Cotrimoxazole in HIV exposed neonates

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Previous Paediatric STG and EML/National Guideline Recommendation

Cotrimoxazole prophylaxis recommended for:
both HIV-exposed and HIV-infected infants

Previous recommendations was made in the context of:

- No maternal ART.
- No infant prophylaxis (HIV).
- Cotrimoxazole showed benefit in those HIV-positive children with very low CD4 counts.

This recommendation was considered during the review of both the Paediatric STGs and EML Review and review of the National ARV Programmatic Guidelines.

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Recent evidence for Botswana and South African studies (1):

No benefit for mortality or morbidity for HIV-exposed uninfected children (HEU)

Botswana study (Lockman _et al_, 2017) :

- Prophylactic cotrimoxazole did not improve 18-month survival in HEU children
- Mortality at 18-months 2.4% in cotrimoxazole group and 2.6% in placebo group, difference 0.2%, 95% CI -0.15 to 1.0%, p = 0.70.

South African Study (Daniels _et al, 2019_):

- No cotrimoxazole was not inferior to daily cotrimoxazole among breastfed HEU infants whose mothers are accessing a PMTCT programme.
- Cumulative probability of the composite primary outcome _(incidence of grade 3 or 4 common childhood illnesses or mortality in breastfed HEU infants by age 12 months)_ was 0.114 (95% CI 0.076 to 0.147; 49 events) for cotrimoxazole group vs 0.0795 (0.044 to 0.115; 39 events) in the no cotrimoxazole group. Risk difference −0·0319.

POTENTIAL HARM

Botswana study (Lockman *et al*, 2017) :
- Cotrimoxazole prophylaxis increased resistance to cotrimoxazole AND amoxicillin (1st line pneumonia treatment).

South African Study (Daniels *et al, 2019*):
- Cotrimoxazole group was associated with microbiome dysbiosis and increase in resistance genes

- Lockman S, et al. Effect of co-trimoxazole on mortality in HIV-exposed but uninfected children in Botswana (the Mpepu Study): a double-blind, randomised, placebo-controlled trial. The Lancet Global Health. 2017;5(5):e491-e500.
- Daniels B, et al. Effect of co-trimoxazole prophylaxis on morbidity and mortality of HIV-exposed, HIV-uninfected infants in South Africa: a randomised controlled, non-inferiority trial. The Lancet Global Health. 2019;7(12):e1717-e27.

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Rationale to change

Assumptions

- 270 000 live births to HIV+ women
- 1,7% viral transmission rate, 83% of transmission in first 6 months
- current definition of high-risk: > 1000 c/ml
- PJP incidence of 9.5 cases per 100 child years in the first year of life **without ART** (Morris, et al)

32520 high-risk infants
- **Thus 552 HIV-positive children (1 in 10 may get PJP if not on ART)**
- **Thus 55 at risk of PJP (if not on ART)**
  In SA with high birth PCR coverage and ART initiation, incidence may be less

- Treating **32 480** high-risk HEIs to benefit 552 HIV-positive children of which **55** may get PJP is against policy norms and even ethics
- **Potential harm to 32 480 children**

The Paediatric STGs and EML updated (aligned with National ARV Programmatic Guidelines)

Current recommendation for cotrimoxazole use only in babies with positive HIV PCR results:

MEDICINE TREATMENT

Cotrimoxazole prophylaxis

Indications:

» According to the current guideline, babies with a positive HIV PCR should be started and continued on cotrimoxazole prophylaxis until criteria for discontinuation are met.

• Cotrimoxazole (sulfamethoxazole/trimethoprim), oral, once daily (every day).

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Thank you