

Assessment of adverse drug reactions in the home management of malaria cases of children under 5 years using artemisinin-based combination therapy in Mfou health district, Center region of Cameroon

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Abstract

Malaria remains one of the major public health concerns in Cameroon. Its treatment is frequently initiated at home, most often with street drugs. The home management of malaria cases entails the prescription of Artemisinin-based combination (ACTs) as first-line therapy for treatment of uncomplicated malaria after having confirmed the malaria case using rapid diagnostic tests. But induced adverse reactions of this therapy are not well known in Cameroon. Thus, a prospective, observational, cohort study of adverse events associated with ACTs was conducted from January 2013 to November 2013 in the health district of Mfou. Children under 5 years receiving ACTs for malaria treatment at home were enrolled. Suspected ADRs and other clinical events were recorded. Data were managed and analysed using Epi Info version 3.5.3 and Statistical Package for Social Sciences, statistical software version 20. Of the 479 children investigated, 56.8% (n=272/479) were males, the age group 25-59 months (49.5%; n=237/479) was most represented, 27.1% (n=130/479) had experienced one form of ADRs, male children (56.2%; n=73/130) and the age group 25-59 months (50.8%; n=66/130) were most affected. No significant association was found between age, sex and incidence of adverse ACTs reactions. The main experienced ACTs reactions were tiredness (43.1%; n=56/130) followed by lack of appetite (24.6%; n=32/130). The incidence ACTs ARDs was found to be relatively low and tolerable. Home management of malaria cases using ACTs should be encouraged and community members should be trained to improve the recognizing and reporting of adverse effects.

Introduction

In the past, only health professionals managed medicines. But nowadays, the community through community health workers is also involved in the management and handling of drugs.¹ This type of partnership is found in areas of malaria intense transmission, where antimalarial drugs are prescribed for the treatment of malaria and suspected cases (fevers).²⁻⁵ Community health workers are community members trained to treat malaria at home after having confirmed the malaria cases using rapid diagnostic tests. They are also involved in the distribution of antimalarial for presumptive treatment of fever in children under five years.²⁻⁵

In response to the resistance observed in previously antimalarial drugs, the World Health Organization (WHO) recommend to use Artemisinin-based combination therapy (ACTs) as first-line therapy for the treatment of uncomplicated *Plasmodium falciparum* malaria.⁶⁻⁸ Two types of ACT have been adopted in Cameroon: Artesunate + Amodiaquine and Arthemether + Lumefantrine.⁹ ACTs are cheap and effective treatment for malaria.⁶⁻⁸ However, they are more efficient when the patient receive the treatment within 24 to 48 hours after the onset of the first symptoms of the disease.⁶⁻⁸ The objective of the National Programme Against Malaria in Cameroon is to ensure the most risky population for malaria infection to have access to effective antimalarial drugs.⁹ That is why considering the limited access to health services for some populations,^{9,10} the strategy for home management of malaria cases (HMMCs) at home was adopted in order to improve the accessibility of all to the rapid and effective treatment of malaria.^{9,10}

According to WHO, Pharmacovigilance (PV) is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems.¹¹ This activity is important and should be continued mostly because clinical trials prior to drugs marketing are conducted on limited number of participants in good health, thus not allowing to detect all potentials drug side effects that may cause unexpected illness, disability and even death in extreme cases.¹¹ The implementation of HMMCs using ACTs in the health district of Mfou was a great opportunity to evaluate the safety of ACTs. Thus, this study aimed to determine the incidence of ADRs related to ACTs and to describe the riskiest groups according to the age and sex.

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Materials and Methods

Study setting

Mfou health district is located in the Center region of Cameroon at 25 km of Yaounde. The health district is a part of two departments (Mefou-Afamba, and Nyong-So'o), and covers the sub-divisions of Mfou, Nkolafamba and Dzeng. The health district of Mfou is spread over 475 Km² with an estimated population of 65 816 (unpublished data, 2013), in 12 health areas. Ewondo and Bene are the dominant population groups mostly Christians (catholic and protestan). Farmers represent a part of population while other people commute to the city of Yaounde daily for work or commerce. Malaria and respiratory infections are diseases most prevalent in the health district of Mfou, followed by sexually trans-

mitted infections, including HIV/Aids which is the cause of 30% of hospital admissions (unpublished data, 2013).

Study design

This was a prospective, observational, cohort study of adverse events associated with ACTs, conducted from January 2013 to November 2013. The study was designed as cohort event monitoring system,¹² of the HMMCs using ACTs implemented in Mfou health district.

Study participants

The study population consisted of children under 5 treated for malaria using ACTs at home.

Sampling size and technique

An exhaustive sampling method was applied for children under 5 treated at home with ACTs prescribed by community health workers during the study period.

Data collection stools and methods

An elaborated PV form was used for data collection and filled by trained community health workers involved in the HMMCs. All suspected ADRs following ACTs administration and other clinical events were recorded.

Data analysis

Data were entered into the computer using Epi Info version 3.5.3 and analysis was done using Statistical Package for Social Sciences (SPSS), statistical software version 20. Frequency tables and cross tabulations were generated and presented as tables. Categorical variables were presented as frequencies and proportions and association between two of them assessed using Chi square test. Level of significance was determined by a P-value of <0.05.

Ethical considerations

The study was approved by the Mfou Health District Authorities. Data collection was conducted confidentially and after obtaining parents' informed consent. Children experiencing adverse reactions after drugs administration were notified to Mfou Health Authority in order to receive appropriate care.

Results

Socio-demographic characteristics of children

As a whole, four hundred and seventy-nine (479) PV forms were filled. There were 56.8% (n=272/479) of males and 43.2%

(n=207/479) of female children under 5. The most represented age group was 25-59 months (49.5%; n=237/479). Table 1 shows the socio-demographic characteristics of treated children with ACTs.

Incidence of adverse reactions in treated children

Out of the total number of children that have been treated with ACTs, 27.1%

(n=130/479) had experienced one form of adverse reactions following drug administration, among them, 43.8% (n=57/130) were females and 56.2% (n=73/130) were males. The main experienced ACTs reactions are shown by Figure 1. All ADRs were common side effects reported in the drug notice as associated to ACTs. Tiredness (43.1%; n=56/130) was the most observed adverse reactions followed by lack of appetite

Table 1. Socio-demographic characteristics of children.

Age groups (months)	Frequency	Proportion (%)
6 – 11	70	14.6
12 – 24	172	35.9
25 – 59	237	49.5
Total	479	100

Table 2. Experienced adverse Artemisinin-based combination therapies reactions according to the age in months.

	6 – 11		12 – 24		25 – 59		Total, n
	n	%	n	%	n	%	
Tiredness	2	3.6	23	41.1	31	55.4	56
Lack of appetite	3	9.4	12	37.5	17	53.1	32
Headache	3	23.1	4	30.8	6	46.2	13
Vomiting	2	13.3	4	26.7	9	60	15
Others	2	14.3	9	64.3	3	21.4	14
Total	12	9.2	52	40	66	50.8	130

Table 3. Prevalence of adverse Artemisinin-based combination therapies reactions according to the sex of children.

	Female		Male		Total, n
	n	%	n	%	
Tiredness	24	42.9	32	57.1	56
Lack of appetite	17	53.1	15	46.9	32
Headache	6	46.2	7	53.8	13
Vomiting	6	40	9	60	15
Others	4	28.6	10	71.4	14
Total	57	43.8	73	56.2	130

Table 4. Occurrence of adverse Artemisinin-based combination therapies reactions according to age and sex.

Age groups (months)	Occurrence of adverse reactions		P-value
	Observed	Non-observed	
	n (%)	n (%)	
6 – 11	12 (9.2)	58 (16.6)	>0.05
12 – 24	52 (40)	119 (34.1)	
25 – 59	66 (50.8)	172 (49.3)	
Sex			
Male	74 (56.2)	182 (52.1)	>0.05
Female	57 (43.8)	167 (47.9)	
Total	130 (100)	349 (100)	

P<0.05 (significant) and P>0.05 (non-significant).

(24.6%; n=32/130). Tiredness was most reported among children aged 25-59 (55.4%, n=31/130) and 12-24 (41.1%; n=23/130), while children aged 6-11 months had most suffered from lack of appetite and headache (25%; n=3/12) (Table 2). According to the sex, both female (42.1%; n=24/57) and male (56.2%; n=32/73) children had most suffered from tiredness after ACTs administration (Table 3).

Association between age, sex and the incidence of adverse ACTs reactions

Table 4 summarizes the association between age, sex and the incidence of adverse ACTs reactions. Adverse reactions were most observed in children aged 25-59 months (50.8%; n=66/130) and male children (56.2%; n=74/130), but not significant association was found.

Discussion

Malaria remains one of the major public health concerns in Cameroon.¹⁰ In spite of enhanced control efforts, malaria is responsible for about 40 – 50% of hospital visits, 30% of hospital admissions, 40% of deaths among children under 5 and 35 – 40% of total deaths in health facilities.¹⁰ Malaria treatment is frequently initiated at home, most of time with street drugs.¹³ No informal used of ACTs for self-treatment of malaria was reported, indicating the effectiveness of the HMMCs strategy, thus the decrease of irrational use of the antimalarial drugs related problems.^{14,15} In the HMMCs

strategy implemented in Cameroon, Artemisinin derivatives were always used in combined form (bi-therapy). This should probably contribute to the decrease of drug resistance and hence the treatment effectiveness.¹⁶⁻¹⁸

ACTs induce side effects, but not systematically.¹⁹ In this study, common adverse ACTs reactions were reported, without life-threatening adverse reactions that could result in the end of treatment. All adverse events observed in children after ACTs administration were already known and listed in package inserts.¹⁹ This confirms the safety of ACTs and their tolerance.^{16,17} Contrary to studies from Nigeria,¹⁹ Kenya,²⁰ and Zambia,²¹ itching, ear and eye disturbances and abdominal pain were not observed among the study population. Tiredness was the most reported adverse effects attributed to ACTs observed in treated children, followed by lack of appetite, vomiting and other side effects (nervousness, diarrhoea, cough, insomnia, dizziness).²² It was documented that adverse ACTs reactions as tiredness, lack of appetite, dizziness are mostly induced by amodiaquine component.²³ This can partially explain why tiredness and lack of appetite were most observed considering that ACTs used in Cameroon include Artesunate + Amodiaquine.⁹

Regarding the age and sex, children aged 12-24 months and male children had most experienced ACTs adverse reactions. Tiredness and vomiting were most reported among male children, while lack of appetite was mostly found in female children.

However, no significant association was found between the incidence of adverse ACTs reactions and age and sex of children. This is similar to the findings of Adisa *et al.*, (2008), in which sex did not appear to have any significant effects on the incidence ACTs adverse reactions.¹⁹

This study had some limitations. Although we worked with children patients receiving antimalarial drugs (ACTs) for treatment of malaria and ADRs collected by community health workers, we did not apply the world health organization assessment scale,²⁴ to classify the adverse drug events as certain, probable, possible, unlikely, and unclassified. In addition, the fact that prescribers (community), were in charge of data collection could also induce some bias.

Conclusions

No informal use of ACTs for self-treatment of malaria was reported and Artemisinin derivatives were always used in combined form (bi-therapy). The prevalence of side effects of ACTs used as first-line therapy for treatment of uncomplicated malaria was found to be relatively low and tolerable. Tiredness was the most adverse reactions reported, age group 25-59 months and male children were most affected, but significant association was found between age, sex and incidence of ACTs adverse reactions. HMMCs using ACTs should be encouraged and effort should be made to continue to involve community health workers in the strategy. Community health workers should be trained in order to improve the recognizing and reporting of adverse effects.

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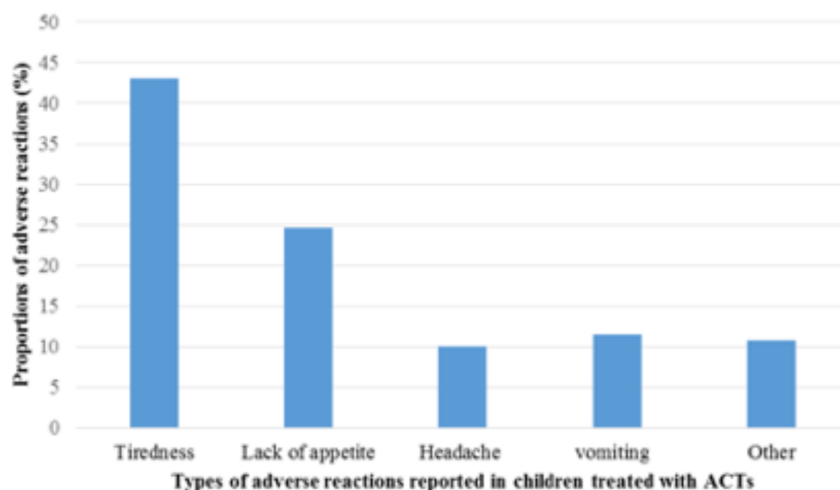


Figure 1 Distribution of reported adverse reactions in treated children with Artemisinin-based combination therapies (other ADRs: nervousness, diarrhea, cough, insomnia, dizziness).

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