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THE LAMBARÉNÉ-ORGAN-DYSFUNCTION SCORE (LODS) IS A SIMPLE CLINICAL PREDICTOR FOR FATAL MALARIA IN AFRICAN CHILDREN

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Plasmodium falciparum malaria accounts for more than a million deaths annually, mostly among young children in sub-Saharan Africa. Identifying those who are likely to die is difficult. Prior studies suggested that quantitative scores (Multi-Organ-Dysfunction Score and simplified Multi-Organ-Dysfunction Score, MODS and sMODS) are useful markers predicting morbidity, but the cohorts were not large enough to detect an association with case fatality. We used stepwise backward logistic regression to select the best predictors out of nine variables evaluated on admission to predict death in 23,800 hospitalised children with P. falciparum malaria. The study was conducted from December 2000 to May 2005 in six hospital-based research units (Banjul in The Gambia, Blantyre in Malawi, Kilifi in Kenya, Kumasi in Ghana and Lambaréné and Libreville in Gabon) in a network established to study severe malaria in African children (SMAC). The Lambaréné-Organ-Dysfunction-Score (LODS) counts how many of the three variables coma, prostration and deep breathing are present. A LODS > 0 (OR = 9.6; 95%CI 8.0-11.4) has a sensitivity of 85% to predict death and a LODS < 3 is highly specific for survival (98%). The LODS is a simple clinical predictor for fatal malaria in African children. This score provides a sufficiently accurate and rapid identification of children needing either referral or increased attention.

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SULFADOXINE-PYRIMETHAMINE VERSUS UNSUPERVISED ARTEMETHER-LUMEFANTRINE VERSUS UNSUPERVISED AMODIAQUINE-ARTESUNATE FIXED-DOSE FORMULATION FOR UNCOMPLICATED FALCIPARUM MALARIA IN BENINESE CHILDREN: A RANDOMIZED EFFECTIVENESS NON-INFERIORITY TRIAL

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In order to measure the potential impact of the 2004 malaria treatment guidelines in Benin that recommend ACTs (artemisinin-based combination therapies: artemether-lumefantrine as first line therapy and amodiaquine-artesunate as second line therapy) in the management of uncomplicated malaria in young children, we conducted an open randomised non-inferiority trial to compare the effectiveness of sulfadoxine-pyrimethamine (SP) to unsupervised artemether-lumefantrine (AL) and to unsupervised amodiaquine-artesunate fixed-dose formulation (ASAQ). The trial took place in southern Benin in children aged 6 to 60 months with fever or a

history of fever, and a 6-weeks follow-up was performed after treatment. The primary objective was a comparison of day 28 PCR-corrected effectiveness rates. 240 children (48 SP, 96 AL and 96 ASAQ) with a mean age of 26 months were randomized from May to October 2007. Before PCR correction, the intention to treat (ITT) analysis (239 patients) showed day 28 effectiveness rates of 20.8%, 78.1% and 70.5% with SP, AL and ASAQ respectively. After PCR correction, day 28 ITT effectiveness rates were 27.1%, 83.3% and 87.4% respectively. The per protocol analysis (217 patients) showed day 28 effectiveness rates of 21.7%, 88.0% and 76.1% with SP, AL and ASAQ respectively. After PCR correction, day 28 effectiveness rates were 28.3%, 94.0% and 93.2% respectively. Comparisons of SP with ACTs were highly significant in any case, whereas there was no significant difference between AL and ASAQ in the PCR-corrected analyses. The rate of new infections was significantly higher in children treated with ASAQ compared to those treated with AL. Two children treated with SP had to be hospitalized for severe anemia. There was no difference between treatment arms in terms of incidence of adverse events. No severe adverse event was related to a study drug. The potential impact on malaria morbidity and mortality of the replacement of SP by ACTs in this study area could be highly significant.

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RISK FOR SEVERE DISEASE IN ADULTS WITH FALCIPARUM MALARIA

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We conducted a clinical study of malaria acquired worldwide in adults in a non-endemic country over a 16 year period to determine risk factors for severe Plasmodium falciparum malaria. All patients managed by our unit from 1991 to 2006 with confirmed malaria were prospectively evaluated. Factors predicting disease severity according to a) strict World Health Organisation (WHO) criteria, b) a composite measure of unfavourable outcome and c) length of hospital stay, were identified through logistic-regression analysis. We evaluated 676 episodes; 482 (71%) due to P. falciparum and 194 to non-falciparum malaria. Black patients were at significantly reduced risk of developing severe disease, an unfavourable outcome or prolonged stay in hospital compared to Asians or whites. Of six patients with falciparum malaria who died, none were black. Patients with parasitemias ≥2% had odds of severe malaria of 12 times higher than patients with <2% parasites. Patients with a history of previous clinical malaria, regardless of ethnicity, were at significantly reduced risk of WHO-definition severe malaria. Ethnicity and parasitemia are important independent risk factors for severe falciparum malaria while a history of previous malaria significantly reduces the risk of severe disease (WHO Criteria). These results have important implications for management guidelines in non endemic countries.

Faucher Jean-François, Aubouy Agnès, Adeothy Adicat, Justin Doritchamou, Kossou H., Amedome H., Massougbodji A., Cot Michel, Deloron Philippe (2008)

Sulfadoxine-pyrimethamine versus unsupervised artemether-lumefantrine versus unsupervised amodiaquine-artesunate fixed-dose formulation for uncomplicated falciparum malaria in beninese children : a randomized effectiveness now inferiority trial. The American Journal of Tropical Medicine and Hygiene, 79 (6), 350-art. 1191