

Effect of artesunate-mefloquine fixed-dose combination in malaria transmission in Amazon basin communities

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INTRODUCTION

- Malaria is a major public health problem in Brazilian Amazon
- Concern about increasing antimalarial resistance to quinine-doxycycline (QD)
- In 2006, QD was first line treatment for Plasmodium falciparum malaria (Pf)
- Artesunate-mefloquine new fixed-dose combination (ASMQ) in development, registration in the country in March '08.

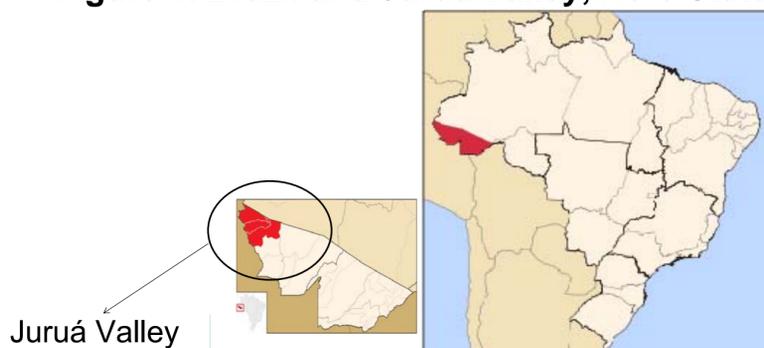
OBJECTIVES

- Evaluate the impact of programmatic use of ASMQ versus QD on Pf incidence

STUDY SETTING

- Acre State in Northeast Brazil at Amazon Basin
- Juruá Valley (Fig 1) 3 municipalities with 103,809 inhabitants, total 86% of malaria cases in Acre State
- Tropical climate, 72-93°F, relative humidity 60-85%, rainy season Oct-Apr.

Figure 1. Brazil and Juruá Valley, Acre State



METHODOLOGY

- Intervention study: July/2006 – December/2008
- Inclusion criteria
 - All patient seen in public health facilities
 - Asexual Pf parasitemia of 250-100,000/uL
 - Consent in participation
- Exclusion criteria
 - Age < 6 months
 - Pregnancy or amenorrhea > 1 month
 - Mixed malaria
 - Signs and symptoms of severe malaria
- Procedures
 - Treatment of P. falciparum infections
 - Juruá Valley - ASMQ 25/55 mg or 100/220 mg po 3 days
 - Other municipalities in Acre State - QD
 - Follow-up: blood smears D7, D40
 - Passive notification on adverse events
- Data collection
 - Regular national malaria information system (Sivep-Malaria)
- Analysis
 - Database duplicities were excluded.
 - Time series analysis: effect estimates and 95%CI for years (trend), months (seasonality), and intervention (ASMQ) on 3 monthly outcomes from Jan 2004 to Dec 2008:
 - Incidence Rates (Falciparum),
 - Ratio Falciparum-Vivax
 - Hospital Admission Rates (malaria)
 - Impact of the ASMQ intervention assessed in comparison with baseline, adjusting for the effects of other years and months.
 - Coefficients of remaining months and years: variation on the log-incidence rates in comparison to July 2004.
 - Quasi-Poisson estimation procedure, with an offset variable. Residual diagnostics were performed for each of the six adjusted models.
 - Software: Tableau 3.5, Microsoft Office Excel 2003, Reclink, and the R (R Development Core Team 2011) version 2.11.

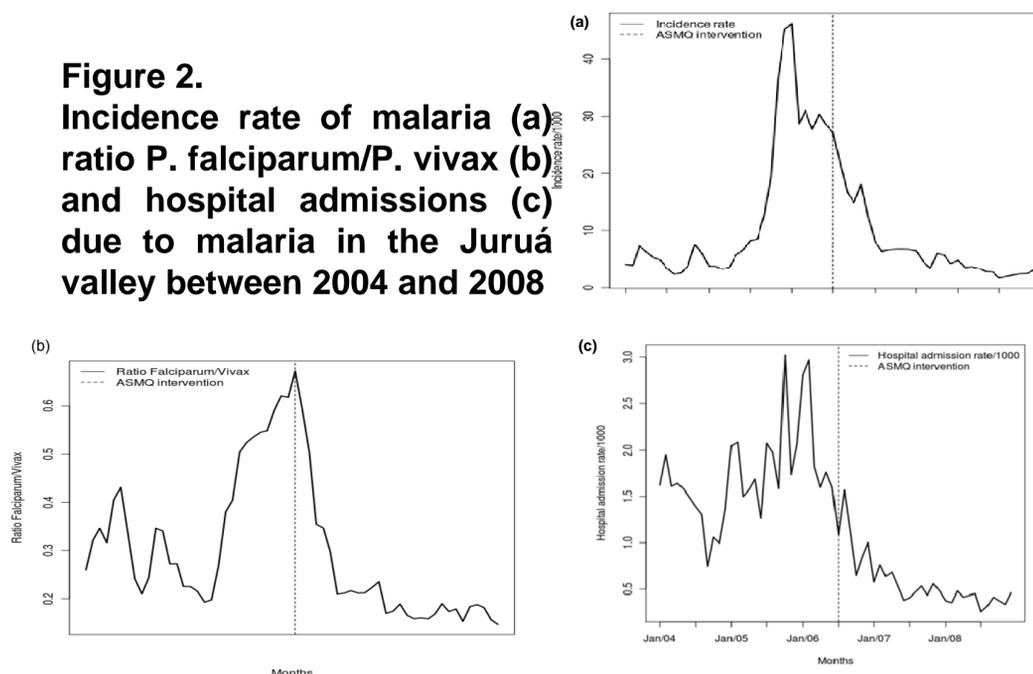
RESULTS

- The total population who received ASMQ between June 2006 and December 2008 numbered 23,845.
- A significant effect of the ASMQ intervention was observed in all evaluated outcomes:
 - Incidence Rate 0.34 (0.20 – 0.58)
 - Ratio Falciparum/Vivax 0.67 (0.50 – 0.89)
 - Admissions 0.53 (0.41 – 0.69) - with a decrease in the mean level of the time series, adjusted for the trend and seasonality
- Interaction effects between months and intervention were also evaluated. An elimination of the end of the year seasonal malaria peak was seen post-intervention.
- No serious adverse events relating to the use of fixed-dose ASMQ were reported.

Table 1. Yearly distribution of ASMQ-treated subjects in the Juruá valley stratified by age.

	<1 year	1 to 6 years	7 to 13 years	≥14 years
2006	86 (0.7%)	2,114 (17.4%)	2,333 (19.2%)	7,682 (62.7%)
2007	72 (0.9%)	1,303 (16.3%)	1,569 (19.6%)	5057 (63.2%)
2008	38 (1.1%)	667 (18.5%)	698 (19.4%)	2,195 (61.0%)
Total	196 (0.8%)	4,084 (17.2%)	4,600 (19.4%)	14,880 (62.6%)

Figure 2. Incidence rate of malaria (a) ratio P. falciparum/P. vivax (b) and hospital admissions (c) due to malaria in the Juruá valley between 2004 and 2008



CONCLUSIONS

- Early detection of malaria by health care workers and treatment with fixed-dose ASMQ was feasible and efficacious in programmatic conditions
- Significant impact of ASMQ in malaria reduction, change in Pf/Pv ratio and malaria-related hospitalisation rates

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