Electronic Drug Monitoring of Infant Adherence to Antiretroviral Therapy Prophylaxis

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Conflict of Interest Disclosure

No conflicts of interest to disclose
PMTCT

• Prevention of Maternal to Child Transmission of HIV (PMTCT) is a public health success story:
  • Rates of maternal to child transmission of HIV: ~40% to < 3%.\(^1\)
• Option B+ is the WHO-recommended PMTCT policy:
  • Lifelong antiretroviral therapy (ART) for all HIV-positive pregnant women.
  • 6 weeks of postnatal ART prophylaxis for exposed infants and early infant diagnosis (EID) at 6 weeks of life
• Poor retention of mother-infant dyads in Option B+ but overall limited knowledge about adherence to infant ART prophylaxis during the infant’s first six weeks of life
Background

- HIV in Uganda:
  - High burden country: 8% prevalence in pregnant women
  - Rapid scale-up of WHO’s Option B+
  - >95% of HIV+ pregnant women on ART by 2015
  - Only 38% of HIV-exposed infants received prophylactic ART postnatally
  - Only 50% of infants were tested for HIV by 6 weeks of life
Electronic Drug Monitoring

- Prior studies in sub-Saharan Africa have used electronic drug monitoring (EDM) devices to measure adherence to pediatric antiretroviral regimens.\textsuperscript{10-11}
- The use of EDM devices in measuring adherence to antiretroviral prophylaxis in HIV-exposed infants has not been investigated.
This pilot study examined the acceptability and feasibility of an EDM device affixed to a bottle containing the standard NVP suspension provided to HIV-exposed infants.
The Uganda Wise Infant Study

• Routine care in Uganda: HIV-exposed infants receive daily nevirapine (NVP) for ART prophylaxis postnatally to 6 weeks of age.

• The EDM bottles provided to mothers had caps, which contained a microchip that records the date and time of each bottle opening and stores this data until downloaded using a specialized cap reader.

• No real-time feedback regarding the EDM usage was given to participants or the study team.

• We used the EDM-generated data as a proxy for adherence to NVP prophylaxis, based on evidence that EDM data are a reliable measure of medication adherence. 11-15
Methods: Enrollment

• Mityana District Hospital in Central Uganda from July to December 2016

• Eligibility: HIV-positive pregnant women with estimated gestational age greater >24 weeks

• Inclusion criteria also included the intent to deliver at Mityana District Hospital.
Data Collection and Analysis

• At enrollment, we administered a survey questionnaire to collect quantitative data on sociodemographic characteristics of the mothers.
  • Maternal age, ethnicity, education, employment, time since maternal HIV diagnosis, reproductive health history, and maternal self-reported ART adherence.
• NVP adherence data were collected via the EDM device after return of the EDM bottle, regardless of how long the EDM bottle was in the possession of the mother.
Methods: Measures

• We estimated adherence to ART prophylaxis by calculating:
  • Proportion of daily doses administered within the first 42 days of EDM possession
  • Proportion of daily doses administered during the entirety of EDM possession, respectively.
  • High adherence was defined as having > 90% adherence to NVP.
  • Bivariate analyses using Fisher’s exact test and Wilcoxon rank sum test, SAS version 9.4 (SAS Institute).
Results

49 women provided consent

28 women received EDM device

- 26 EDM devices with data
- 1 missing device

2 EDM devices without data

1 unutilized device

21 women did not receive EDM device

- Lost To Follow-Up: 10
  - Not Received: 6
  - Refused: 1
  - Home Delivery: 1
  - Other Health Facility: 1
  - Maternal Death: 1
  - Neonatal Death: 1
### Baseline Maternal Characteristics (n=26)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%) or Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>26.6 (4.6)</td>
</tr>
<tr>
<td>Parity</td>
<td>1.8 (1.5)</td>
</tr>
<tr>
<td>Maternal ART duration (years)</td>
<td>2.4 (1.9)</td>
</tr>
<tr>
<td>Household size</td>
<td>3.4 (1.4)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>4 (15.4)</td>
</tr>
<tr>
<td>Primary</td>
<td>14 (53.9)</td>
</tr>
<tr>
<td>Secondary</td>
<td>8 (30.8)</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
</tr>
<tr>
<td>Housewife</td>
<td>13 (50.0)</td>
</tr>
<tr>
<td>Employed outside home</td>
<td>13 (50.0)</td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>N = 26</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of EDM possession, days, median (range)</strong></td>
<td>45 (34 – 85)</td>
</tr>
<tr>
<td><strong>Infants who missed at least one dose in first 42 days, n (%)</strong></td>
<td>24 (92.3)</td>
</tr>
<tr>
<td><strong>Missed doses in first 42 days, median (range)</strong></td>
<td>10 (2 – 40)</td>
</tr>
<tr>
<td><strong>Infants who missed at least one dose during EDM possession, n (%)</strong></td>
<td>25 (96.2)</td>
</tr>
<tr>
<td><strong>Missed doses during EDM possession, median (range)</strong></td>
<td>11 (2 – 51)</td>
</tr>
<tr>
<td><strong>Infants with double or more openings of EDM device, n (%)</strong></td>
<td>14 (53.9)</td>
</tr>
<tr>
<td><strong>Days with double or more openings of EDM device, mean (sd)</strong></td>
<td>3.4 (2.3)</td>
</tr>
<tr>
<td><strong>Percent adherence in first 42 days, mean (sd)</strong></td>
<td>69.9 (26.4)</td>
</tr>
<tr>
<td><strong>Percent adherence during EDM possession, mean (sd)</strong></td>
<td>63.6 (27.8)</td>
</tr>
<tr>
<td><strong>Adherence in first 42 days, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>High adherence (≥ 90%)</td>
<td>7 (26.9)</td>
</tr>
<tr>
<td>Low adherence (&lt; 90%)</td>
<td>19 (73.1)</td>
</tr>
</tbody>
</table>
Results

NVP Adherence in first 42 days of EDM Possession (n=26)
# Infant Adherence by Maternal Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>High adherence (n = 7)</th>
<th>Low adherence (n = 19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>25 (22 – 28)</td>
<td>27 (24 – 30)</td>
<td>0.557</td>
</tr>
<tr>
<td>Parity, median (IQR)</td>
<td>1 (0 – 1)</td>
<td>2 (1 – 3)</td>
<td>0.121</td>
</tr>
<tr>
<td>Maternal ART, median (IQR)</td>
<td>1 (0.3 – 2.0)</td>
<td>2 (1.5 – 5.0)</td>
<td>0.106</td>
</tr>
<tr>
<td>Household size, median (IQR)</td>
<td>3 (2 – 4)</td>
<td>4 (2 – 5)</td>
<td>0.409</td>
</tr>
<tr>
<td>Education, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>2 (50.0)</td>
<td>2 (50.0)</td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>3 (21.4)</td>
<td>11 (78.6)</td>
<td>0.608</td>
</tr>
<tr>
<td>Secondary</td>
<td>2 (25.0)</td>
<td>6 (75.0)</td>
<td></td>
</tr>
<tr>
<td>Employment, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Housewife</td>
<td>4 (30.8)</td>
<td>9 (69.2)</td>
<td>1.000</td>
</tr>
<tr>
<td>Employed outside home</td>
<td>3 (23.1)</td>
<td>10 (76.9)</td>
<td></td>
</tr>
</tbody>
</table>
Feasible and Acceptable?

• To our knowledge, this pilot study evaluating the feasibility of EDM in measuring adherence to ART prophylaxis among HIV-exposed infants in Uganda is the first to utilize EDM devices in assessing adherence to PMTCT in HIV-exposed infants.

• Nearly half of enrolled women did not get the device as intended
  • Study site?
  • More intensive formative work needed?

• Qualitative data regarding acceptability still being analyzed
Take-home results

- Utilization of the EDM devices varied among the participants.
  - Median time of EDM possession: 45 days (range: 34 – 85 days).
  - Almost all infants (92.3%) missed at least one dose of ART prophylaxis in the first 42 days of therapy.
  - Median number of missed doses of NVP was 10 (range: 2 – 40).
  - The mean infant adherence in the first 42 days of therapy was 69.9% and only 26.9% of infants were at least 90% adherent.

- More than half of the infants had double openings of the cap (or more frequent) during EDM possession.
  - May be attributed to EDM devices not being the standard of practice accustomed to the mothers for infant prophylaxis,
  - May indicate that NVP was inappropriately being given.
Limitations

• Pilot study

• Small sample size
  • Cannot determine significant associations.
  • Only EDM data, used here as a proxy for ART adherence, but no other measures of infant adherence, such as serum NVP levels for the exposed infants.
  • No ‘real-time’ data regarding the usage of the device.
  • EDM data not captured before conducting in-depth interviews to facilitate more informative discussions with the mothers.
Conclusions

- Revealed low adherence levels to ART prophylaxis among HIV-exposed infants: < 1/3 of infants demonstrated high (>90%) adherence.
- HIV-exposed infants are a special population: require high adherence to a single daily dose of ART for a relatively short period of time.
- Methods of ensuring good adherence to ART prophylactic regimens for exposed infants remain important for PMTCT efforts.
- Demonstrated the potential feasibility of using an EDM device to measure adherence to ART prophylaxis.
- This study is the first study to utilize EDM technology in this population, with potential for EDM to possibly be used as an intervention to ensure adequate adherence for HIV-exposed infants.
Wise Infant Study Team and Acknowledgments

Boston University School of Public Health
- Osaremien Omorogie, MPH
- Lora Sabin (PhD)
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University of New England
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Mildmay Uganda
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- Barbara Mukasa (MPH)
- Joseph Kyebuzibwa
- Mary Odit

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