Use of Rapid Diagnostic Tests for Diagnosis of Malaria in the United States

In the September issue, performance of the BinaxNOW Malaria for the diagnosis of malaria in a major U.S. academic medical center was reported (2). Herein, we report performance of this test in a second large academic medical center in the U.S. BinaxNOW was introduced at our institution as a component of routine blood parasite examination, along with thick and thin blood smear microscopy in January 2011. In 2007-2011, BinaxNOW was also selectively performed on specimens that were positive for malaria by microscopy, as part of laboratory verification studies. In total, 251 parasite blood exams from 244 patients were performed. Of these, 239 (95.2%) were negative by microscopy. The remaining 12 positive specimens included 4 Plasmodium falciparum, 5 Plasmodium vivax and 3 Plasmodium malariae, with corresponding parasitemias of <0.01% - 0.5%. BinaxNOW resulted in 9 positive results. Three false negative BinaxNOW results were obtained, all in patients with P. malariae infection and parasitemia < 0.1%. One false-positive BinaxNOW result was obtained, in a 17 month old child with two weeks recurrent fevers and travel history to a malaria endemic region one year prior to symptoms. Clinical index of suspicion for malaria in this case was low. All discrepant results were confirmed by repeat testing using BinaxNOW, and reevaluation of blood smears. Overall sensitivity, specificity, positive predictive value, and negative predictive value for BinaxNOW was found to be 72.7%, 96.8%, 88.8% and 98.8%, respectively (Table). When patients with P. malariae infection or parasitemia <0.1%, neither of which are covered by BinaxNOW FDA performance claims, were removed from analysis, sensitivity improved to 100%.

Based on the results of our study, our laboratory uses BinaxNOW as an adjunct to thin and thick smear microscopy, primarily to aid with species identification when only early trophozoites are observed by microscopy, and to provide a rapid preliminary positive result identifying P. falciparum from non-falciparum. A rapid identification of P. falciparum is critical in cases of severe malaria which necessitate
prompt treatment. In particular, intravenous artesunate has recently been made available by the Centers for Disease Control and Prevention for this indication, under an investigational new drug protocol (http://www.cdc.gov/malaria/diagnosis_treatment/artesunate.html).

Performance data for BinaxNOW indicate this test cannot replace microscopy, as we and others have observed both false-negative and -positive results (1, 3-5). Clinical ramifications of reporting false-negative results are of most pressing concern, in particular as many patients seen in the U.S. with falciparum malaria will have low level parasitemia that is below the limit of detection of BinaxNOW. False negative results may also be obtained at high level parasitemia, due to prozone phenomenon, or possibly mutation in HRP-2 antigen detected by the test (2, 5).

It is unquestionable that maintaining expertise in malaria diagnostics at the hospital level in the U.S. is challenging, due to regulatory and budget considerations and the fact that laboratories may encounter only 0-2 cases of malaria per year. As such, the promise of a rapid, low-complexity test that can replace labor-intensive microscopy techniques is highly attractive. However, current technologies have not yet achieved a sensitivity and specificity to allow the laboratory to discontinue microscopy. Only 17% of laboratories in the U.S. use rapid diagnostic tests such as BinaxNOW (1), the majority in conjunction to microscopy. We urge laboratories that are considering implementation of this test to ensure capacity for microscopy diagnostics is maintained. Nevertheless the implementation of the rapid diagnostic test can be very useful in providing physicians with quick preliminary results allowing for appropriate clinical management of the patient.

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Table. Performance of BinaxNOW for 251 blood specimens evaluated for malaria at a large academic hospital laboratory 2007 - 2012

<table>
<thead>
<tr>
<th>Overall Performance</th>
<th>Performance for FDA-approved claims only (P. falciparum and P. vivax, &gt;0.1% parasitemia)</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>72.7 % 39.3-92.7 % 100% 59.8-100.0%</td>
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<tr>
<td>Specificity</td>
<td>99.6 % 97.3-99.9 % 99.6% 97.3-99.9%</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>88.9 % 50.7-99.4 % 88.9% 50.7-99.4%</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>96.4 % 93.1-98.2 % 100% 98.0-100.0%</td>
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References


