EVALUATION OF THE KAT™-QUICK MALARIA RAPID TEST FOR RAPID DIAGNOSIS OF FALCIPARUM MALARIA IN THAILAND

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Abstract. In recent years, several rapid diagnostic tests for falciparum malaria have been developed. KAT™ test results were compared with microscopy on 90 consecutive patients hospitalized at the Hospital for Tropical Diseases, Bangkok, Thailand. Fifty-one patients had *P. falciparum* infections while 49 had malaria due to other plasmodium species. For a geometric mean ±SD (Min;Max;range) parasitemia of 11,481 ± 5.0 (88;713,838;713,750), the sensitivity of the KAT test was 96% (95% CI=86-99.5), the specificity was 92% (95% CI=80-99), the accuracy was 94% and the reliability was 85%. These findings suggest that the KAT™ test is of potential interest in the diagnosis of *falciparum* malaria in Thailand.

INTRODUCTION

Although the detection of asexual parasites by light microscopy of Giemsa-stained thick and thin blood films is still the gold standard for the diagnosis of malaria (Makeler *et al*, 1998; Hanscheid *et al*, 1999; Craig *et al*, 2002), the World Health Organization has repeatedly emphasized the urgent need for simple and cost-effective diagnostic tests for malaria that can overcome the deficiencies of light microscopy (World Health Organization, 1996). Microscopy is time consuming, unreliable at low parasite densities and requires trained personnel and regular quality control to be reliable. Several rapid tests based on the immunodetection of plasmodium antigens have been successfully developed and recommended by the WHO. Some are cost-effective, require neither laboratory facilities nor electricity, are quickly performed and are easily interpreted. Most rapid tests, however, cannot quantify parasitemia and remain positive after viable parasites are no longer circulating. They are not necessarily better than microscopy at detecting low level parasitemia. *Plasmodium falciparum* is the most lethal malarial parasite and its reliable detection in febrile patients is crucial (Manson's Tropical Diseases, 2003). The KAT-Quick Malaria test (KAT™ Medical, Johannesburg) was designed for rapid diagnosis of malaria where microscopic examination is not available or feasible. An antigen-capture assay detecting the presence of a specific soluble protein, histidine-rich protein II (PfHRP-II), which is present in, and released from, infected red blood cells. The test is designed as a simplistic, rapid qualitative method of testing for the presence of *P. falciparum* malaria *in vitro*. The KAT-Quick Malaria test did not cross-react with any of the following species of malaria: *P. malariae, P. ovale*, and *P.vivax*. The purpose of this study was to determine the sensitivity and specificity of the KAT™ test in using microscopy as the gold standard.

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MATERIALS AND METHODS

The study was performed between June and

December 2000 at the Hospital for Tropical Diseases in Bangkok, Thailand. The study was approved by the Ethics Committee of the Faculty of Tropical Medicine, Mahidol University. Ninety consecutive patients with microscopically diagnosed malaria (*P. falciparum, P. vivax, P. malariae* or *P. ovale*) were recruited after informed consent. The fingerprick blood samples were used to prepare thick and thin blood films, which were stained with 10% Giemsa solution and examined microscopically at 1,000 x magnification. The microscopists at the Hospital for Tropical Diseases are highly experienced in the diagnosis of malaria and quality control is regular. The number of malaria parasites per microliter of blood was determined by counting the number of parasites per 1,000 red blood cells in thin films and per 200 white blood cells on thick films. In cases where thick blood films were missing or uncountable (too many parasites), the number of malaria parasites was calculated using a thin blood film and red blood cells. Blood films were considered negative if no parasites were seen in 200 oil-immersion fields on a thick blood film.

Another 10 µl of blood was collected into a microcapillary tube and immediately tested using the KAT™-Quick Malaria Rapid Test following the manufacturer's instructions. The test consists of a strip encased in a plastic housing in which blood and buffer are added.

The principle of this test is to immobilize a capture monoclonal antibody on the nitrocellulose strip. The red blood cells are lysed releasing PfHRP-II which binds selectivity to this antibody as the blood is wicked up the strip. The signal reagent is coated with specific antibodies which bind with the antibody-antigen complex, producing a red line (the procedural control line) demonstrates the test has been performed correctly.

RESULTS

Of the ninety cases, 50 (56%) cases were *P. falciparum*, 38 (42%) cases were *P. vivax*, 1 (1%) case was *P. malariae*, and 1 (1%) case was *P. ovale*. Geometric mean ± SD (Min, Max) parasite counts for falciparum and vivax malaria were 11,481 ± 5.0 (88;713,838). Only 1 patient with *P. falciparum* infection had a parasitemia below 500/µl. These numbers were insufficient to explore the performance of the test at low parasitemia.

The sensitivity and specificity of the KAT™ test in using microscopy as the gold standard were calculated by STATA 6.0 licensed software (STATA™, Stata Corporation, 4905 Lakeway Drive, College Station, Texas 77845, USA) using the formulae of Galen (1975).

True positive for *P. falciparum* : 48
False positive for *P. falciparum* : 3
True negative for *P. falciparum* : 37
False negative for *P. falciparum* : 2
Sensitivity [TP/(TP + FN)] = 96%; 95%CI = 86.3, 99.5
Specificity [TN/(TN + FP)] = 92.5%; 95%CI = 79.6, 98.4
Positive predictive value [TP/(TP + FP)] = 94.1%; 95%CI = 83.8, 98.8
Negative predictive value [TN/(TN + FN)] = 94.9%; 95%CI = 82.7, 99.4
Reliability [(TP + TN)/total] = 85/90 = 94.4%
Accuracy [(TP x TN)-(FP x FN)]/[(TP + FN)(TN + FP)] = 88.5%

DISCUSSION

There were not enough patients with very low parasitemia to establish if there was a decrease of sensitivity at parasitemias less than 500 per microliter as have been previously described with rapid tests (Forney *et al*, 2001; Iqbal *et al*, 2002). However, for higher parasitemias the KAT™ rapid test was sensitive and specific for diagnosing *P. falciparum* malaria, as was found by other investigators (Craig *et al*, 2002). The finding of this study for sensitivity was remarkably similar to the standard of the KAT test with 96%. However, the absence of cross-rection with 1 case of *P. vivax* and the presence of false positive results of the KAT test for fever cases indicates its specificity (92.5%) lower than the screening capability of 99.7% that was similar to the experience of a previous study (Cong *et al*, 2002).

The KAT™test therefore does permit the early diagnosis and treatment of potentially fatal *falciparum* malaria. Moreover, given the spread of malaria drug resistance and the increasingly

expensive new antimalarial compounds, rapid tests may avoid presumptive treatments, which are expensive and may exert drug pressure. It is thus a potentially useful and cost effective tool in circumstances where laboratory facilities are absent, or in pregnant women in whom placental sequestration of falciparum parasites can produce a negative blood smear (Leke *et al*, 1999).

Conclusion

Since the KAT™ test detect only falciparum malaria, we therefore recommend that this test should be used in an endemic area where falciparum malaria is the predominant species. Definite clinical diagnosis should not be made until the physician has evaluated the results in combination with other clinical and laboratory findings.

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