EARLY DIAGNOSIS AND TREATMENT OF FALCIPARUM MALARIA IN CAMBODIAN TRAUMA PATIENTS

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Abstract. Asymptomatically infected patients with falciparum malaria may develop symptomatic malaria infection secondary to injury or surgery. This complication increases the risk for postoperative wound infection and adds to the burden of trauma. The aims of the present study were to investigate the preventive effect of early antimalaria treatment of *Plasmodium falciparum* infected trauma patients, and to study the validity and accuracy of a rapid test to identify those infected. An open, non-randomized, interventional multi-center, cohort study was carried out at six district hospitals in northwestern Cambodia. Two hundred twenty-two trauma patients was examined for *P. falciparum* by dipstick test soon after injury. The patients testing positive were immediately treated with artesunate-mefloquine. A subset of 108 patients from Pailin, an area considered highly endemic for falciparum malaria, was used for the main analysis. Of 28 *P. falciparum* rapid test-positives, 21 developed symptomatic post-injury malaria despite early antimalarial treatment. The agreement between the dipstick test and blood smear examination was good (kappa 92.5; 95%CI 84.5 - 100). Early pre-operative treatment of parasite carriers does not seem to prevent symptomatic malaria after injury and surgery. The rapid test for falciparum malaria was reliable in early identification of asymptomatic *P. falciparum* infected patients.

INTRODUCTION

Post-operative malaria attacks are a known problem for surgeons working in *Plasmodium falciparum* endemic areas. As stated in Manson's Tropical Diseases: "Many patients, especially children, may remain fit to work and play but can have malarial parasites in their blood. The stress of surgery commonly provokes a severe attack of malaria with marked hemolysis and possible cerebral involvement. Fever within 48 hours of surgery is most likely malaria. Any patient with a hemoglobin below 9 g/dl needs investigation. Those in whom malaria parasites are found should have a course of antimalarial treatment and surgery should be delayed for several days. In an emergency situation, antimalarial drugs may be started soon after surgery" (Gordon and Alimuddin, 2008). Some surgical centers in malaria-endemic areas recommend routine antimalarial chemoprophylaxis for patients undergoing surgery (Gibney, 1990). The problem of post-

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operative malaria is of clinical importance; in previous studies from Cambodia we reported that more than one third of trauma victims living along the Thai-Cambodian border developed postoperative symptomatic malaria, the prevalence increasing with increasing injury severity (Husum *et al*, 2002). The complication adds to the burden of disease; we found that post-injury malaria enhances the risk for bacterial wound infections and prolongs recovery after surgery (Sundet *et al*, 2004; Heger *et al*, 2005). The problem of post-injury malaria is of global importance; the communities in Latin America, Africa and Asia hardest struck by local wars, land mines, and natural disasters also host the falciparum parasite. As many as 85% of the Southeast Asian population of 1,200 million people are cohabitants with the parasite, 35% of them are estimated to live in moderate to high-risk areas (WHO, 2003).

Persons living in areas where *Plasmodium falciparum* malaria is highly endemic acquire natural immunity. However, the acquired immunity is rarely, if ever, sterile; immune individuals living in highly endemic areas without symptomatic disease almost always have low-grade blood parasitemia. The immunity is thus a protection against symptoms but not against the parasite itself. T cells play a crucial role in both induction and maintenance of this immunity. CD8 + T cells are the principal effector cells against pre-erytrocytic stages of malaria parasites, and an increase in the capacity to produce *P. falciparum*-specific and non-specific INF-gamma appear to be the main cellular correlates of naturally acquired immunity (Troye-Blomberg *et al*, 1994; Stevenson *et al*, 1995; Doolan and Martinez-Alier 2006; Schofield and Mueller, 2006). Trauma, hemorrhage, and surgery affect inflammatory mediators and cause immunodepression with risk for bacterial infections due to impairment in cell-mediated immunity. This causes us to consider if post-traumatic immunodepression also causes susceptibility to malaria infection in asymptomatic parasite carriers.

Trauma and surgery result in impaired cellular immunity with the result of aTH1/TH2 shift with down-regulation of the pro-inflammatory cytokine INF-gamma and up regulation of IL-10. IL-10 has been shown to suppress protective immunity against malaria. IL-12-induced protection against blood-stage parasites requires INF-gamma. Induction of a strong TH2 response early in the infection may result in a severe or even lethal outcome to the malaria infection (Faist *et al*, 1996; Menger and Vollmar, 2004). One could postulate that the immune response to malaria is impaired due to the TH1/TH2 shift, and this may be a reason why asymptomatic malaria infected patients are at risk for developing symptomatic post-injury malaria.

Down-regulation of the immune response is initiated within hours of injury. One would think injured asymptomatically malaria infected patients would benefit from early antimalarial treatment, especially in scenarios where prehospital transit times are long. Dipstick rapid-tests for falciparum malaria make it possible to identify those infected with the malaria parasite early. However, the sensitivity and specificity of the dipstick tests in trauma patients remains to be investigated.

The primary aim of the trial was to study the effect of early in the field diagnosis and treatment of injured *P. falciparum* asymptomatically infected patients using the rate of postoperative symptomatic malaria as the main outcome. The second study aim was to examine the diagnostic validity and accuracy of a dipstick test for in the field *P. falciparum* identification.

MATERIAL AND METHODS

This was an open, non-randomized,

interventional multi-center cohort study which began in May 2002 and concluded in October 2005.

Study population

The study area was located in the most land mine infested part of Cambodia with a high incidence of land mine injuries and road traffic accidents (Fig 1). The study area has previously reported a high prevalence of *P. falciparum* infection (Husum *et al*, 2002) although rates have decreased over the past five years. Trauma paramedics operate in a local trauma system, the Trauma Care Foundation (TCF), and provide early in-field life support before evacuating trauma victims to rural district hospitals for primary trauma surgery. Patients with light injuries not needing hospital admission, female patients during the first trimester of pregnancy, patients with known liver disease, patients evacuated to hospitals outside Battambang Province and patients treated recently with quinine within 24 hours were excluded from the study but those treated with antimalarials more than 24 hours previously were not excluded.

Test and treatment

Paracheck Pf® (dipstick test, Orchid Biomedical Systems) is a rapid self performing, qualitative, two-site sandwich immunoassay for determination of *P. falciparum* specific histidine rich protein -2 (Pf HRP-2) in whole blood samples. PfHRP-2 is a water soluble protein released from parasitized erythrocytes of infected individuals and is assumed to be specific to *P. falciparum*. Initial antimalarial treatment was given according to Cambodian national standards (WHO, 1990). One initial dose of Artemeter or artesunate 3.2 mg/kg was given as a single intravenous injection to all test-positive study patients as soon as possible after injury, preferably before surgery. Further in-hospital treatment of *P. falciparum* infected patients consisted of two doses of Artemeter 1.6 mg/kg followed by a single oral dose of mefloquine 20 mg/kg. In patients with postoperative symptomatic malaria infection further treatment was given according to the Cambodia national guidelines (WHO, 1990). Fake antimalarial drugs have been reported in Southeast Asia (Rozendaal and Thy, 1999). The pharmacological composition of random artemisin samples used in the study was therefore determined at the University Hospital North Norway. This analysis confirmed molecule mass and concentration of racemic artemeter according to specifications given by the producer. The paramedic providing immediate life support at first encounter, during evacuation and in the hospital emergency room, when the patient was initially stabilized performed the dipstick test and gave immediate antimalarial treatment to all test-positive patients. Blood smears of all trauma patients were taken on hospital admission. In patients developing symptomatic post-injury malaria, smears were also taken during the course of treatment.

Variables and data gathering

The main outcome variable in the study was post-injury malaria infection defined as a positive blood smear for malaria and fever in a trauma patient. Cases with post-injury malaria infection were further classified as either non-complicated or severe in accordance with classification criteria in the WHO guidelines (WHO, 1990). Demographic factors, diagnosis, life support procedures, and time factors were registered by the medics providing care (Fig 2). The physiological severity score (PSS) similar to the Revised Trauma Score (Champion *et al*, 1990) was registered at the first medic encounter in the field and again on hospital admission. The difference in PSS ratings (△ PSS) was used as an indicator for prehospital treatment effect (Table 1). The Injury Severity Score (ISS) was used to classify the anatomi-

Table 1
Physiological Severity Score (PSS) as a function of physiological indicators.

	Respiratory rate/minute		Level of consciousness		Systolic blood pressure (mmHg)	
Rating	4	10-29	4	13-15	4	>89
	3	>29	3	9-12	3	76-89
	2	6-9	2	6-8	2	50-75
	1	1-5	1	4-5	1	1-49
Conversion factor	0.2908		0.9369		0.7326	
PSS	1.1632		3.7476		2.9304	
	0.8724		2.8107		2.1978	
	0.5816		1.8738		1.4652	
	0.2908		0.9369		0.7326	

cal injury severity (Association for the Advancement of Automotive Medicine, 1998). The hospital staff registered outcome variables, previous history of malaria, hemoglobin on admission, duration of surgical operations, volume of blood transfused, and nutritional status based on clinical assessment (Fig 2). Cases with positive blood smears and hyperpyrexia (≥40.0ºC) were classified as having severe malaria (http://www.biomedcentral.com/content/pdf/cc2183.pdf; http://www.medal.org/visitor/www%5CActive%5Cch24%5Cch24.01%5Cch24.01.07.asp). The study data were collected and validated monthly by the study supervisor (SCH). All data were translated to English by experienced Khmer medical staff.

Statistical analysis

Assumed continuously distributed variables are expressed by mean values with 95% confidence intervals (95%CI) constructed by the Student procedure (Kleinbaum, 1997). Variables of time-to-event type are expressed by Kaplan-Meier plots (Agresti, 2002). Categorical data are expressed in contingency tables. Prevalences and proportions are given in percentages with 95% confidence intervals constructed by the Bernoulli procedure (Kleinbaum *et al*, 1998). Kappa estimates (κ) with 95 % confidence intervals were used to measure the agreement between methods of discrete recording. Comparison of groups based on continuous variables was performed using Analysis of Variance. Contingency table analysis was used for comparison of groups regarding categorical data. All comparisons of groups were performed two-tailed, differences were considered significant if $p<0.05$.

Ethical considerations

According to Cambodian national standards all patients with confirmed falciparum parasitemia immediately treated with antimalarials. For this reason the study was not designed as a randomized controlled trial. The study protocol was approved by the National Malaria Center in Phnom Penh and all data processed according to permission from the Norwegian Social Science Data Service (ref no. 13702).

RESULTS

The total study sample consisted of 32 women and 190 men, with a mean age of 27.5 years (range 2 - 64 years). Of these patients, 30 were falciparum dipstick test-positive. Two patients were excluded because

Table 2
Comparison of subsamples (means and rates expressed with 95% confidence intervals).

	Factors and variables	Dipstick test		Post-injury malaria	
		Negative (n = 80)	Positive (n = 28)	Negative (n = 4)	Positive (n = 21)
Factors	Gender (% male)	85 (75 - 92)	93 (77 - 99)	75 (19 - 99)	95 (76 - 100)
	Nutritional status (% malnutrition)	2.5 (1 - 9)	11 (2 - 28)	0 (0 - 60)	10 (1 - 30)
	Previous symptomatic malaria (%)	12 (5 - 22)	56 (34 - 76)	75 (19 - 99)	47 (25 - 71)
	Age (years)	31 (28 - 33)	31 (27 - 35)	34 (15 - 52)	30 (25 - 35)
	Positive blood smear (%)	0 (0 - 7)	92 (74 - 99)	50 (7 - 93)	100 (84 - 100)
	Low parasitemia (%)	[a]	52 (31 - 73)	100 (16 - 100)	48 (26 - 70)
Outcome variables	Wound infection (%)	12 (5 - 22)	43 (25 - 63)	0 (0 - 60)	52 (30 - 74)
	Duration of hospital stay (days)	11 (10 - 13)	13 (10 - 16)	10 ([a])	14 (11 - 17)
	Fever (%)	21 (13 - 33)	89 (72 - 98)	50 ([a])	100 (84 - 100)
	Parasite clearance (days)	[a]	5 (4 - 6)	5 ([a])	5 (3 - 6)
Explanatory variables	Time injury - first aid (hours)	1.5 (1.2 - 1.9)	1.0 (0.7 - 1.5)	1.3 (0 - 8.0)	1.0 (0.6 - 1.4)
	Total prehospital transport time (hours)	1.7 (1.4 - 2.1)	1.3 (0.9 - 1.7)	1.5 (0 - 14.2)	1.2 (0.8 - 1.6)
	Injury severity score	6.4 (5.4 - 7.4)	8.3 (6.5 - 10.1)	6.3 (0 - 16.9)	8.9 (6.9 - 10.8)
	Delay in antimalarial treatment (hours)	[a]	[a]	2.3 (0 - 4.5)	2.7 (2 - 4.1)
	Physiological severity in-field	11.0 (10.7 - 11.2)	10.2 (9.7 - 10.8)	10.8 (9.3 - 12.0)	10.0 (9.4 - 10.7)
	Physiological severity on admission	11.7 (11.5 - 11.8)	11.3 (11.0 - 11.6)	11.8 (10.9 - 12.0)	11.1 (10.9 - 12.0)
	Hemoglobin hospital admission (g/100 ml)	9.9 (9.2 - 10.6)	7.9 (7.0 - 8.9)	7.7 (2.5 - 12.8)	8.2 (7.2 - 9.0)
	Received blood transfusion (%)	8 (3 - 11)	19 (6 - 38)	33 (1 - 90)	19 (6 - 42)
	Underwent surgery (%)	83 (72 - 90)	93 (77 - 99)	100 (40 - 100)	96 (76 - 100)
	Duration of surgical operation (hours)	1.7 (3.0 - 6.6)	2.0 (1.7 - 2.3)	2.1 (0.8 - 3.5)	2.0 (1.7 - 2.4)

[a]Insufficient number of observations for statistical analysis

Table 3
Diagnostic accuracy of the dipstick test.

Criterion	Material	Classification	Study patients dipstick test		Study patients (total)	Kappa with 95% CI
			Negative	Positive		
Blood smear	Total sample	Negative	89	3	92	
		Positive	0	24	24	92.5 (84.5 - 100)
		Missing data	103	3	106	
		Sum	192	30	222	
	Pailin subsample	Negative	51	2	53	
		Positive	0	23	23	93.9 (85.5 - 100)
		Missing data	29	3	32	
		Sum	80	28	108	
Blood smear +Fever	Total sample	Negative	72	5	77	
		Positive	0	21	21	86.1 (74.1 - 98.1)
		Missing data	120	4	124	
		Sum	192	30	222	
	Pailin subsample	Negative	34	4	38	
		Positive	0	21	21	85.8 (71.8 - 99.8)
		Missing data	46	3	49	
		Sum	80	28	108	

they died from the trauma before data could be gathered. No patients were excluded due to pregnancy or liver disease. *P. vivax* was detected on blood smear in one patient who developed post-injury malaria; this patient was excluded from the study. Except for two cases, all *P. falciparum* positive patients came from Pailin District (Fig 1). The Pailin subsample (n = 108) was used for analysis of the main study question. The subsample consisted of 14 women and 94 men, with a mean age of 30.8 years (SD 10.7). Of the 108 patients, 28 were dipstick-positive. Eighty-eight patients in the Pailin sample were injured in land mine accidents and 20 were injured in other events. The mean ISS was 6.9 (SD 4.5), with a range from 1 to 25. The mean time from injury to first aid was 2.6 hours (95% CI 1.4 - 3.8) and the mean duration of surgical operation was 2.1 hours (SD 0.6). All patients with a positive dip stick test received antimalarial treatment, the initial treatment being provided at a mean of 1.4 hours after the accident.

Outcome indicators

Parasites were identified by microscopy in 23 of the 28 dipstick-positive patients. Twenty-one of these patients had fever on the first postoperative day, and were classified as having symptomatic post-injury malaria (Table 2). In the dipstick-negative group (n = 78), 51 patients had a blood smear examined, all of them were negative for *P. falciparum*. Of the patients with symptomatic post-injury malaria, 52% had moderate to high parasitemia. Eight malaria patients were classified as having severe malaria indicated by hyperpyrexia above 40ºC. The prevalence and duration of fever was significantly greater in the dipstick-positive group (Table 2). The mean duration of fever

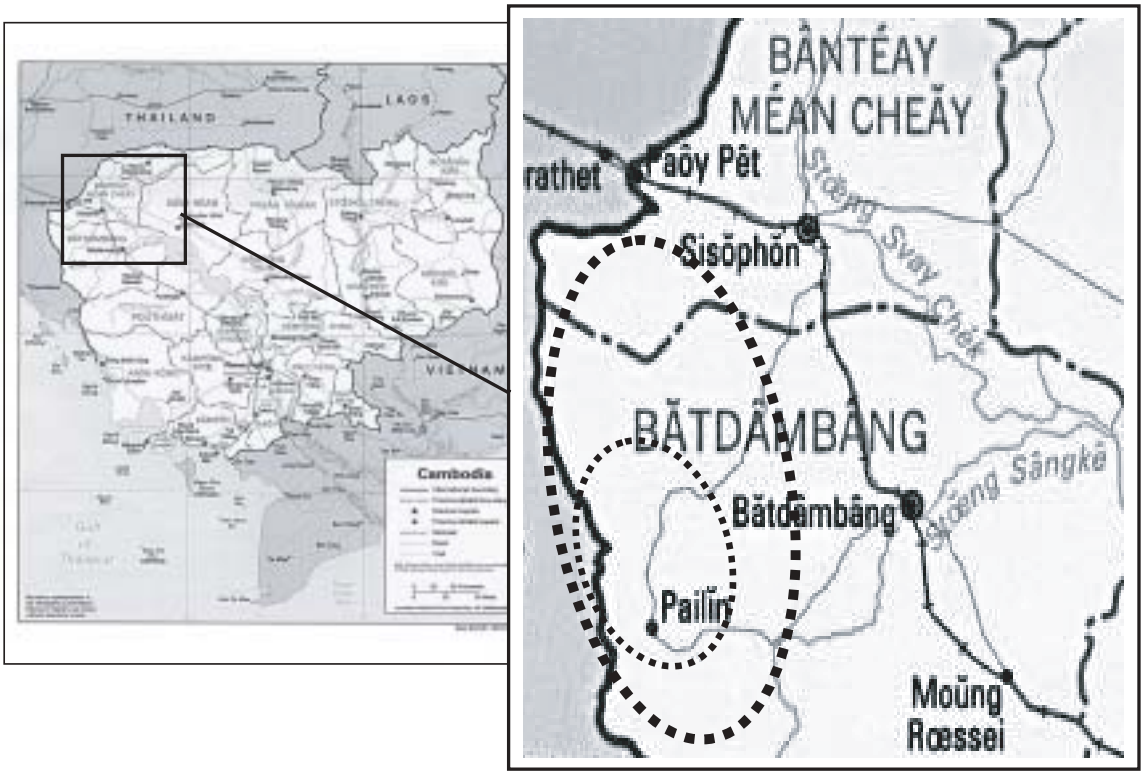

Fig 1–The study area in northwestern Cambodia.

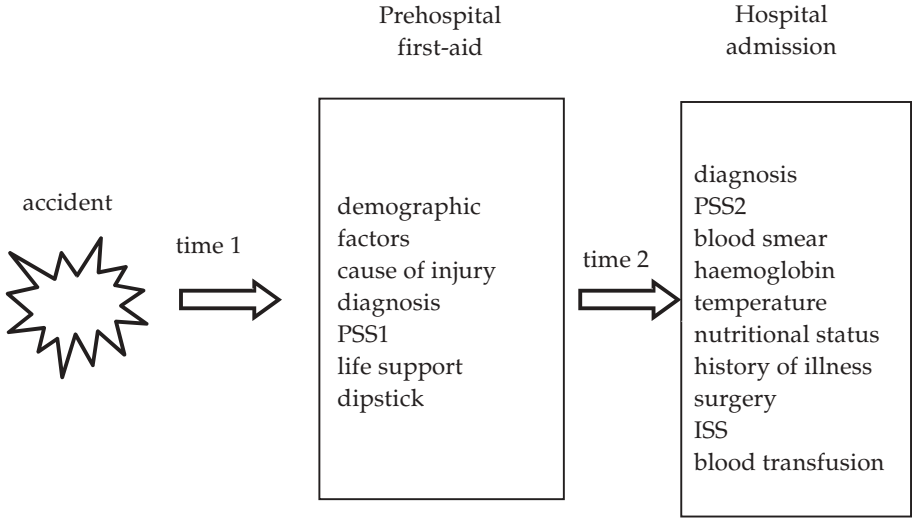

Fig 2–Data-gathering flow chart.

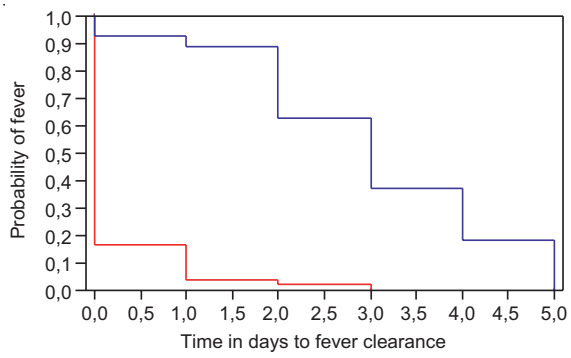

Fig 3–Comparison of dipstick categories for fever clearance. The results are expressed by Kaplan and Meier plots.

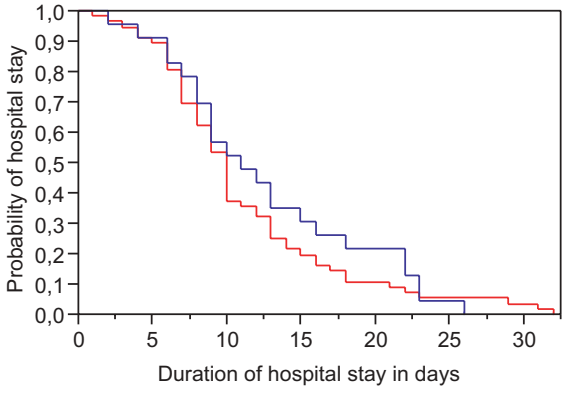

Fig 4–Comparison of dipstick categories for duration of hospital stay. The results are expressed by Kaplan and Meier plots.

among dipstick-positive patients was three days; no patients had a fever for more than five days (Fig 3).

No significant difference was found in the duration of hospital stay between test-positive and test-negative cases. Comparing duration of in-hospital stay, the two groups were nearly identical up to ten days of hospital stay; for longer in-hospital times there was a difference in the pattern of the probability curves indicating the dipstick-positives tended to stay longer in the hospital than the dipstick-negative patients (Fig 4).

Bacterial wound infection was detected in 20 patients. The rate of wound infection was higher in patients with post-injury symptomatic malaria ($p = 0.1$). Patients with bacterial wound infection had significantly longer hospital stays and durations of fever (Table 2). Agreement analysis was applied to check for misclassifications between post-injury malaria and wound infection. There was a significant positive agreement between wound infection and post-injury malaria when comparing the group with post-injury malaria ($n = 21$) with the rest of the study sample ($n = 87$) ($\kappa = 0.5$; 95% CI 0.2 - 0.7). The agreement was also significant between wound infection and positive dipstick result ($\kappa = 0.34$; 95% CI 0.14 - 0.50) and between wound infection and post-injury malaria when comparing the post-injury malaria group ($n = 21$) with the rest of the dipstick-positive group ($n = 4$) ($\kappa = 0.26$; 95% CI 0.02 - 0.50).

Variables affecting the outcome

Of the assumed explanatory variables, the hemoglobin level, systolic blood pressure and level of consciousness at first in-field encounter, Δ PSS, and duration of prehospital care explained 42% of the variation in the dipstick test results. The proportion of patients that had malaria in their previous medical history was higher among the dipstick-positive patients compared with the dipstick-negative group (Table 2). The prevalence of malnutrition was higher in the dipstick-positive group, but the difference was not significant. Patients in the dipstick-positive group were more severely injured as measured by their physiological indicators. The anatomical severity score was significantly higher and hemoglobin levels on hospital admission significantly lower in the dipstick-positive patients. No other significant differences were detected between the two groups. Comparison of dipstick-positive

patients with and without post-injury malaria demonstrated the patients developing symptomatic malaria were more severely injured. The post-injury malaria group had a lower prevalence of previous malaria infections but the difference was not significant ($p = 0.1$).

Validity and accuracy of dipstick test

Blood smears were collected in 116 patients from the total sample and in 76 from the Pailin subset (Table 3). In both samples the agreement between the dipstick test and the blood smears was very good. Using blood smear microscopy as a reference test, the sensitivity of the dipstick test was 100% in both samples; the specificity was 96.7% (95%CI 90.8 - 99.3) in the total sample and 96.2% (95%CI 87.0 - 99.5) in the Pailin subset. Two patients with a positive dipstick test result and a negative blood smear had recently been treated for malaria. The agreement between post-injury malaria and the dipstick-test was also very good (Table 3). Measured against clinically defined post-injury malaria the dipstick test specificity was 100% and sensitivity 94.7% (95%CI 7.1 - 98.6) in the total study sample, and 89.5% (95%CI 90.8 - 99.3) in the Pailin subset.

DISCUSSION

The main aim of the intervention was to prevent symptomatic post-injury malaria in injured falciparum infected patients by early antimalarial treatment. By giving prehospital antimalarial treatment to all parasite carriers, one would expect very few parasite carriers would develop post-injury malaria. One would further expect the parasite carriers would have the same outcome when it comes to morbidity factors, such as fever, wound infection and recovery. However, according to the definition given in this study, most parasite carriers among the study patients did develop post-injury malaria and had high postoperative morbidity. On the other hand, it was found the malaria infected patients had more severe injuries with higher physiological impact, had lower hemoglobin levels and a higher prevalence of malnutrition. This could explain the increased morbidity. Antimalarial treatment would not affect these variables. Even if the lack of direct treatment effect was surprisingly low, we do not know if the malaria infected patients would have been worse off without early treatment. The local medical teams participating in the study were not disappointed by the seemingly poor treatment effect; they considered it to be normal for injured malaria infected patients to have fever for a few days during treatment, and held that the reappearance of parasitemia might have been more severe and prolonged without early antimalarial treatment.

Still, the lack of firm antimalarial treatment effect raises several queries. The diagnosis of post-injury malaria is not straightforward and there is a risk that post-injury malaria may have been over-diagnosed, thus obscuring the treatment effect. In a study in Sri Lanka only 19% of patients given the tentative diagnosis of malaria on clinical grounds in fact had positive blood films for parasites. There were no important differences in signs and symptoms between those with positive and those with negative blood films (Van der Hoek *et al*, 1998). Postoperative fever in a dipstick-positive patient may well be caused by other conditions, such as wound hematoma, wound infection, respiratory tract infection, or the trauma itself. Diagnostic microscopy may have limited clinical significance: detection of parasites in a blood film from a febrile patient does not necessarily indicate clinically symptomatic malaria (Trape, 1985; Smith *et al*, 1994).

The study did not include mapping of

clinical signs of malaria infection prior to injury. Some study patients classified as post-injury malaria may have had symptoms at the time of injury. We believe the number of such patients was small because most study patients were injured by landmines while working the rice fields or in the forest. It is unlikely a person suffering from symptomatic falciparum malaria would be capable of heavy physical efforts.

The study shows a significant positive agreement between wound-infection and post-injury malaria, when comparing the wound-infection group to the total study sample, and comparing the group to the patients in the dipstick positive group who did not develop post-injury malaria. These results indicate there might have been misclassification between post-injury malaria and wound infection. Study patients defined as having post-injury malaria might have had another cause for their fever, such as bacterial wound infection.

Various parasite clearance times are reported in clinical trials for artesunate and artemisin, from 24 hours to 60 hours (Alin *et al*, 1995; Krudsood *et al*, 2003). During this time period malaria symptoms may develop even if the patients had the drug administered within three hours of injury. We cannot rule out inadequate blood concentrations of the active drug which may have contributed to treatment failure. Some study patients, contrary to protocol, had the artemisin administered by intramuscular route; in hypotensive trauma patients the absorption of intramuscular drugs may be slow. A recent Vietnamese study documents delayed uptake of intramuscular Artemeter in patients with severe malaria (Hien *et al* 2004). Another uncontrolled variable is time of treatment. A few malaria infected patients (n = 5/28) did not get the first dose of antimalarial until after the operation because the patient was in need of urgent surgical care. In these cases, the stress of surgery would probably add to the stress caused by the trauma, increasing immune depression and risk of post-injury malaria.

The poor treatment outcome observed in the study may have been real, caused by resistant strains of *P. falciparum*. Since 2003, evidence has been accumulating that artemisin-based combination therapy is becoming less effective in the treatment of falciparum malaria along the Thai-Cambodian border, probably due to local emergence of parasite strains resistant to artemisin-based derivatives. Interim data from Pailin confirm parasites have emerged which exhibit prolonged clearance times during treatment with artesunate as single drug and also artesunate-mefloquine combinations (WHO, 2008). The fact that patients recently treated with antimalarials were included in the study may have affected the study outcome, especially those recently treated with mefloquine, since the elimination half-life of that drug is as long as three weeks. These patients would have supplementary antimalarial protection, mefloquine plus artesunate. The fact that almost all malaria infected patients did developed post-injury malaria indicates any mefloquine effect must have been small or absent.

We should also consider whether malaria parasites could have been transmitted by post-injury blood transfusion in the study patients. A study from Africa shows that 33.5% of blood donors harbored malaria trophozoites (Gazard *et al*, 2000). However, the pattern of early postoperative signs of symptomatic malaria and the agreement between dipstick test-positives and verified post-injury malaria makes transfusion transmission unlikely in the study.

HIV is another uncontrolled variable with obvious impact on immune responses.

The study patients were not screened for HIV infection even though the prevalence of HIV is high in the study area. HIV-1 infection is associated with an increased frequency of clinical malaria and parasitemia. HIV-infected persons appear to have more severe and complicated malaria (Whitworth *et al* 2000).

The study found that the dipstick test performed with reasonable accuracy in populations with low and high prevalences of falciparum malaria. However, the confidence intervals in the dipstick tests are relatively wide, since many patients were excluded due to invalid or missing data (Table 3). This reflects the challenge of gathering solid scientific data in facilities where a tradition of medical documentation is not well established. Other studies of the rapid test report high test sensitivity, although with larger variations in specificity. False-positive test results are reported in patients recently treated for malaria (Mboera *et al*,2006; Swarthout *et al*, 2007). Smear microscopy is time-consuming and may delay trauma intervention. The diagnostic accuracy of microscopy may vary, even in trained hands (Hemme and Gay, 1998; Coleman *et al* 2002). In areas where the quality of health worker training is suboptimal it seems reasonable to recommend the rapid test as the diagnostic tool of choice in emergency care. At a cost of one US dollar per patient the rapid test is a feasible tool for in-field and emergency room identification of non-symptomatic malaria infected patients.

In conclusion, post-injury malaria is a clinically significant problem in trauma patients in falciparum malaria endemic areas of northwestern Cambodia. *P. falciparum* parasitemia is a risk factor for postoperative complications in trauma patients. Early identification of asymptomatic parasite carriers by rapid test should be a part of trauma care where *P. falciparum* is endemic. Despite early treatment with antimalarials it is difficult to prevent post-injury symptomatic falciparum malaria infection. Due to a lack of case-controls we could not determine if the intervention had some effect; post-injury malaria could have been more severe and protracted without early antimalarials. It is a pharmacological characteristic of artemisin that parasite clearance is relatively slow. The preventive effect of early preoperative antimalarials may have been greater in scenarios with protracted evacuations. Trials of prehospital antimalarial treatment with larger cohorts in rural trauma with long transport times should be carried out.

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