Low plasma arginine concentrations in children with cerebral malaria and decreased nitric oxide production

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Summary

Nitric oxide (NO) production and mononuclear cell NO synthase 2 (NOS2) expression are high in healthy Tanzanian children but low in those with cerebral malaria. Factors that downregulate NOS2 also diminish factors involved in cellular uptake and biosynthesis of L-arginine, the substrate for NO synthesis. We therefore postulated that L-arginine concentrations would be low in individuals with cerebral malaria. We measured concentrations of L-arginine in cryopreserved plasma samples from Tanzanian children with and without malaria. L-arginine concentrations were low in individuals with cerebral malaria (mean 46 μmol/L, SD 14), intermediate in those with uncomplicated malaria (70 μmol/L, 20), and within the normal range in healthy controls (122 μmol/L, 22; $p<0{\cdot}0001$). Analysis by logistic regression showed that hypoargininaemia was significantly associated with cerebral malaria case-fatality. Hypoargininaemia may contribute to limited NO production in children with cerebral malaria and to severe disease.