Assessment of three new parasite lactate dehydrogenase (pan-pLDH) tests for diagnosis of uncomplicated malaria

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Background
- Microscopy is the recommended method for malaria diagnosis, but:
  - Trained staff
  - Quality equipment
  - Supervision

- Rapid diagnostic tests (RDT) are useful for malaria diagnosis where high standard microscopy is not available:
  - Easy to use
  - Simple to interpret

Study rationale
- Most common RDT detect Histidine Rich Protein 2 (HRP2)
- HRP2 tests have 2 major drawbacks:
  - Only detect *P. falciparum*
  - Remain positive for weeks after treatment
- New RDTs detect parasite Lactate Dehydrogenase (pLDH):
  - Identify all Plasmodium species
  - Become negative quickly after treatment

Objectives
- Primary objective
  - Measure validity of 3 new pLDH tests and that of one HRP2 test (Paracheck®)
- Secondary objectives
  - Measure % of positive tests after effective treatment
  - Evaluate ease of use
  - Measure inter-reader reliability

Methods

Inclusion
- Screening at OPD of Mbarara hospital (Uganda)
- Inclusion:
  - Symptoms of simple malaria
  - Signed informed consent
  - Two age groups: “under 5” and “5 and above”

- Sample size: 200 blood smear [+ ] and 200 blood smear [-]
- All tests double read, blinded and compared to microscopy
- Reading of blood smears controlled in Thailand

Methods (continued)

Tests performed

<table>
<thead>
<tr>
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<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<tbody>
<tr>
<td>1</td>
<td>Vistapan® (Mitra, India)</td>
<td>Parabank® (Orchid/Zephyr, India)</td>
<td>Paracheck® (AccessBio, USA)</td>
<td>Carestart® (AccessBio, USA)</td>
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Follow-Up
- Patients:
  - Positive BS on D0
  - Or at least 1 positive RDT on D0
  - Positive BS on D0 treated with Coartem®

- Pregnant women were excluded

- Procedures on D3 & D14:
  - Clinical examination
  - Blood smear
  - All tested RDTs

Results

Validity

<table>
<thead>
<tr>
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<th>Sensitivity (N=248)</th>
<th>Specificity (N=212)</th>
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<tbody>
<tr>
<td>Parabank®</td>
<td>94% [90.2 - 96.6]</td>
<td>87.3% [82.0 - 91.4]</td>
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<tr>
<td>Vistapan®</td>
<td>91.9% [87.8 - 95]</td>
<td>89.6% [84.7 - 93.4]</td>
</tr>
<tr>
<td>Carestart®</td>
<td>95.6% [92.2 - 97.8]</td>
<td>91.5% [86.9 - 94.9]</td>
</tr>
<tr>
<td>Paracheck®</td>
<td>84.7% [79.6 - 88.9]</td>
<td>94.3% [90.3 - 97.0]</td>
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Sensitivity by group

- Parasite density:
  - Sensitivity decreased with parasitemia
  - Parasitaemia <100 parasites/µL (from 41.9% [Parabank®] to 67.7% [Carestart®])

- Age group:
  - Sensitivity increased in under 5’s
  - From 95.3% [Parabank®] to 97.7% [Vistapan® / Carestart®]

Conclusions
- Carestart® and Vistapan® proved better than:
  - Parabank® (poorly sensitive)
  - Paracheck® (high % of positives at D14)

- Carestart® and Vistapan® could replace Paracheck® for malaria diagnosis in sub-Saharan Africa

- However, pLDH tests have slightly higher costs ($0.6 to $0.7 vs $0.45 for Paracheck®)