Treatment Outcomes of the Modified Directly Observed Therapy (MDOT) Program of Infected Children Receiving HAART

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Phnom Penh, Cambodia
Cambodian MDOT Study

Objective: To evaluate the method of modified directly observed therapy (MDOT) at National Pediatric Hospital in Phnom Penh, Cambodia

Cohort: 26 ARV therapy naïve HIV+ children

Observation schedule:
Month 1 5 days/week 1 of 2 doses observed
Month 2 3 days/week 1 of 2 doses observed
Month 3 2 days/week 1 of 2 doses observed
After Month 3 visits tapered to 1 day/week, 2 times/month, then 1 time/month
Adherence to HIV medication has been identified as a critical element to successful outcomes. Treatment failure has been associated with decreased adherence to the drug regimen. DOT is a strategy to improve adherence in marginalized population. DOT programs for TB have improved cure rates in a wide range of settings.
TB treatment program in NPH:

- Provides a minimum of 1wk.of inpatient anti. TB drug to children with active TB.

- Caregivers/children come for a week supply of medication and adherence education.

- After one month the visits decrease in frequency upon the clinical improvement and adequate adherence.
Should MDOT be applied to HIV infected children in our poor setting?

The primary goal would be to increase adherence to HIV therapy.

Learning from some successful programs and our existing program, we propose a pilot study on the feasibility of a MDOT-HAART program in children in NPH.
Study Population: 26 HIV-infected children.

Inclusion criteria:
- Under 15 years; naïve to ART
- Meet the clinical & immunologic criteria for ART of NPH Guidelines.
- Meet the social criteria: live with family; not live > 20km from NPH; Biological mother must be linked to medical care for HIV. Accepted the informed consent.

Exclusion criteria:
- Acute severe infections.
- Congenital conditions with prevent the ability to take medication.
## Baseline characteristics

<table>
<thead>
<tr>
<th>Status of parents</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two parents alive</td>
<td>13 (50%)</td>
</tr>
<tr>
<td>Lost one parent</td>
<td>9 (34.6)</td>
</tr>
<tr>
<td>Lost two parents</td>
<td>4 (15.4)</td>
</tr>
</tbody>
</table>
Baseline characteristics
CDC stage & HBV

| CDC category A | 2 (7.7%) |
| CDC category B | 21 (80.8%) |
| CDC category C | 3 (11.5) |
| HBsAg+         | 2 (7.7)  |
## Cambodian MDOT Study

### Baseline Cohort Summary

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age (yrs)</th>
<th>%CD4</th>
<th>CD4/CD8</th>
<th>Viral Load</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>13</td>
<td>1.1 – 12</td>
<td>1 – 19</td>
<td>0.02 – 0.51</td>
</tr>
<tr>
<td>Female</td>
<td>13</td>
<td>(5.5)</td>
<td>(4.5)</td>
<td>(0.13)</td>
</tr>
</tbody>
</table>
**ARV Regiment**

**Started ART in August 2004**

**3TC + d4T + NVP**
- 3TC 150mg and Syrup 10mg/mL
- d4T 15mg, d4T 20mg (Capsule)
- NVP 200mg and Syrup 10mg/mL

Then switch NVP to EFV:

**3TC + d4T + EFV** for 5 children
Preparing ARV for the child
### Cambodian MDOT Study

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<tr>
<td>Male 13</td>
<td>1.1 – 12</td>
<td>1 – 19</td>
<td>0.02 – 0.51</td>
<td>1.5x10⁴ - 5.2x10⁶</td>
</tr>
<tr>
<td>Female 13</td>
<td></td>
<td></td>
<td>(0.13)</td>
<td>7.5x10⁵</td>
</tr>
<tr>
<td></td>
<td>(5.5)</td>
<td>(4.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>6 Months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male 12</td>
<td>1.6 – 11.5</td>
<td>5 – 30</td>
<td>0.12 – 0.99</td>
<td>&lt;400 - 1.5x10⁵</td>
</tr>
<tr>
<td>Female 11</td>
<td></td>
<td></td>
<td>(0.3)</td>
<td>&lt;400</td>
</tr>
<tr>
<td></td>
<td>(3 died)</td>
<td>(5.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(15.6)</td>
<td></td>
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<td><strong>12 Months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male 12</td>
<td>2.1 – 12</td>
<td>8 – 32</td>
<td>0.12 – 1.13</td>
<td>&lt;50 - 9.3x10⁴</td>
</tr>
<tr>
<td>Female 11</td>
<td></td>
<td></td>
<td>(0.49)</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>(3 died)</td>
<td>(6)</td>
<td></td>
<td>83% &lt;400</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(20)</td>
<td></td>
<td>35% &lt; 50</td>
</tr>
<tr>
<td><strong>18 Months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male 12</td>
<td>2.6 – 12.5</td>
<td>10 – 36</td>
<td>0.22 – 1.28</td>
<td>&lt;50 - 5.9x10⁴</td>
</tr>
<tr>
<td>Female 11</td>
<td></td>
<td></td>
<td>(0.51)</td>
<td>&lt;50</td>
</tr>
<tr>
<td></td>
<td>(3 died)</td>
<td>(6.5)</td>
<td></td>
<td>87% &lt;400</td>
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<tr>
<td></td>
<td></td>
<td>(23)</td>
<td></td>
<td>52% &lt; 50</td>
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#### 6 Months Cohort Summary

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<td></td>
<td></td>
<td>87% &lt;400</td>
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Response in Z-score over 18 months (n=23)

Months of follow up

-3.5 -3 -2.5 -2 -1.5 -1 -0.5 0

-3.5 -3 -2.5 -2 -1.5 -1 -0.5 0

Z-Score

Height for Age (HAZ)
Weight for Age (WAZ)
Weight for Height (WHZ)
Adherence assessment

- Pill count:
- Measurement of ARV syrup
- Self report

**Result:** A few participants missed one or two doses in the self administration phases.

**Conclusion:** Good adherence (all most 100%)
Response through 18 month
Median of CD4 & CD8 percentage and CD4/CD8 ratio

Study Month

Baseline M6 M12 M18

CD4%
4.5 15.6 20 22.6

CD4/CD8 ratio
0.13 0.3 0.5 0.5

CD8%
58.8 48.5 44.9 40.2
Increase of CD4 percentage during ART

Period of Time on ART

- M0-M6
- M6-M12
- M12-M18

CD4 percentage

- 0
- 2
- 4
- 6
- 8
- 10
- 12

CD4 percentage increases over time on ART.
Decrease of CD8 percentage

<table>
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<th>Time Interval</th>
<th>CD8 Percentage Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0 - M6</td>
<td>-11.3</td>
</tr>
<tr>
<td>M6 - M12</td>
<td>-3.6</td>
</tr>
<tr>
<td>M12 - M18</td>
<td>-4.7</td>
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Changes in CD4 percentage (by individual)
Immune Reconstitution Syndrome

- Total: 5 (19.2%)
- Timing: 45 days
- 3 had CD4=1%
- 2 had CD4=2%
- TB-IRS: (1: Pleurisy; 1: Pulmonary; 1: Lymphadenopathy; 2: TB/MAC?)
- 3 died: Mean duration of 79 days after ART
## Risk factor for IRS
### CD4<5%

<table>
<thead>
<tr>
<th>IRS</th>
<th>Non-IRS</th>
</tr>
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<tr>
<td>5 (41.7%)</td>
<td>7 (58.3%)</td>
</tr>
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</table>

![Pie chart showing the distribution of IRS and Non-IRS cases]
CD4:2%; IRS-TB
MDOT 28; CD4 2%
Plasma Viral Load (copies/ml)

Response through 18 months

Study Month
Cambodian MDOT Study

Response at 12 months

Viral Load

log decrease 1.4 – 4.9 (3.9)

Number <400 19 (83%)

Number <50 8 (35%)
Cambodian MDOT Study

Response at 18 months

Viral Load

log decrease 1.2 – 5.0 (4.1)

Number <400 20 (87%)

Number <50 12 (52%)

Plasma Viral Load (copies/ml)
Conclusion

- Good adherence (appears to be a feasible strategy to optimize medication adherence).
- Good clinical, immunological and virological outcomes.
- Burden of IRS, very low CD4% (<5%)
AKNOWLEDGEMENT

- All children and caregivers in the study
- NPH Team, Cambodia
- Fogarty Program, Brown University, USA
- CFAR, University of Massachusetts, USA
- Pasteur Institute, Cambodia
- French Red Cross
Thank you