

In vivo sensitivity of *Plasmodium falciparum* to chloroquine and sulfadoxine-pyrimethamine

Burundi

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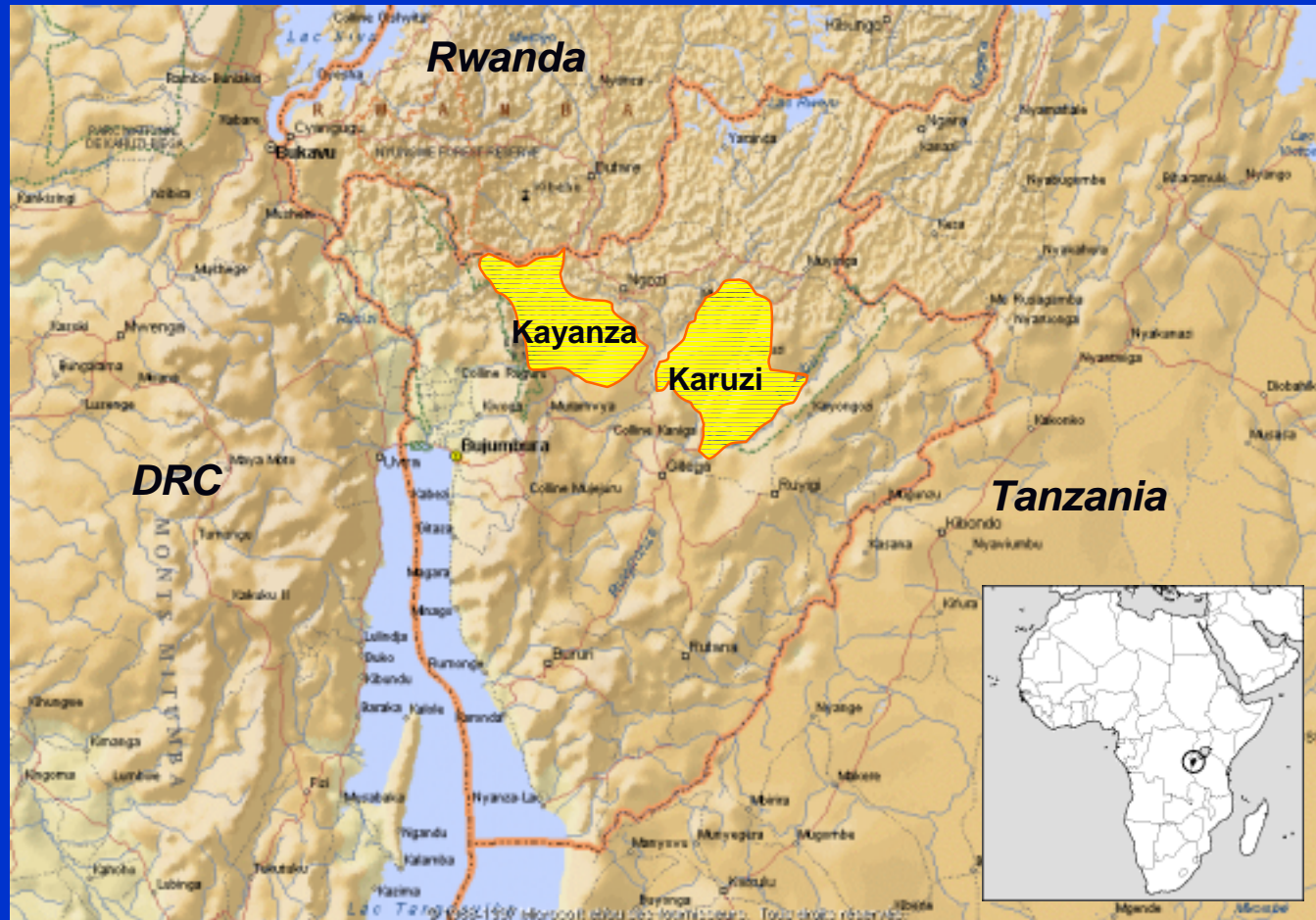
Rationale

- Major malaria epidemic in Burundi
- Chloroquine (CQ) seemed less effective
- 1995: CQ failure of 44% (children < 5)
- S/P as second-line treatment
- Use of CQ+S/P in Kayanza province

Objectives

- To assess the *in vivo* sensitivity of *P. falciparum* to chloroquine, S/P, and CQ+S/P
- To provide baseline data for malaria treatment policies

Study site



Methods (1)

- Recruitment in Health Centres
- Medical and laboratory support
- Protocol: MOH - WHO 1996
 - 6 - 59 months
 - Uncomplicated falciparum malaria
 - Follow-up during 14 and 28 days
- Drug tested: CQ, S/P, CQ+S/P

Methods (2)

- **Parasitological failure**

- Day 3 parasitaemia $> 25\%$ Day 0
- Day 3 $\leq 25\%$ Day 0, then positive during follow-up
- Day 7 negative, then positive during follow-up

If $<$ day 7 : Early Parasitological Failure (EPF)

If \geq day 7 : Late Parasitological Failure (LPF)

- **Sensitive**

- Day 3 $\leq 25\%$ Day 0, then negative during follow-up

- **Non assessable**

CQ parasitological failure rate at day 14

	Kayanza			Karuzi		
	(N = 50 - 7 na* - 0 lost†)			(N = 58 - 13 na* - 0 lost†)		
	N	%	CI	N	%	CI
EPF	14	32.6	[19.5 - 48.7]	21	46.7	[31.9 - 62.0]
LPF	29	67.4	[51.3 - 80.5]	23	51.1	[36.0 - 66.1]
Total	43	100.0	[89.8 - 100.0]	44	97.8	[86.8 - 99.9]

* Non assessable

† Lost to follow-up

S/P parasitological failure rate at day 14

	Kayanza (N = 127 - 8 na* - 1 lost†)			Karuzi (N = 111 - 22 na* - 2 lost†)		
	N	%	CI	N	%	CI
EPF	6	5.1	[2.1 - 11.7]	12	13.8	[7.6 - 23.2]
LPF	81	68.6	[59.4 - 76.7]	66	75.9	[65.3 - 84.1]
Total	87	73.7	[64.7 - 81.2]	78	89.7	[80.8 - 94.9]

* Non assessable

† Lost to follow-up

S/P parasitological failure rate at day 28, Karuzi

(N = 111 - 22 na* - 2 lost†)

Outcomes	N	%	CI
EPF	12	13.8	[7.6 - 23.2]
LPF	74	85.1	[75.4 - 91.5]
Total Failures	86	98.9	[92.9 - 99.9]
Sensitive	1	1.1	[0.1 - 7.1]

* Non assessable

† Lost to follow-up

CQ+S/P parasitological failure rate at day 14, Kayanza

(N = 119 – 6 na* - 9 lost†)

Outcomes	N	%	CI
EPF	4	3.8	[1.2 - 10.1]
LPF	53	51.0	[41.0 - 60.8]
Total Failures	57	54.8	[44.8 - 64.5]
Sensitive	47	45.2	[35.5 - 55.2]

* Non assessable

† Lost to follow-up

Observed parasitological failure rates summary

	CQ	S/P		CQ+S/P
	<i>14 Days</i>	<i>14 Days</i>	<i>28 Days</i>	<i>14 Days</i>
Kayanza	100.0	73.7	-	54.8
Karuzi	97.8	89.7	98.9	-

Discussion

- High level of resistance to CQ and to S/P
- CQ and S/P need to be replaced as first-line treatment
- Malaria treatment policies
 - Access to effective treatments
 - Accurate diagnosis/prescription

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- All people involved in the study

Baseline characteristics of the patients

Site (drug used)	N (= 465)	Mean age (months)	Par. density (per μ L)	Mean temp. (° Celsius)
Kayanza				
CQ	50	28.6	14,413	38.2
S/P	127	28.0	14,537	38.3
CQ + S/P	119	24.2	13,176	38.4
Karuzi				
CQ	58	34.2	11,785	38.3
S/P	111	31.0	14,241	38.3

Overall Classification of Therapeutic Response (1)

Early Treatment Failure

- Development of danger signs or severe malaria on Day 1, Day 2 or Day 3, in the presence of parasitaemia
- Axillary temperature $\geq 37.5^{\circ}\text{C}$ on Day 2 with parasitaemia $>$ of Day 0 count
- Axillary temperature $\geq 37.5^{\circ}\text{C}$ on Day 3 in the presence of parasitaemia
- Parasitemia on Day 3 $\geq 25\%$ of count on Day 0

Late Treatment Failure

- Development of danger signs or severe malaria on any day from Day 4 to Day 14, without previously meeting any of the criteria of early treatment failure
- Axillary temperature $\geq 37.5^{\circ}\text{C}$ in the presence of parasitaemia on any day from Day 4 to Day 14, without previously meeting any of the criteria of early treatment failure

Overall Classification of Therapeutic Response (2)

Adequate Clinical Response

- Absence of parasitaemia on Day 14 irrespective of axillary temperature, without previously meeting any of the criteria of early or late treatment failure
- Axillary temperature $< 37.5^{\circ}\text{C}$ irrespective of the presence of parasitaemia, without previously meeting any of the criteria of early or late treatment failure