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[Diagnostic Test Accuracy Review]

Rapid diagnostic tests for diagnosing uncomplicated non-falciparum or Plasmodium vivax malaria in endemic countries

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ABSTRACT

Background

In settings where both *Plasmodium vivax* and *Plasmodium falciparum* infection cause malaria, rapid diagnostic tests (RDTs) need to distinguish which species is causing the patients' symptoms, as different treatments are required. Older RDTs incorporated two test lines to distinguish malaria due to *P. falciparum*, from malaria due to any other *Plasmodium* species (non-falciparum). These RDTs can be classified according to which antibodies they use: Type 2 RDTs use HRP-2 (for *P. falciparum*) and aldolase (all species); Type 3 RDTs use HRP-2 (for *P. falciparum*) and pLDH (all species); Type 4 use pLDH (from*P. falciparum*) and pLDH (all species).

More recently, RDTs have been developed to distinguish P. vivax parasitaemia by utilizing a pLDH antibody specific to P. vivax.

Objectives

To assess the diagnostic accuracy of RDTs for detecting non-falciparum or *P. vivax* parasitaemia in people living in malaria-endemic areas who present to ambulatory healthcare facilities with symptoms suggestive of malaria, and to identify which types and brands of commercial test best detect non-falciparum and *P. vivax* malaria.

Search methods

We undertook a comprehensive search of the following databases up to 31 December 2013: Cochrane Infectious Diseases Group Specialized Register; MEDLINE; EMBASE; MEDION; Science Citation Index; Web of Knowledge; African Index Medicus; LILACS; and IndMED.

Selection criteria

Studies comparing RDTs with a reference standard (microscopy or polymerase chain reaction) in blood samples from a random or consecutive series of patients attending ambulatory health facilities with symptoms suggestive of malaria in non-falciparum endemic areas.



Data collection and analysis

For each study, two review authors independently extracted a standard set of data using a tailored data extraction form. We grouped comparisons by type of RDT (defined by the combinations of antibodies used), and combined in meta-analysis where appropriate. Average sensitivities and specificities are presented alongside 95% confidence intervals (95% CI).

Main results

We included 47 studies enrolling 22,862 participants. Patient characteristics, sampling methods and reference standard methods were poorly reported in most studies.

RDTs detecting 'non-falciparum' parasitaemia

Eleven studies evaluated Type 2 tests compared with microscopy, 25 evaluated Type 3 tests, and 11 evaluated Type 4 tests. In meta-analyses, average sensitivities and specificities were 78% (95% CI 73% to 82%) and 99% (95% CI 97% to 99%) for Type 2 tests, 78% (95% CI 69% to 84%) and 99% (95% CI 98% to 99%) for Type 3 tests, and 89% (95% CI 79% to 95%) and 98% (95% CI 97% to 99%) for Type 4 tests, respectively. Type 4 tests were more sensitive than both Type 2 (P = 0.01) and Type 3 tests (P = 0.03).

Five studies compared Type 3 tests with PCR; in meta-analysis, the average sensitivity and specificity were 81% (95% CI 72% to 88%) and 99% (95% CI 97% to 99%) respectively.

RDTs detecting P.vivax parasitaemia

Eight studies compared pLDH tests to microscopy; the average sensitivity and specificity were 95% (95% CI 86% to 99%) and 99% (95% CI 99% to 100%), respectively.

Authors' conclusions

RDTs designed to detect *P. vivax* specifically, whether alone or as part of a mixed infection, appear to be more accurate than older tests designed to distinguish *P. falciparum* malaria from non-falciparum malaria. Compared to microscopy, these tests fail to detect around 5% of *P. vivax* cases. This Cochrane Review, in combination with other published information about in vitro test performance and stability in the field, can assist policy-makers to choose between the available RDTs.

12 April 2019

No update planned

Review superseded

This Cochrane Review has been superseded by Choi 2019 https://doi.org/10.1002/14651858.CD013218

PLAIN LANGUAGE SUMMARY

Rapid tests for diagnosing malaria caused by Plasmodium vivax or other less common parasites

This review summarises trials evaluating the accuracy of rapid diagnostic tests (RDTs) for diagnosing malaria due to *Plasmodium vivax* or other non-falciparum species. After searching for relevant studies up to December 2013, we included 47 studies, enrolling 22,862 adults and children.

What are rapid tests and why do they need to be able to distinguish Plasmodium vivax malaria

RDTs are simple to use, point of care tests, suitable for use in rural settings by primary healthcare workers. RDTs work by using antibodies to detect malaria antigens in the patient's blood. A drop of blood is placed on the test strip where the antibodies and antigen combine to create a distinct line indicating a positive test.

Malaria can be caused any one of five species of *Plasmodium* parasite, but *P. falciparum* and *P. vivax* are the most common. In some areas, RDTs need to be able to distinguish which species is causing the malaria symptoms as different species may require different treatments. Unlike *P. falciparum*, *P. vivax* has a liver stage which can cause repeated illness every few months unless it is treated with primaquine. The most common types of RDTs for *P. vivax* use two test lines in combination; one line specific to *P. falciparum*, and one line which can detect any species of Plasmodium. If the *P. falciparum* line is negative and the 'any species' line is positive, the illness is presumed to be due to *P. vivax* (but could also be caused by *P. malariae*, or *P. ovale*). More recently, RDTs have been developed which specifically test for *P. vivax*.

What does the research say

RDTs testing for non-falciparum malaria were very specific (range 98% to 100%) meaning that only 1% to 2% of patients who test positive would actually not have the disease. However, they were less sensitive (range 78% to 89%), meaning between 11% and 22% of people with non-falciparum malaria would actually get a negative test result.



RDTs which specifically tested for *P. vivax* were more accurate with a specificity of 99% and a sensitivity of 95%, meaning that only 5% of people with *P. vivax* malaria would have a negative test result.