Antimicrobial resistance

PO - (8542) - CLINICAL ILLNESS AND OUTCOMES IN NIGERIAN CHILDREN WITH PERSISTENT EARLY APPEARING ANAEMIA FOLLOWING ARTEMISININ-BASED COMBINATION TREATMENTS OF UNCOMPLICATED FALCIPARUM MALARIA

Akano, Kazeem (Nigeria)¹; Fatunmbi, Bayo (Uganda)²; Ntadom, Godwin (Nigeria)³; Alebiosu, Omobolaji T. (Nigeria)¹; Akpoborie, Odafe (Nigeria)¹; Okafor, Chukwuebuka (Nigeria)¹; Sowunmi, Akintunde (Nigeria)¹

1 - Department of Pharmacology and Therapeutics, University of Ibadan; 2 - National Malaria Elimination Programme, The Federal Ministry of Health, Abuja, Nigeria; 3 - World Health Organization, Country Office, Kampala

**Background:** Early appearing anaemia (EAA) is not uncommon in malarious children following artemisinin-based combination treatments (ACTs) of uncomplicated infections and it may become persistent (PEAA). There is little evaluation of the factors contributing to and the kinetics of the resolution of haemoglobin deficit characteristic of ACT-related PEAA.

**Methods:** PEAA was defined as haemoglobin concentration <10g/dL for at least 1 week post-treatment initiation with artemether-lumefantrine, artesunate-amodiaquine or dihydroartemisinin-piperaquine in malarious children with haemoglobin ≥10g/dL pre-treatment. Drug-attributable fall in haemoglobin (DAFHB) was defined as the difference between pre-treatment and the lowest recorded haemoglobin value in the first week post-treatment initiation. Stepwise multiple logistic regression model was used to evaluate independent predictors of PEAA. Time-course of deficits in haemoglobin from baseline was used to estimate the disposition kinetics of haemoglobin deficits using a one compartment model.

**Results:** Asymptomatic PEAA occurred in 46 of 540 children. A duration of illness ≤3days before presentation, haemoglobin <11.7g/dL pre-treatment and 8.3g/dL 1 day post-treatment initiation, DAFHB ≥2g/dL and treatment with dihydroartemisinin-piperaquine independently predicted PEAA. Time to 90% reduction in haemoglobin deficit was significantly longer in artemether-lumefantrine-treated children compared with other treatments. Declines in haemoglobin deficits were monoexponential with the following overall estimated parameters: Cmax 2.6g/dL (95%CI 2.3-2.9), Tmax 3.2days (95%CI 2.2-4.1), AUC 31.9g.dL⁻¹.day (95%CI 25-38.8), Kₑ 0.3day⁻¹ (95%CI 0.3-0.4), t½ 3.9days (95%CI 2.6-5.1), CLp 0.6L.day⁻¹ (95%CI 0.5-0.7), and Vd 2.4L (95%CI 1.7-3). Overall, mean anaemia recovery time of 17.9days (95%CI 15.5-20.2, n=39) was equivalent to 5 multiples of half-time of haemoglobin deficit on Bland-Altman analysis. Eight children, after recovery from PEAA progressed to asymptomatic late-appearing anaemia (LAA).

**Conclusion:** Asymptomatic PEAA, which may progress to LAA, is not uncommon in young children following ACTs. Its occurrence, and progression to LAA, may have implications for case management and control efforts for ACT-related anaemia in sub-Saharan Africa.