Treatment of malaria in Myanmar

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Medical Action Myanmar

Comparison 5 ACT’s in Myanmar

- Background malaria in Myanmar & study area.
- Comparison 5 ACT’s in Myanmar
- Achievements and needs
In 1994 MSF-H started in Rakhine state, Western Myanmar

Proposal
• Cooperation with 20 DoH clinics
• Training microscopists
• Staff ask a small fee (0.10-0.15 USD)
• Mefloquine-Artesunate
Malaria in Myanmar in 1994

- Population = 50-55 million
- Malaria cases 500,000, 75% clinical diagnosis.
- WHO / DoH; CQ and SP still effective
- Malaria protocol 1st chloroquine 2nd fansidar.

Failure rates after chloroquine for 3 age groups

(Study WHO / MOH)
14 days follow up, adults only
"Chloroquine still effective"
Failure rates after sulfadoxine-pyrimethamine for 3 age groups

- Children < 5 years
- Adults
- Children 5 – 14 years

Failure rates after mefloquine (15mg/kg) for all ages

- 7% reappearance of parasites at day 42

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1996; DoH agreed the project to use M 15mg/kg + A 4 mg/kg for children as a ‘study’
2001

M 25mg/kg +
A 4mg/kg x 3 days

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Comparing the effectiveness of 5 artemisinin combination treatment regimen

1. AA  Artesunate-amodiaquine
2. AL  Artemether-lumefantrine
3. AM-F  Artesunate-mefloquine Fixed dose combination
4. AM-L  Artesunate-mefloquine Loose tablets
5. DP  Dihydroartemisinin-piperaquine

Half patients with primaquine 0.75 mg/kg (sd) and half without.

Sample size ; 800

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Recurrence of P.falciparum

![Graph showing recurrence of P.falciparum over time for different treatment regimens.]

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Outcome day 63

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>Pf +</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>155</td>
<td>28</td>
</tr>
<tr>
<td>AL</td>
<td>162</td>
<td>15</td>
</tr>
<tr>
<td>AM-FDC</td>
<td>169</td>
<td>5</td>
</tr>
<tr>
<td>AM-LT</td>
<td>161</td>
<td>7</td>
</tr>
<tr>
<td>DP</td>
<td>162</td>
<td>14</td>
</tr>
</tbody>
</table>

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PCR results recurrent *P. falc*

- 38 new infection
- 20 recrudescence
- 11 indeterminate
Recurrence of *P. falc* day 63

<table>
<thead>
<tr>
<th>Compared to AM-FDC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>0.0000</td>
</tr>
<tr>
<td>AL</td>
<td>0.014</td>
</tr>
<tr>
<td>AM-LT</td>
<td>0.430</td>
</tr>
<tr>
<td>DP</td>
<td>0.023</td>
</tr>
</tbody>
</table>

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Recrudescence of *P. falc* day 63

<table>
<thead>
<tr>
<th>Compared to AMFDC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>0.0001</td>
</tr>
<tr>
<td>AL</td>
<td>0.138</td>
</tr>
<tr>
<td>AM-LT</td>
<td>0.138</td>
</tr>
<tr>
<td>DP</td>
<td>0.141</td>
</tr>
</tbody>
</table>

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## Recrudescence of *P. falc* day 63

<table>
<thead>
<tr>
<th>Compared to AM-FDC</th>
<th>P value confirmed (+ indet term)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>0.0001 - 0.0000</td>
</tr>
<tr>
<td>AL</td>
<td>0.138 - 0.019</td>
</tr>
<tr>
<td>AM-LT</td>
<td>0.138 - 0.035</td>
</tr>
<tr>
<td>DP</td>
<td>0.141 - 0.021</td>
</tr>
</tbody>
</table>

## Recrudescence rates (+ indeterminate)

- AA: 10.3 – 12.5%
- AL: 1.4 – 3.5%
- AML: 1.4 – 2.8%
- AMF: 0%
- DP: 1.4 – 3.4%
Cumulative new infections with P. falciparum

Outcome day 63

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Recr.</th>
<th>Indeterminate</th>
<th>New inf</th>
<th>LTF</th>
<th>Neg</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>155</td>
<td>14</td>
<td>3</td>
<td>11</td>
<td>8</td>
<td>119</td>
</tr>
<tr>
<td>AL</td>
<td>162</td>
<td>2</td>
<td>3</td>
<td>10</td>
<td>10</td>
<td>137</td>
</tr>
<tr>
<td>AM-FDC</td>
<td>169</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>8</td>
<td>156</td>
</tr>
<tr>
<td>AM-LT</td>
<td>161</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>17</td>
<td>137</td>
</tr>
<tr>
<td>DP</td>
<td>162</td>
<td>2</td>
<td>3</td>
<td>9</td>
<td>9</td>
<td>138</td>
</tr>
</tbody>
</table>
Effect on P. Vivax

Patients with at least 1 vivax appearance after treatment

Significant difference between AM-FDC and AL (p<0.001) and AM-LT (p=0.01)
### Vivax appearance after treatment

<table>
<thead>
<tr>
<th>ACT</th>
<th>N</th>
<th>P.vivax ≥1</th>
<th>1x</th>
<th>&gt;1</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>155</td>
<td>59</td>
<td>47</td>
<td>12</td>
</tr>
<tr>
<td>AL</td>
<td>162</td>
<td>85</td>
<td>52</td>
<td>33</td>
</tr>
<tr>
<td>AM-FDC</td>
<td>169</td>
<td>55</td>
<td>49</td>
<td>6</td>
</tr>
<tr>
<td>AM-LT</td>
<td>161</td>
<td>75</td>
<td>57</td>
<td>18</td>
</tr>
<tr>
<td>DP</td>
<td>162</td>
<td>56</td>
<td>46</td>
<td>10</td>
</tr>
</tbody>
</table>

**Proportions of patients with P.vivax**

- **AA**
- **AL**
- **AM FDC**
- **AM LT**
- **DP**

Patients with vivax (%)

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Effect on gametocytes

Proportion of patients positive for gametocytes after treatment (no PQ)
Gametocytaemia after ACT’s (no PQ)

<table>
<thead>
<tr>
<th></th>
<th>Episodes</th>
<th>Person time</th>
<th>Inc rate ratio *</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM-FDC</td>
<td>21</td>
<td>718</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>66</td>
<td>699</td>
<td>3.2</td>
<td>2.0-5.6</td>
<td>0.0000</td>
</tr>
<tr>
<td>AL</td>
<td>41</td>
<td>704</td>
<td>2.0</td>
<td>1.1-3.5</td>
<td>0.005</td>
</tr>
<tr>
<td>AM-LT</td>
<td>23</td>
<td>664</td>
<td>1.2</td>
<td>0.6-2.2</td>
<td>0.29</td>
</tr>
<tr>
<td>DP</td>
<td>75</td>
<td>665</td>
<td>3.9</td>
<td>2.4-6.6</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

* Compared to AM-FDC

Gametocyte positivity rate

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Gametocytaemia after ACT +/- PQ

Gametocytaemia after ACT with PQ and without PQ

| ACT + PQ | 18 | 3279 |
| ACT     | 226 | 3450 | 11.9 | 7.4-20.5 | 0.0000 |

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Effect on gametocytes and transmission

*person-gametocyte-weeks (PGW)*

1. The 5 treatment regimen had a similar PGW when primaquine was added. [average 12.2]
2. However, when primaquine was not added, the 5 regimen had significantly different PGW
   - AA 206
   - AL 127
   - AMF 66
   - AML 74
   - DP 239

Side effects
Artesunate + Mefloquine

- 1630 patients studied
- > 1 million patients treated with Artesunate and Mefloquine combination
- Never very severe side effect observed !?!
- Sometimes serious dizziness
- Sometimes repeated vomiting among children => other drugs

After AM more dizziness than after AL (p=0.004) and DP (p=0.015)
Summary

• AM, DP and AL are effective for treatment uncompl. Falciparum malaria
• AM FDC had no recrudescence and
  – Less new infections with P.falc
  – Least vivax after treatment
  – Less gametocytes after treatment
  – More dizzyness …. but compliance seems OK
  – …… AM is more expensive ……

How to deal with artemisinin resistance in Myanmar

• Use the most effective ACT available.
• At a large scale.
• Reduce transmission by adding PQ.
ODA per capita

GNI per capita

ODA Per Capita 2005

Needs

- It is possible to set up effective projects
- Health investment is too low.
- Myanmar people the lowest recipients of ODA…. for political reasons?
- Lobby groups ‘anti-aid-to-Burma’, Politicians / donors afraid
- Most malaria treatment is uncontrolled.
- Resistance to artemisinin..........
Thank you

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