WHO Malaria RDT Web Reviews

Ratsimbasoa 2007

Summary Table

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| RDT product(s): | CareStart Malaria test, Access Bio Inc, Monmouth Junction, NJ, USA SD Malaria Antigen Bioline, Standard Diagnostics, Suwon City, South Korea OptiMAL-IT, Diamed AG, Cressier sur Morat Switzerland |
| Target antigens: | Pf specific and pan-malaria pLDH |
| Comparative standard(s): | Microscopy of thick/thin blood films |
| Trial type: Accuracy / Cost-benefits/public health impact/ease of use/behavioral: | Accuracy of three RDT to diagnose malaria in Madagascar/cost benefits were compared/public health impact was considered/ease of use and cost was discussed |

*Usefulness of paper (rated by reviewers): 4/5

Major findings/implications:

- CareStart Malaria Test was comparable to OptiMAL-IT in detecting *P falciparum* and *P vivax* in symptomatically diagnosed patients.
- All 3 RDT were less sensitive in detecting non-falciparum malaria
- SD Malaria antigen Bioline sensitivity was lower than the other two RDT for the diagnosis of all malaria and a higher number of false negative results occurred
- Ease of use for all three RDT was good, stability was not analysed in this study

**Country:** Madagascar

**Trial type**

A laboratory and rural field evaluation by the NMCP Madagascar of the accuracy of three RDT’s for malaria diagnosis compared to microscopy of thick and thin blood slides. An additional study to test absolute parasite detection limits was also conducted.

**Methods**

**Field study**

A field study was conducted in PHC's in rural areas of Mahasolo and Saharevo, both in the Highland foothills during October and November 2005. This area has low, predominately seasonal malaria.

EDTA Blood samples were collected from febrile patients with typical malaria symptoms, who gave informed consent and had axillary temperatures ≥ 37.5°C or history of fever in the last 24hrs. Pregnant women and severe complicated malaria cases were excluded.

Thick and thin blood films were prepared and the Giemsa stained blood films were examined by an experienced technician blinded to results of RDT. A Minimum 200 fields were examined in the thick film before declaring negative. Parasites were counted against 200-500 WBC in the thick film and parasite density estimated assuming 8000 WBC/µl. 0% of slides were independently checked at the end of the study by another expert microscopist and no discrepancies were found.

The three RDT’s were performed according to the manufacturers’ instructions by a second technician. All three RDT’s were used according to manufacturers’ instructions. All kits were maintained at room temperature until opened and used immediately to avoid humidity effect.

**Absolute parasite detection sensitivity**
Two samples of EDTA anti-coagulated blood containing approximately 10,000 *P. falciparum* parasites/µl and 1000 *P. vivax* parasites/µl were collected in the PHC at Mahasolo and sent to the Malaria Unit laboratory within 8 hours in a controlled 4°C cool box. Parasitaemia was again confirmed by microscopy.

Both samples were diluted with uninfected blood to give a range of 7 dilutions from 10000-150 *P. falciparum* parasites/µl and five dilutions ranging from 1000-65 *P. vivax* parasites/µl. No details for this procedure are described. Further serial dilutions of the samples were prepared with mixed *P. falciparum* and *P. vivax* containing 2500 Pf and 1000-125 *Pv* parasites/µl and 4 dilutions containing 1000 parasites/l of *P. vivax* and serially diluted 1250-150 parasites of *P. falciparum*.

Each dilution was tested in duplicate by two independent technicians with the three RDT. The proportion of serial dilutions testing positive gave the absolute parasite detection limits for each.

**Results and analysis:**

Analysis was made using Epi Info version 3.3.2 software. Chi square test was used to compare performances between the three RDT and microscopy. *P* values < 0.05 indicated significant differences.

194 patients were recruited from both centres. 17% had previous anti-malaria therapy (Chloroquine 57.6%, SP 30.3%, Tetracycline 6.1%, Chloroquine+SP 3% and Quinine 3 %.). 90/194 (46.4%) were diagnosed with malaria by microscopy. 80% with *P. falciparum*, 10% with *P. vivax* and 6.7% with *P. malariae*. There were mixed infections with Pf/Pv in 3%.

**Tabulated results**

Results are shown for
- Comparative results from the field study positive for Plasmodium spp. by microscopy, CareStart Malaria Test, SD Malaria antigen Bioline, OptiMAL-IT.
- Diagnostic performance of the three RDT tests in detecting Plasmodium spp. in the study patients
- Sensitivity of the three RDT in detecting different levels of *P. falciparum* parasitaemia in study patients.
- pLDH threshold detection levels at different levels of parasitaemia in a laboratory study.

**Sensitivity:**

For detection of 95% of results for ≥100 parasites/l (WHO recommendation), only CareStart Malaria Test (96.8% CI 95%) and OptiMAL-IT (95% CI 95%) achieved this sensitivity.

For detection of > 500 parasites/µl of *P. falciparum* CareStart Malaria Test and OptiMAL-IT had 100% sensitivity and SD Malaria Antigen Bioline sensitivity was 90%.

For detection of ≤500 parasites/µl the sensitivity decreased to 60% for CareStart Malaria Test and OptiMAL-IT and 57.1% for SD Malaria Bioline.

Overall sensitivity for detection of *P. falciparum* was 89.4% for SD Malaria Antigen Bioline, 92.6% for OptiMAL-IT and 97% for CareStart Malaria Test. There was a significant difference between SD Malaria Antigen Bioline and CareStart Malaria Test (*P* = 0.005)

For detection of *P. falciparum* antigen specificity was 94.1% for CareStart Malaria Test, 97.1% for SD Malaria antigen Bioline and 100% for OptiMAL-IT. There was a significant difference between CareStart Malaria Test and OptiMAL-IT (*P*=0.002)

PPV OptiMAL-IT was 100% with CareStart Malaria Test 91.4% (*P* = 0.001) and SD Malaria antigen Bioline 95.1% (*P* = 0.005)
NPV had no significant differences between the three RDT.

For detection of non-falciparum malaria the decline in sensitivity began at <5000 parasites/µl for all three RDT.

*pLDH threshold detection levels*

All three RDT had a minimum threshold detection of 150 parasites/µl for *P falciparum*, but no non-falciparum bands were observed at all parasitaemia for SD Malaria Antigen Bioline and only at > 1250 parasites/µl for CareStart Malaria Test.

*False positive/False negative results detected by all three RDT*

Reasons for the few detected were explained as either false microscopic readings or parasite densities below detection microscopic levels. Two samples with parasitaemias of 500 and 2520 parasites/µl were false negative with 2 RDTs and these were not explained.

*Ease of use and cost benefits*

Because this was an evaluation to try to find a candidate to supply a National program, ease of use and cost benefit was necessary.

No large differences between the three were seen and all were fairly easy to use and interpret, results were stable and were simple to store with no cold chain necessary. Stability and shelf life were not assessed.

CareStart Malaria Test was the least costly ($1.11/test) and SD Malaria antigen Bioline most costly ($1.35/test).

*Usefulness of paper (rated by reviewers): 4*

* 1. No direct relevance.  2. Very unlikely to influence current practice.  3. Likely to influence current practice in some settings.  4. Likely to influence current practice in many areas.  5. Highly likely to influence current practice in many areas.

Disclaimer:

The views expressed in this report are those of the independent reviewers and do not necessarily reflect the views or policies of the World Health Organization.