contexts of the country [27, 28].

Eradication of onchocerciasis attributed to CDTI was successful in Senegal and Mali. Thus, some African countries have set the target of controlling onchocerciasis by 2020, whilst other nations such as DRC, are expected to reach 80% of control by 2025. Challenges to achieve such objectives in endemic countries include armed conflicts, which delay or interrupt control programmes, transboundary foci, the potential emergence of ivermectin-resistant parasitic strains, and co-endemicity with loiasis, another vector borne parasitic disease which hinders or restricts the implementation of CDTI [28]. Our results confirmed these observations in the way that insecurity impairs door-to-door ivermectin supply in villages. We fear that the 2025 WHO target of onchocerciasis control will not be achieved in DRC due to untreated villages and unsecure conditions prevailing in the country. According to Hopkins, controlling the disease, as a public health problem, is achieved by implementing sustainable control measures, in order to prevent disease recurrence [27].

Three factors explaining independently the absence of treatment were identified by the multivariable analysis: insecurity, due to the presence of armed groups in some villages, the fear of serious side effects and geographical inaccessibility. These factors are a result of the weaknesses of the National Program for Onchocerciasis Control (NPOC) in DRC. The success of treatment requires an active participation of the population and the community ownership of ivermectin delivery. This objective can only be achieved through contact with leaders, notables and the whole population. Advantages of a long-term treatment should be explained to the population, as well as the importance of its entire responsibility along the whole delivery process. Such community integration was not followed up appropriately in some projects. Meanwhile, a correct coverage and a better ownership will allow to avoid reinfection and prevent the vector from transmitting new parasites at each blood meal. That is why the population should actively celebrate the success of control programmes through health education about community participation, as Shu and Col described in their study [29].

The fear of developing serious side effects, such as (non)neurological encephalopathies, tiredness, headaches, digestive problems (nausea, diarrhoea and vomiting), rash, swollen limbs and face, muscle pain, fever and swollen groin lymph nodes, reported on patients who are delivered ivermectin for the first time, was another reason for non-treatment. Such fear of side effects, in villages where onchocerciasis and loiasis are co-endemic, could be explained by the absence of a well organised sanitary information system, but also the lack of motivated service providers, supervision and follow-up. Such problems were previously mentioned by Makenga and collaborators in a study assessing the situation of onchocerciasis in DRC [10]. These side effects have discouraged the population from starting/continuing the treatment. To our opinion, one

of NPOC weaknesses is the lack of importance given to education and/or public awareness which are crucial aspects leading to therapy acceptance, as demonstrated by Kuesel in his study [30]. We are convinced that onchocerciasis eradication will not be achieved without the entire cooperation of the population. Indeed, it is essential to inform local populations so that they can fully cooperate during treatment in order to guarantee a global therapeutic coverage. Making the population aware of treatment discontinuation and post-treatment surveillance concepts is essential as well. Otherwise, community members may refuse to participate to post-treatment surveys if they do not understand why treatment is stopped while they feel positive effects [27].

Geographical inaccessibility reported in Kasai, Masisi-Walikale and Rutshuru Goma was responsible for non-treatment, which confirms the conclusions of Makenga and collaborators, who also mentioned expired tablets in different CDTI projects of the country [10]. Insecurity due to the presence of armed groups explained a high proportion of untreated villages, especially in eastern DRC projects. Makenga and collaborators previously reported in their publication illustrating the challenges of onchocerciasis control in post-war DRC, that climate of war was a reason for non-treatment, [10]. Insecurity impaired the timely transport of tablets to the point of making some of them obsolete and leading to stock-outs.

To our opinion, the NPOC should be radically reformed in order to refine the operational criteria and address CDTI weaknesses, i.e. awareness, organisation and management so as to regain control of the fight against onchocerciasis in DRC, or even stop mass treatment timely, as suggested by Stolk and collaborators [28]. The world programme for the control of river blindness will have to rely on the development of new tools (medicine, vaccines, biomarkers) in order to achieve its 2025 target [31]. The bi-annual treatment with ivermectin could also improve the chances to achieve control objectives by 2020/2025. It would potentially generate programme savings in highly endemic environments, as suggested by Turner and collaborators [32]. Our opinion is similar to Crump's, who mentioned that eliminating onchocerciasis by 2025 because of its impact on public health, will not be achieved (even though well advanced) in some sub-Saharan countries, due to untreated villages and hyper-endemicity [33]. Decreasing the proportion of untreated villages is not the only mean to achieve the WHO target of 80% therapeutic coverage. Other major changes in the programme, through efforts targeting specific objectives, could help eradicating onchocerciasis by 2025, at the world level, as suggested by Mackenzie and collaborators [34].

The proportions of non-treated villages have progressively decreased between 2001 and 2014, i.e. from 90.7% to 1.7%, respectively. The peaks observed in 2001 and 2002 were related to the progressive disappearance of projects. In 2005, the discontinuation of treatment after serious side effects explained the peak recorded in Bas Congo; the Rapid Assessment Procedure for loiasis (RAPLOA) surveys also started during that period. The 2008-peak was consecutive to Mectizan stock-out in Kasai, which was encompassing more than 25% of the therapeutic weight in DRC. Factors such as demotivation, abandonment of community-based distributors and the launch of the Ituri-Sud CDTI project account for the small peak observed in 2011. Between 1996 and 2016, DRC experienced armed conflicts that impaired the correct course of CDTI process. . Serious side effects related to the co-endemicity of loiasis and onchocerciasis were recorded during this period affected also the CDTI process. The situation has thus worsened and the population turned away from CDTI. Our results confirm the conclusions of Makenga and collaborators who demonstrated that armed conflicts impaired CDTI in several provinces of DRC [10]. The present study also highlights that ivermectin, delivered as recommended, would not be appropriate to prevent the occurrence of serious side effects, as previously reported by Kamgno and collaborators [35].

Limitations

Our study had some limitations that need to be pointed out. Indeed, the statistical unit we considered was the untreated village, and not the untreated person. Some individual data which may provide information on factors associated with non-treatment, treatment refusal or discontinuation was lacking. A study on perception of illness, mortalities, serious side effects and the comparison of prevalence in treated vs. non treated areas should be encouraged.

Conclusion

The existence of untreated villages, as observed in several CDTI projects, could make it difficult to achieve the 2025 WHO target of onchocerciasis control in DRC.

Insecurity, instability, the fear of serious side effects consecutive to treatment and the geographical inaccessibility are the main factors explaining the non-

treatment, as highlighted in our study. Expected therapeutic and geographical coverages were not achieved, which enhances the transmission of onchocerciasis and the persistence of clinical signs and/or complications of the disease.

We would recommend to the WHO and the NOCP to plan other interventional alternatives to control the disease for eradication such as: strengthening the NOCP coaching in management and steering through the appointment of consultants, strengthening the implementation of supportive activities such as supervision and regular evaluation by technical advisers, and leading the planning with policy makers to stabilise the staff and maintain national human expertise used as a battle tool in onchocerciasis control.

Acknowledgements

We thank DRC Ministry of Health and all participants who enabled this study to be realised.

Declarations

Ethics approval and consent to participate: The Scientific Committee, School of Public Health, approved the study and provided a document authorizing field data collection (No. approval: ESP/CE/068/16).

Authors' contributions

JCMB is the main author: he designed the study, participated to data collection and analysis. FNT participated to the writing of the manuscript, data analysis and marking of the final version. DMM and PMM took part in data analysis and marking of the final version. FII took part in data collection and analysis. YC participated to the writing of the manuscript, methodology and read-through. All authors were involved in the preparation of the manuscript, editing and finalization of the version to be published and agreed to be accountable for all aspects related to the integrity of the work.

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Conflict of interests: No conflict of interests is declared.