

THE EFFECT OF FERROUS SULPHATE THERAPY FOR IRON DEFICIENCY ON NEUROPSYCHOLOGICAL FUNCTION AMONG UGANDAN CHILDREN WITH SEVERE MALARIA.

ABSTRACT

Background: Severe malaria is a public health problem especially in children less than 5 years of age in low and middle income countries (LMICs). These pre-schoolers usually suffer significant co-morbid conditions such as iron deficiency and severe anaemia that increases their risk of morbidity, hospitalisation and mortality. Therefore, this thesis explored the effects of severe malaria, iron deficiency, severe anaemia and the use of ferrous sulphate therapy on the neuropsychological functioning among Ugandan children below five years of age.

Methodology: Three sub-studies were conducted: Sub study 1 was a systematic review of the association of malaria infection on cognition and behaviour among children living in LMICs. Sub study 2 was a hospital based prospective cohort study to investigate the neurocognitive and neurobehavioral outcomes among children below five years surviving severe anaemia conducted at Lira Regional Referral Hospital, in Northern Uganda. We enrolled children between the ages 6-42 months with severe anaemia [SA] (n=180) on admission to the paediatric ward and healthy community controls [CC] (n=90) of similar age at the time of cognitive testing. Sub-study 3: a randomised controlled trial (NCT01093989) to compare neurocognitive and neurobehavioral outcomes at 6 and 12-months of children with severe malaria treated for iron deficiency (ferrous sulphate on admission [immediate group] vs. ferrous sulphate one month after admission [delayed group]) and healthy community controls). We enrolled 79 children with Cerebral Malaria (CM) and 77 children with Severe

Malaria Anaemia (SMA) on admission at the paediatric ward and 83 healthy community children (CC); all aged between 18 months and 5 years.

Results: Sub study 1: Severe malaria, uncomplicated malaria and asymptomatic malaria among children were associated with poor cognitive and behavioural performance with severity of deficits increasing along the disease spectrum. Sub study 2: The prevalence of neurodevelopmental impairment was 2.3% (95% CI: 0.8–6.1) for cognition, 1.7% (95%: 0.6–5.3) for language and 3.5% (95% CI: 1.6–7.6) for motor scales and 4.6% (95% CI: 2.3–9.1) for deficits in ≥ 1 area of neurodevelopment. The severe anaemia group performed worse on cognition [adjusted mean score, (Standard error, SE), P-value] [-0.20, (0.01) vs. 0.00, (0.01), $P = 0.02$]; language [-0.25, (0.01) vs. 0.00, (0.01), $P < 0.001$]; motor [-0.17, (0.01) vs. 0.00, (0.01), $P = 0.05$] and socio-emotional [-0.29, (0.05) vs. 0.01, (0.08), $P = 0.002$] behaviour. Sub study 3: All children with CM or SMA and 35 CCs had iron deficiency (zinc protoporphyrin concentration ≥ 80 $\mu\text{mol/mol}$ heme). No significant differences were seen at 12-month follow-up in overall cognitive ability, attention, associative memory, or behavioural outcomes between immediate and delayed iron treatment (mean difference (standard error of mean) ranged from -0.2 (0.39) to 0.98 (0.5), all $P \geq 0.06$).

Conclusion: The findings reveal an important burden on cognition and behaviour in the short and long-term among Ugandan children who suffer severe malaria, iron deficiency and severe anaemia. These deficits can have a long-lasting impact on the children's lives preventing them from achieving their full potential.