Post-exposure prophylaxis for reducing Mother-To-Child Transmission of HIV

CITATION

RESEARCH QUESTION
What post-exposure prophylaxis regimen given to newborns shortly after birth is more effective for reducing mother-to-child transmission of HIV: nevirapine (NVP) plus zidovudine (ZDV) or nevirapine alone?

STUDY DESIGN
Randomised, open-label clinical trial

STUDY SETTING AND DATE
Clinics in Blantyre, Malawi; April 2000 to January 2002
IRB approval obtained. Written informed consent obtained.

PARTICIPANTS
Included: singleton babies, mother HIV positive and presented in advanced labour
Excluded: babies who were preterm or had abnormalities/serious illnesses

INTERVENTIONS
1. NVP 2mg/kg as a single oral dose plus ZDV 4mg/kg orally twice daily for 7 days
2. NVP 2mg/kg, single oral dose

OUTCOMES
Primary: HIV infection at 6-8 weeks in babies not infected at birth; HIV-1 RNA test
Other: Adverse events related to treatment

RISK OF BIAS

Selection bias – negligible risk
Computer-generated randomisation. Permuted blocks of 10 with 1:1 allocation, stratified by clinic. Allocation concealed using sequentially-numbered, sealed, opaque envelopes Baseline characteristics balanced (*Table 1*)

Performance bias – small risk
Mothers and providers not blind. Breastfeeding rates > 99% in both groups Adherence to ZDV was not reported.

Detection bias – small risk
Main outcome was objective and laboratory staff were blind. Trained research nurses and clinicians recorded the type and severity of adverse events.
Attrition (exclusion) bias – small to moderate risk

See Trial profile pg 1173
For primary outcome:
NVP plus ZDV 118/562 (21%) randomized babies excluded from analysis. But if babies HIV positive at birth (50) and those with HIV negative mothers (7) not taken into account then exclusions 61/505 (12%)

NVP 136/557 (24%) excluded from analysis. But if babies HIV positive at birth (56) and those with HIV negative mothers (6) not taken into account then exclusions 61/562 (11%). Ignoring babies HIV positive at birth then exclusions 74/495 (15%)

STUDY FINDINGS

HIV positive at 6-8 weeks but not at birth

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Event rate</th>
<th>RRR (95% CI)</th>
<th>ARR (95% CI)</th>
<th>NNT (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVP/ZDV</td>
<td>34/444 (7.7%)</td>
<td>36% (3 to 69%)</td>
<td>4.4 (0.4 to 8.4)</td>
<td>23 (12 to 239)</td>
</tr>
<tr>
<td>NVP</td>
<td>51/421 (12.1%)</td>
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HIV positive at 6-8 weeks regardless of HIV status at birth (closer to ITT)

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</tr>
</thead>
<tbody>
<tr>
<td>NVP/ZDV</td>
<td>74/484 (15.3%)</td>
<td>27% (3 to 50%)</td>
<td>5.6 (0.7 to 10.5)</td>
<td>18 (10 to 140)</td>
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<tr>
<td>NVP</td>
<td>98/468 (20.9%)</td>
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Adverse events
Low rates in both groups, mostly mild and few attributable to treatment.

Total infant deaths: NVP/ZDV 8.5% vs NVP 11.8% the majority in those testing positive at birth.

COMMENTS
Interventions feasible in resource-poor settings and findings likely to be generalisable

BOTTOM LINE
Short-course, post-exposure prophylaxis with NVP and ZDV given to neonates born to HIV-infected mothers presenting late in pregnancy appears to be an effective and safe option for reducing MTCT of HIV

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