OPERATIONAL TRIAL OF PARASIGHT™-F (DIPSTICK) IN THE DIAGNOSIS OF FALCIPARUM MALARIA AT THE PRIMARY HEALTH CARE LEVEL

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Abstract. The rapid manual ParaSight™-F test of *Plasmodium falciparum* malaria, an antigen capture test for detecting trophozoite-dirived histidine rich protein-2 (PF HRP-2), is simple to perform and provides a definite diagnosis within 10 minutes. During an operational trial at health centers and mobile malaria units where microscopical diagnosis is not available and using defined symptom screening criteria, 3,361 subjects were tested yielding 618 positives (18.4%) for PF-HRP-2 by ParaSight™-F. Microscopic examination of the same subjects by thick blood film examined 7 days later at a malaria clinic showed 578 falciparum, and 349 vivax and mixed infection (F+V) 41. The technology proved highly effective in detecting falciparum malaria at the peripheral levels where access to malaria laboratory services are difficult, thus allowing immediate administration of a complete course of treatment in the absence of a microscopic examination.

INTRODUCTION

The World Health Organization's new strategy for Global Malaria Control (WHO, 1992), and Antimalarial Drug Policies (WHO, 1994) identifies, as a major objective, early diagnosis and treatment of malaria at the village or PHC levels. The control strategy aims at the elimination of mortality and reduction of morbidity and suffering by providing effective treatment at the earliest possible time following the onset of clinical symptoms. In district-based health centers (HC) diagnosis by paramedical staff is normally made on the bases of crude clinical symptoms, generally fever, and presumptive treatment with an anti-malarial, usually sulfadoxine-pyrimethamine, is administered. Blood slides collected are forwarded to a Malaria Clinic (MC) for microscopic examination, after which radical treatment is provided. A period of some 3 to 7 days may elapse before this treatment is administered. The provision of a simple and reliable diagnostic test that can be applied at the peripheral level would allow immediate administration of a complete course of radical treatment to the positive cases and eliminate the need to provide presumptive treatment. We describe an operational trial of the "ParaSight™-F" test at the primary health care level.

The primary objective was to evaluate the operational use of the ParaSight™-F in the diagnosis of malaria at the primary health care level (health center), and by malaria field staff. A secondary objective was to determine an appropriate set of simple clinical symptoms as improved criteria for application of the dipstick technology.

MATERIALS AND METHODS

The ParaSight™-F, a dipstick malaria antigen detection wick is a rapid technique for the diagnosis of falciparum malaria by the detection of *P. falciparum* histidine-rice protein-2 (Pf HRP-2), a water-soluble antigen released from the blood stages of *P. falciparum*. If the test is successful after processing, a broken pink line, as a quality control, appears at the upper part of the dipstick test strip. If a solid unbroken line also appears at the lower part of the test strip then the test is positive for *P. falciparum* HRP-2 antigen. If there is no unbroken pink line the test is negative. The entire test can be completed within 10 minutes. Materials for conducting the "ParaSight™-F" test are supplied in a test kit.

Study design

The study was conducted as an operational trial

to determine the practical use of the ParaSight™-F at health centers and malaria mobile units to diagnose falciparum infections without microscopic examination. The trial was determined to demonstrate the possibility of making a reliable diagnosis of falciparum malaria at the PHC level by peripheral health staff that would allow prompt and appropriate treatment and eliminate the need for blood slide collection, presumptive treatment, and the presently practised delay of 3-7 days required for microscopic examination at a malaria clinic before effective radical treatment can be administered.

The operational trial was conducted at 22 malaria mobile units and 34 health centers in the provinces of Chiang Mai and Mae Hong Son, located in high malaria receptive areas of Thailand close to the Thai-Burmese border.

Following a brief 2-3 hours training (including demonstration and practice) given to the peripheral health workers, ParaSight™-F test kits and other basic equipment were provided. After this initiation and with very limited supervision, the health workers carried out the diagnosis and provided treatment of falciparum infections as determined by the dipstick technology. Selection of possible malaria cases was made on specified criteria that included oral thermometer graded temperatures of ≥ 37.5°C with or without headache. Thick blood films were also collected in order to determine reliability of the test system as carried out by the health workers and also to test for possible of *Plasmodium vivax* infections, the ParaSight™-F having the capability of detecting only *Plasmodium falciparum*. All thick blood films were forwarded by standard procedure to the nearest malaria clinic for microscopic examination. Patients having the defined symptoms but negative by ParaSight™-F were provided with single dose chloroquine (600 mg) as presumptive treatment and instructed to report to the hospital if symptoms had not subsided within 24-48 hours. Patients having a positive ParaSight™-F, indicating the presence of *P. falciparum* HRP-2 antigen were administered standard mefloquine and primaquine treatment.

The selection system by defined clinical symptoms detected a total of 968 malaria cases (TBF Table 1) giving a SPR of 28.8%. Efforts were made to determine possible reason(s) for the remaining negative samples, 2,390 or 71.2%, that had similar symptoms. Field staff reported focal outbreaks of para-typhoid as being a major possibility.

Blood films and ParaSight™-F dipsticks were forwarded to the Malaria Regional Center, Chiang Mai, for expert review that included dipstick reactions, confirmation of parasite species and parasitemia by thick blood film microscopic examination.

RESULTS AND DISCUSSION

The ParaSight™-F is a simple diagnostic system requiring, beside the test materials supplied by the manufacturer in the basic kit, only blood lancets, cotton wool and alcohol swabs. The training period is limited to a short 2-3 hours and can easily be mastered by health workers at primary health care level. The rapid diagnosis followed by full appropriate treatment has become most popular with both health center staff and patients. The patients acceptance has been reflected in the increase of symptomatic cases seeking examination and also their expressed offer of participation in the financial cost of providing the diagnostic system. The fact that patients could observe the rapid diagnosis and return home with full radical treatment instead of having to wait a number of days was greatly appreciated.

A total 3,361 patients were selected having the criteria for ParaSight™-F diagnostic test of which 618 (18.4%) were positive for PF HRP-2 antigen. Microscopic examination of thick blood films at the Malaria Clinic showed 578 falciparum, 349 vivax and 41 mixed infections (F+V) (Table 1). It is noted that although all patients had the required thermometer temperature (≥ 37.5°C) some 96% had also headache. Comparative results of Table 1 do seem to suggest that the criteria applied allowed the detection of the majority of *P. falciparum* infections.

Table 1

Collection results.

System	Exam	Pf	Pv	Mixed (F+V)	Total
Dipstick	3,361	618	-	-	618
TBF	3,361	578	349	41	968

Table 2

Comparison with TBF.

DS	TBF +	TBF -	Total
+	598	20	618
-	21	2,722	2,743
Total	619	2,742	3,361

Sensitivity	$= \frac{598}{619} =$	96.6%
Specificity	$= \frac{2,722}{2,742} =$	99.2%
Positive predictive value	$= \frac{598}{618} =$	96.8%
Negative predictive value	$= \frac{2,722}{2,743} =$	99.2%

The accuracy of the ParaSight™-F in detecting a falciparum infection as confirmed by the TBF parallel microscopic examination, sensitivity = 96.6% and specificity = 99.2% is most encouraging. The fact that some few *P. falciparum* cases were detected by TBF but undetected by ParaSight™-F does not reduce the value of the system. Of the cases undetected 1 had gametocytes only and the remainder had a few ring forms. Mature gametocytes do not produce histidine rich protein-2 while a very low trophozoite number may not provide sufficient levels of antigen to be detected by the dipstick. However, all cases that were demonstrated as having sufficient levels of antigen proved to have parasitemias that would have required prompt treatment. Unnecessary suffering has been prevented and when one considers that more than 40% of all falciparum cases detected were children below the age of 15 years, so that possibly some instances of mortality were prevented.

The operational trial had a major objective to attempt to determine simple clinical symptoms as criteria for application of the dipstick diagnosis. Records of the blood collections by the malaria control program during 1995 at the health centers and mobile malaria units within the operational trial provinces show that 292,219 blood films collected 3,744 positives were detected, an SPR of 1.3%. This high collection and low SPR indicated a need for a more accurate criteria at the pheripheral level. The criteria of ≥ 37.5°C thermometer temperature with or without headache as used in the trial has greatly improved the detection system. As an example data from sector 13, Chiang Mai Province shows that the PCD at health centers had an SPR increase from 16% to 36%. Using this approach the ACD determined by malaria mobile units rose from 0.8% to ~ 25%.

We are aware that in Thailand in most malaria transmission areas *Plasmodium vivax* infections play a major role. In this operational trial some 349 *P. vivax* cases were given presumptive treatment with single dose chloroquine (600 mg) that was

Table 3

Comparison collections 1995-1996 in operational trial area, Sector 13.

	Health centers (10)			Malaria mobile units (2)		
	1995	1996		1995	1996	
	Routine	Routine	Operation trial	Routine	Routine	Operation trial
I Total TBF						
Exam	1,957	1,229	741	3,313	2,145	154
Total pos	354	197	269	30	17	38
SPR %	18.0	16.0	36.3	0.9	0.8	24.7
II ParaSight-F						
Pos	-	-	170	-	-	22
Pos rate %	-	-	23.0	-	-	14.7

followed by the full course of treatment 3-7 days later. *Plasmodium vivax* while normally not being life-threatening can produce severe illness. The presumptive treatment assists in clearing the erythrocytic stages and provide relief from symptoms.

Manufacturers of the ParaSight™-F are presently developing a dipstick technology that will diagnose in a similar manner the presence of both *Plasmodium falciparum* and *Plasmodium vivax*. This technology that will function on a single stick is scheduled to be field validated in Thailand in 1996.

Conclusions

The operational trial has clearly demonstrated the reliability of the ParaSight™-F in detecting falciparum malaria. The diagnostic system is simple and peripheral health workers can perform the test after a short 2-3 hours training. By using defined symptomatic criteria the selection of positive cases has been highly accurate, although there remains room for further improvement. The addition of fever history over the past 72 hours is suggested.

The provision of a service with prompt diagnosis and treatment for falciparum infections has been achieved, thus reducing suffering and removing the need for the 3-7 days delay before radical treatment. A total of 618 falciparum malaria cases having been diagnosed by the ParaSight™-F were provided on the spot full radical treatment. Although *P. vivax* infections amounted to 349, the method of single dose chloroquine has possibly been beneficial to these patients. The large number of *P. vivax* cases clearly indicates the need for dipstick to diagnose this species.

The service of prompt diagnosis and treatment has been most welcomed by both patients and health center staff. It is expected that attendance at health centers will increase as the community become more aware of the service provided. Although the cost effective for the ParaSight™-F diagnostic system as compared with the thick blood film method involving delayed microscopical examination is not yet completed, preliminary observations make the dipstick favorable.

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