

FIRST LINE ANTIMICROBIALS IN CHILDREN WITH COMPLICATED SEVERE ACUTE MALNUTRITION (FLACSAM)

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Background

Children with severe malnutrition admitted sick to hospitals have high mortality in hospital and after discharge, usually because of infection. WHO recommend all children with complicated severe malnutrition (SAM) admitted to hospitals are treated with antibiotics (currently recommended penicillin or gentamicin plus gentamicin). Ceftriaxone, recommended as second line, is being used sometimes as first line treatment, however there is no evidence whether it is more effective, and it carries a much greater risk of inducing antimicrobial resistance affecting patients themselves and the community. A second area of uncertainty is the use of metronidazole to reduce malabsorption and inflammation from bacterial growth in the small bowel and parasitic infections. However, WHO guidelines acknowledge divergent expert opinion and no evidence from trials.

Methods

In phase 1 (completed), we determined the pharmacokinetics of ceftriaxone and metronidazole in sick, severely malnourished children, and undertook surveillance of carriage of antimicrobial at admission and discharge. In phase 2 (ongoing), we are conducting a multicentre 2x2 factorial randomised trial of first line:

- Ceftriaxone vs. Penicillin plus Gentamicin (open label)
- Metronidazole vs. placebo (double-blind)

The primary endpoint is mortality; secondary endpoints: safety, readmission, growth. Invasive bacterial disease at index admission, during admission and after discharge and carriage of antimicrobial resistance are being monitored. An economic evaluation of costs of care to facilities and families, cost effectiveness and costs associated with antimicrobial resistance

Results

In sick, malnourished children, for ceftriaxone IV, 80mg/kg daily achieves a therapeutic concentration. For metronidazole oral, 7.5 mg/kg three times daily was slow to reach therapeutic levels, and 10-15mg/kg twice daily was selected as a more appropriate dosage. The FLACSAM trial is now ongoing in Mombasa, Mbagathi, Kilifi and Mbale in Uganda.

Conclusions

Evidence from the FLACSAM trial is expected to rationalize, effective antibiotic guidelines.