Poster: 5359

Resistance markers to sulfadoxine-pyrimethamine and amodiaquine in the context of seasonal malaria chemoprevention in Burkina Faso

Cheick Compaore,[1] Craig Bonington,[2] Kevin Baker,[2] Paul Sondo,[3] Adama Traore,[1] Clotaire Tapsoba,[1] Boulaye Dao,[4] Ambroise Ouedraogo,[4] Sidzabda Kompaore,[4] Gauthier Tougri,[5] Halidou Tinto[3]

[1] Malaria Consortium, Burkina Faso
[2] Malaria Consortium, United Kingdom
[3] Institut de Recherche en Sciences de la Santé, Clinical Research Unit of Nanoro, Burkina Faso
[4] Ministry of Health, Permanent Secretary for Malaria Elimination, Burkina Faso
[5] Ministry of Health, Malaria National Research and Training Centre, Burkina Faso

Sulfadoxine-pyrimethamine and amodiaquine remain effective after eight years of SMC implementation in Burkina Faso.

Introduction

In 2022, 8.3 million maria cases were reported in Burkina Faso. Since 2014, seasonal malaria chemoprevention (SMC), using antimalarial medicines sulfadoxine-pyrimethamine (SP) and amodiaquine (AQ), has been implemented. However, there are no data on molecular resistance markers for these drugs. This study assessed resistance to SP and AQ by examining specific molecular markers in blood samples from the Boussé district before and after SMC in 2022.

Methods

- Cross-sectional surveys were conducted in health facilities from 8–10 July 2022 (prior to SMC) and 7–11 November 2022 (after SMC).
- A total of 300 positive rapid diagnostic tests were collected: 150 were collected before the first SMC round and 150 were collected after the first SMC round.
- Parasite deoxyribonucleic acid (DNA) was extracted using quiagen kitand mutations in *Plasmodium falciparum* chloroquine resistance transporter (Pfcrt) codon 76. *Plasmodium falciparum* multi drug resistance (Pfmdr) codon 86, 184, 1034, 1042 and 1246 were detected by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).

Results

- No significant change in the prevalence of dihydrofolate reductase (dhfr) and dihydropteroate synthetase (dhps) alleles was observed before or after SMC (Table 1).
- However, a higher prevalence of the mutant alleles 437G, 51I, 59R and 164L was observed (Table 1).
- A low prevalence of dhps double mutant was observed in the area before and after SMC (Table 2).
- Multiple quintuple mutants were observed but their prevalence was low (Table 2).
- A significant increase in the mutant Pfcrt 76T allele was observed after the SMC round, yet no selection for a specific allele in Pfmdr 1 gene was evident (Table 3).
- The mutation rate in Pfmdr codon 86 was extremely low. By contrast, a higher prevalence of mutations in Pfmdr1 codon 184 was observed before and after SMC (Table 3).
- No mutations were observed in Pfmdr1 codons 1034, 1042 and 1246.

Conclusion

There was a noticeable observance of the Pfcrt 76T mutant allele after SMC in 2022. While no selective pressure was observed for a particular Pfmdr1 allele, the high prevalence of the Pfmdr1 184F mutant allele is of interest. The presence of quintuple mutants with consistent prevalence is also significant. Close monitoring of resistance markers and continued implementation of SMC are required.

Results

Table 1: Resistance to sulfadoxine-pyrimethamine: pfdhps and pfdhfr polymorphism frequencies before and after SMC

	Level	Overall (%)	Pre-SMC (%)	Post-SMC (%)	p value
n		300	150	150	
A437G	Wild	32 (11.5)	18 (13.0)	14 (10.0)	0.544
	Mutant	246 (88.5)	120 (87.0)	126 (90.0)	
K540E	Wild	278 (99.6)	138 (99.3)	140 (100.0)	0.997
	Mutant	1 (0.4)	1 (0.7)	0 (0.0)	
A581G	Wild	273 (96.8)	139 (98.6)	134 (95.0)	0.175
	Mutant	9 (3.2)	2 (1.4)	7 (5.0)	
A613S	Wild	245 (86.9)	126 (88.7)	119 (85.0)	0.452
	Mutant	37 (13.1)	16 (11.3)	21 (15.0)	
N51I	Wild	26 (9.5)	19 (13.9)	7 (5.1)	0.025
	Mutant	247 (90.5)	118 (86.1)	129 (94.9)	
C59R	Wild	26 (9.4)	15 (10.7)	11 (8.0)	0.562
	Mutant	252 (90.6)	125 (89.3)	127 (92.0)	
S108NT	Wild	13 (4.8)	10 (7.1)	3 (2.3)	0.107
	Mutant	260 (95.2)	130 (92.9)	130 (97.7)	
I164L	Wild	155 (100.0)	130 (100.0)	25 (100.0)	NA

Table 2: Mutation combinations frequencies by period

	Level	Overall	Pre-SMC	Post-SMC	p value
n		300	150	150	
dhps_double	No	278 (99.6)	138 (99.3)	140 (100.0)	0.997
	Yes	1 (0.4)	1 (0.7)	0 (0.0)	
dhps_triple	No	283 (100.0)	142 (100.0)	141 (100.0)	NA
dhfr_double	No	27 (10.3)	20 (14.8)	7 (5.5)	0.022
	Yes	236 (89.7)	115 (85.2)	121 (94.5)	
Quintuple	No	278 (99.6)	138 (99.3)	140 (100.0)	0.997
	Yes	1 (0.4)	1 (0.7)	0 (0.0)	
Sextuple	No	283 (100.0)	142 (100.0)	141 (100.0)	NA

Table 3: Resistance to amodiaquine pfmdr1 and pfcrt polymorphism frequencies

	level	Overall (%)	Pre-SMC (%)	Post-SMC (%)	p value
n		300	150	150	
Crt-K76T	Wild	261 (92.2)	136 (95.8)	125 (88.7)	0.044
	Mutant	22 (7.8)	6 (4.2)	16 (11.3)	
N86Y	Wild	276 (98.2)	140 (98.6)	136 (97.8)	0.981
	Mutant	5 (1.8)	2 (1.4)	3 (2.2)	
Y184F	Wild	121 (43.2)	63 (44.7)	58 (41.7)	0.705
	Mutant	159 (56.8)	78 (55.3)	81 (58.3)	
D1246Y	Wild	282 (100.0)	141 (100.0)	141 (100.0)	NA

Acknowledgements

The SMC programme is funded through philanthropic donations received as a result of being awarded Top Charity status by GiveWell, a non-profit organisation dedicated to finding outstanding giving opportunities.

Reference

1) World Health Organization. World malaria report 2022. World Health Organization, 2022.