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-doxycline (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.

METHODOLOGY

- Intervention study: July/2006 – December/2008
- Inclusion criteria:
  - All patient seen in public health facilities
  - Asexual Pf parasitemia of 250-100,000/μL
  - 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-Poison 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.

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<td>86 (0.7%)</td>
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<td>1 to 6 years</td>
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Table 2. Yearly distribution of ASMQ-treated subjects in the Juruá valley stratified by age.

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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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