Slow parasite clearance, absent K-13 propeller gene polymorphisms and adequate artesunate levels among patients with severe malaria - A prospective observational cohort study from South India.

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ABSTRACT

Artemisinin-based combination therapy (ACT) has been the standard of care for management of severe malaria. The efforts at elimination faced a setback following the emergence of resistance. Artemisinin clearance has been postulated to be slower in patients with severe malaria due to the high parasite burden(2).

Objective: We designed a prospective observational study to assess the parasite clearance rates, artesunate pharmacokinetics and sequence the K–13 propeller region of Plasmodium falciparum in a longitudinal cohort of patients with severe malaria in South India.

METHODS

Participants were recruited if they were aged more than 16 years, with microscopy confirmed malaria with either Plasmodium falciparum or Plasmodium vivax, identified according to the World Health Organization clinical practice guidelines 2015(1). The study participants received intravenous artesunate at dose of 2.4 mg/kg to 6.0 mg/kg (or falciparum or vivax) based on the WHO treatment guidelines. The parasite clearance following an effective antimalarial treatment is a first order process, resulting in killing of a fixed fraction of the parasite population in each cycle and can be considered at the reciprocal of parasite multiplication times, which was obtained from plasma samples taken every 24 hours following 2–4 mg/kg artesunate treatment.

RESULTS

The full length K13 propeller gene was sequenced from 35 isolates collected over the three year study period.

DISCUSSION

We report the parasite clearance kinetics and correlation between the presence of K-13 polymorphisms among patients with severe malaria in South India. Surveillance studies conducted in the northeast India report treatment failure of 9.9% to AS/SP(3). In the report by Nour et al. (16 out of 384 samples, non-synonymous mutations in the propeller region were found in four patients from the northeasten states, but their presence did not correlate with ACT treatment failures.

CONCLUSIONS

Our study reports the parasite clearance kinetics and correlation between the presence of K-13 polymorphisms among patients with severe malaria in South India. Surveillance studies conducted in the northeast India report treatment failure of 9.9% to AS/SP(3). In the report by Nour et al. (16 out of 384 samples, non-synonymous mutations in the propeller region were found in four patients from the northeasten states, but their presence did not correlate with ACT treatment failures.

REFERENCES

1. WHO: World Malaria Report 2015