Compliance with artesunate and quinine + tetracycline treatment of uncomplicated falciparum malaria in Thailand

W. Fungladda,[1] E.R. Honrado,[2] K. Thimasarn,[3] D. Kitayaporn,[1] J. Karbwang,[4] P. Kamolratanakul,[5] & R. Masngammueng[6]

A randomized, controlled, malaria-clinic-based field trial was conducted to compare compliance with a 7-day quinine + tetracycline regimen and a 5-day 700-mg artesunate regimen for the treatment of uncomplicated falciparum malaria in a community in Thailand. Of 137 patients, aged 15–60 years attending a malaria clinic, 77 received artesunate and 60 received quinine + tetracycline. Compliance and cure rates were evaluated on days 5 (artesunate) and 7 (quinine + tetracycline) using patient interview/residual pill counts and peripheral blood smear, respectively. Data were analysed using the intention-to-treat approach, and the reasons for compliance and noncompliance were investigated.

Compliance was significantly higher (98.4%) with artesunate than with quinine + tetracycline (71.7%) (relative risk adjusted for sex (aRR) = 1.39 (95% C.I. = 1.15–1.68); referent: quinine + tetracycline). Cure rate (100%) was higher in those receiving artesunate than quinine + tetracycline (77.4%) (aRR = 1.32 (95% C.I. = 1.12–1.55)). Reasons for compliance included the desire to be cured and to follow the advice of malaria staff/employer, and the simple dosing regimen. Noncompliance was mostly due to adverse reactions and forgetting to take the drugs.

These results can serve as a baseline for designing and evaluating new interventions to improve compliance, as well as for studying cost-effectiveness to help drug policy decision-making. We recommend a strategy which integrates a short-course, once-a-day regimen (with minimal adverse reactions), a better delivery system for antimalarial drugs and health education, and an enhanced advisory role of malaria staff. Considering the higher compliance rate and curative effectiveness of artesunate, we recommend its use instead of quinine + tetracycline for the treatment of uncomplicated malaria in clinics in Thailand.

Introduction

Multidrug resistance of *Plasmodium falciparum* to currently available antimalarial drugs, which has been one of the main obstacles to control of malaria in Thailand, continues to be a major public health problem in the country (*1*). Drug pressure, resulting from subcurative dosing due to noncompliance, is the principal causative factor for multidrug-resistant falciparum malaria (*2*). Efforts to prevent deterioration of this problem are, therefore, at present directed towards finding novel ways of intervening to improve compliance and prevent the irrational use of currently available multidose antimalarial drugs. However, before strategies to augment compliance can be devised and implemented, baseline data on the prevailing compliance level with these drugs when used in the community, as well as the reasons for compliance/noncompliance, must first be established. So far, these data are not available. Although the quinine–tetracycline combination is well known (*3*, *4*) for poor compliance when used for home treatment, there has never been a report to quantify this. These data could serve as a baseline for designing innovative control measures and for evaluating their effectiveness.

Data on compliance with antimalarial drugs in the community can also be used for cost-effectiveness analysis studies to guide decisions on drug policies. For countries where resources are scarce, drug policy-makers would certainly like to find answers to

[1] Associate Professor, Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

[2] Associate Professor, Cebu Doctors' College of Medicine, Cebu City, Philippines.

[3] Director, Malaria Division, Ministry of Public Health, Thailand.

[4] Professor, Department of Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

[5] Professor, Department of Preventive and Social Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

[6] Researcher, Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

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the following question: "What is the financial loss to the malaria control programme due to drugs that are given for therapeutic cure, but are not ingested?"

This study was, therefore, conducted to (1) compare the compliances with the currently used standard 7-day quinine + tetracycline regimen and the 5-day 700-mg oral artesunate regimen for treatment of uncomplicated falciparum malaria in a malaria clinic in Thailand, and (2) to determine the reasons for compliance/noncompliance.

Materials and methods

Study area. The study was conducted from October 1994 to August 1995 in a malaria clinic in Tabsai Subdistrict, Pong Nam Ron District of Chanthaburi Province, eastern Thailand. The study area lies along the Thai–Cambodian border, which is a known epicentre for multidrug-resistant falciparum malaria in the country (*4*). In Thailand, the malaria clinics are part of the epidemiological early-warning system for malaria, accounting for more than 60% of the malaria cases reported by the Malaria Control Programme. They have played a major role in reducing mortality and limiting transmission by early case detection and treatment (*2, 5, 6*).

Study population. Patients, aged 15–60 years who attended the Tabsai malaria clinic and were found to have slide-confirmed (thick film, Giemsa stained) uncomplicated falciparum malaria (*7, 8*), were recruited into the study. Pregnant women, patients with manifestations of severe or complicated malaria, and those with a history of renal and/or hepatic disease, allergy to artesunate, quinine or tetracycline were excluded.

Sample size. The sample size was calculated using the Epi Info version 5.01b assuming 65% compliance in the quinine + tetracycline group and 95% in the artesunate group, with a two-tailed significance level at 5% probability and power of 80% (*9*). A 20% contingency for losses to follow-up (*10*) was added. Since compliance with these two drugs in the field was not known, the assumptions on the compliance rates were based on the use of adverse reactions, particularly tinnitus, as the surrogate index for compliance and on expert opinion (Thimasarn, 1994). A hospital-based study (*11*) comparing the two regimens revealed that there was an 88% difference ($P < 0.05$) in the occurrence of tinnitus between the two drugs. For this study, we allowed for a 30% difference in the rate of compliance between the two regimens as already used in the community.

This study was approved by the Ethical Review Committee of the Ministry of Public Health of Thailand.

Study design

After written, free and informed consents were obtained from patients who were eligible for the study, the subjects were randomly allocated (simple randomization) into two treatment groups. Group I received artesunate orally for 5 days, while Group II received quinine + tetracycline for 7 days. The full course of the respective drugs was placed in one packet and given to patients to take home (following the standard practice of the Malaria Control Programme in the malaria clinics). Structured questionnaire-interviews were used to extract data on the sociodemographic profile of the study population.

Patients in the artesunate group were asked to take six tablets (50mg/tablet) while still in the malaria clinic (i.e., day 0) and instructed to take two tablets (100 mg) after breakfast, as a single dose daily, at home from day 1 to day 4. Those in the quinine + tetracycline group were also requested to take the first doses of two quinine tablets (300mg/tablet) and two capsules of tetracycline (250mg/capsule) while still in the clinic and advised to take the prescribed subsequent doses (i.e., two tablets of quinine three times a day after meals and two capsules of tetracycline two times a day after meals) from day 1 to day 6 at home. Patients were followed up on day 5 (artesunate group) and day 7 (quinine + tetracycline group) to assess their compliance, using patient interviews and residual pill counts. Compliance was defined as: adherence to the protocol or not missing a single dose of the prescribed treatment, as reported by interview, or absence of residual pills on follow-up visit to the malaria clinic.

Curative effectiveness was evaluated by the results of the peripheral blood smear (either positive or negative for *P. falciparum*) on day 5 (artesunate) and day 7 (quinine + tetracycline). We used the day-5/day-7 cure rate as the index of curative effectiveness (instead of day 28) because, in community trials conducted in endemic areas, the interpretation of positive results of blood smears obtained on day 28 would have to differentiate between a reinfection and a recrudescence. Moreover, the marked attrition of study subjects (i.e., 30% or more) due to absence in follow-up would cast serious doubts on the validity of the results on day 28 (*12*).

Data analysis

Epi Info version 5.01b was used for data entry and analysis (*9*). To further reduce bias from losses to

follow-up, compliance rates were analysed using the intention-to-treat approach assuming best ("compliant") and worst ("not compliant") outcomes for those lost to follow-up (*12–14*). Cure rates were analysed in the same manner. The χ^2-test for two independent proportions or Fisher's exact test was used, whenever appropriate, to compare the data (*15*). Differences in means and medians were tested using Student's *t*-test and Kruskal–Wallis test (*16*), while adjusted relative risks (aRR) were tested using the Mantel–Haenszel test (*12*).

Results

Sociodemographic characteristics of the study population

A total of 137 patients were recruited into the study, with 60 allocated to the quinine + tetracycline regimen (control) and 77 to artesunate. The subjects in both groups were comparable in their sociodemographic characteristics ($P > 0.10$ for any variable) (Table 1), except for sex distribution where a significantly greater proportion of males than females was included in the quinine + tetracycline group than in the artesunate group ($P = 0.002$). Of the 137 subjects who were initially enrolled, 114 (83.2%) came back for follow-up within the first week, with no significant difference in the loss to follow-up between the two groups ($P > 0.05$): 11.7% on day 7 for the quinine + tetracycline regimen, and 20.8% on day 5 for the artesunate group. The baseline profile of those who were lost to follow-up was comparable with those who returned ($P > 0.3$), except with regard to place of residence and occupation ($P < 0.0005$). The majority (52.2%) of those who did not come back for follow-up were from districts other than Pong Nam Ron District or districts outside Chanthaburi Province. A significantly higher proportion (84%) of patients who remained were indigenous residents of the study area ($P = 0.0004$). Most (74%) of those who were lost to follow-up were working in the logging industry, and no one was

Table 1: **Sociodemographic characteristics of the study population (quinine + tetracycline group vs. artesunate group)**

Variable	Quinine + tetracycline group ($n = 60$)	Artesunate group ($n = 77$)	*P*-value
Age (years):			
Mean ± S.D.	31.9 ± 11.5	30.8 ± 9.4	0.52[a]
Sex:			
No. of males	59 (98.3)[b]	61 (79.2)	0.002[c]
No. of females	1 (1.7)	16 (20.8)	
Marital status:			
Married	33 (55.0)	48 (62.3)	0.49[d]
Others	29 (45.0)	29 (37.7)	
Residence:			
Pong Nam Ron	48 (80.0)	59 (76.6)	0.66[d]
Other districts in Chanthaburi	5 (8.3)	5 (6.5)	
Districts outside Chanthaburi	7 (11.7)	13 (16.9)	
Occupation:			
Agriculture	20 (33.3)	21 (27.3)	0.33[d]
Logging	19 (31.7)	34 (44.1)	
Others	21 (35.0)	22 (28.6)	
Monthly family income (in baht):			
Median	3550	4080	0.245[e]
p25	2500	2500	
p75	5100	7000	
Education:			
<Primary school	4 (6.7)	11 (14.3)	0.18[d]
Primary school	47 (78.3)	60 (77.9)	
≥Secondary school	9 (15.0)	6 (7.8)	

[a] Student's *t*-test.
[b] Figures in parentheses are percentages.
[c] Fisher's exact test.
[d] χ^2 test.
[e] Kruskal–Wallis test.

Table 2: **Comparison of compliance with artesunate (Art) and quinine + tetracycline (QT) treatment (1) among those who stayed in the study, (2) assuming those "lost" to follow-up were compliant ("best" case), and (3) assuming those "lost" to follow-up were noncompliant ("worst" case)**

Treatment group	Number compliant	Number noncompliant	aRR[a]	95% C.I.	*P*-value[b]
Stayed in the study:					
Art	60 (98.4)[c]	1 (1.6)	1.39	1.15–1.68	0.0003
QT	38 (71.7)	15 (28.3)	1.00[d]		
			Crude RR: 1.37		
Assuming "lost" were compliant:					
Art	76 (98.7)	1 (1.3)	1.33	1.13–1.56	0.0001
QT	45 (75.0)	15 (25.0)	1.00[d]		
			Crude RR: 1.32		
Assuming "lost" were noncompliant:					
Art	60 (77.9)	17 (22.1)	1.19	0.93–1.53	0.21
QT	38 (63.3)	22 (36.7)	1.00[d]		
			Crude RR: 1.23		

[a] Relative risk adjusted for sex.
[b] χ^2 test (Yates corrected)..
[c] Figures in parentheses are percentages.
[d] Based on QT as referent.

engaged in agriculture. This was in contrast ($P = 0.0002$) to the distribution of the occupation of those who remained in the study, where only 32% were involved in logging and 36% were in agriculture.

Compliance/noncompliance rates

The intention-to-treat approach of analysis assuming "best" and "worst" outcomes for those lost to follow-up (*14*) established the following three categories of compliance rates: (1) compliance rate in those who remained in the study, (2) compliance rate if those lost to follow-up were assumed to be compliant ("best" case), and (3) compliance rate if those lost to follow-up were assumed noncompliant ("worst" case). The two study groups differed significantly in sex distribution (Table 1).

As shown in Table 2, among those who completed the study nearly all the subjects (98.4%) complied with artesunate treatment, compared with only 71.7% with quinine + tetracycline. Those who received artesunate were 39% more likely to be compliant than those treated with quinine + tetracycline (aRR = 1.39 (95% C.I. = 1.15–1.68), referent: quinine + tetracycline, $P = 0.0003$). If those lost to follow-up were assumed to be compliant ("best" case), then the compliance rate for the quinine + tetracycline group would be significantly lower than that of artesunate (75% vs. 98.7%, respectively). Those receiving artesunate had 33% higher probability of being compliant than those given quinine + tetracycline (aRR = 1.33 (95% C.I. = 1.13–1.56), $P = 0.0001$). On the other hand, if the "worst" case were assumed for those lost to follow up, the compliance rate for quinine + tetracycline would be 63.3%, compared with 77.9% for artesunate. The probability for compliance in the artesunate group would be higher by 1.19-fold in the artesunate group than in the quinine + tetracycline group (aRR = 1.19 (95% C.I. = 0.93–1.53)), although this was no longer found to be statistically significant. However, the point estimates of the three "scenarios" did not differ much from each other.

In summary, the balance of evidence suggests that, if assumptions on losses to follow-up were taken into consideration, a significantly higher compliance rate is observed among the artesunate recipients than in those receiving quinine + tetracycline. Patients given artesunate are 19–39% more likely to be compliant than those treated with quinine + tetracycline. The compliance rate for artesunate when it is given in the malaria clinic ranges from 77.9% to 98.7%, while that for quinine + tetracycline ranges from 63.3% to 75%.

Reasons for compliance and noncompliance

The reasons for compliance or noncompliance consisted of one or a combination of the factors listed in Table 3. The most common reason for compliance was the desire to be cured, followed by adherence to the advice given by the malaria staff. Other reasons include heeding the advice of the employer and sim-

Table 3: **Reasons for compliance and noncompliance with the prescribed treatment (artesunate (Art) or quinine + tetracycline (QT)) among the study population**

	No. treated by regimen:		
	QT	Art	Total
Reasons for compliance:[a]			*n* = 98
Advised by employer	0	3	3 (3.1)[b]
Advised by malaria staff	40	30	70 (71.4)
Wanted to be cured	29	46	75 (76.5)
Easy to take	0	2	2 (2.0)
Reasons for noncompliance:			*n* = 16
Adverse reactions	6	0	6 (37.5)
Forgot to take the drugs	4	0	4 (25.0)
Given intravenous fluids by relatives	2	0	2 (12.5)
Others[c]	3	1	4 (25.0)

[a] The reason for compliance was either one or a combination of any one of those listed.
[b] Figures in parentheses are percentages.
[c] Did not adhere to the protocol and residual pill count suggested noncompliance.

plicity of dosing, particularly for the artesunate treatment group.

The major reason for noncompliance was the occurrence of adverse reactions followed by forgetting to take the drug. These were observed only in the quinine + tetracycline treatment group. Stopping oral drug intake because they were given intravenous fluids by their relatives was also another reason for failing to comply with prescribed treatment in the quinine + tetracycline group, but only to a minor degree. Among the artesunate group there was only one patient who did not comply, the reason being his non-adherence to the protocol which was confirmed by the returned pill count.

Curative effectiveness

Table 4 shows that among those who remained in the study, all the subjects who received artesunate were cured by day 5, while a significantly lower proportion (77.4%, $P < 0.05$) of those who received quinine + tetracycline were cleared of the parasites by day 7 (aRR = 1.32 (95% C.I. = 1.12–1.55)). It was revealed that all those who complied with the artesunate regimen and even the patient who was noncompliant (i.e., missed one dose) were cured by day 5 (data not shown). In contrast, only about 79% of those who were compliant and 73% of those who were noncompliant with the quinine + tetracycline regimen were cleared of the parasites by day 7.

If the "best" case were assumed for those lost to follow-up, the cure rate for the quinine + tetracycline group would be significantly lower than that of the artesunate group (80% vs 100%, respectively), with the artesunate recipients being approximately 1.3 times more likely to be cured than the quinine + tetracycline group after controlling for sex (aRR = 1.27 (95% C.I. = 1.10–1.45), $P = 0.0002$). On the other hand, if the "worst" case were assumed for

Table 4: **Comparison of the day-5 cure rate in the artesunate (Art) treatment group and the day-7 cure rate in the quinine + tetracycline (QT) group, with their respective relative risks, (1) among those who stayed in the study, (2) assuming those "lost" to follow-up were cured ("best" case), and (3) assuming those "lost" to follow-up were not cured ("worst" case)**

Treatment group	No. cured	No. not cured	aRR[a]	95% C.I.	*P*-value[b]
Stayed in the study:					
Art	61 (100.0)[c]	0 (0)	1.32	1.12–1.55	0.0004
QT	41 (77.4)	12 (22.6)	1.00[d]		
			Crude RR: 1.29		
Assuming "lost" were cured:					
Art	77 (100.0)	0 (0)	1.27	1.10–1.45	0.0002
QT	48 (80.0)	12 (20.0)	1.00[d]		
			Crude RR: 1.25		
Assuming "lost" were not cured:					
Art	61 (79.2)	16 (20.8)	1.13	0.89–1.42	0.32
QT	41 (68.3)	19 (31.7)	1.00[d]		
			Crude RR: 1.16		

[a] Relative risk adjusted for sex.
[b] χ^2 test (Yates corrected).
[c] Figures in parentheses are percentages.
[d] Based on QT as referent.

those lost to follow-up, the cure rate for quinine + tetracycline would be approximately 68%, while that of artesunate would be about 79%. The probability for cure (after adjusting for sex) would be 1.13-fold higher (95% C.I. = 0.89–1.42) in the artesunate group than the quinine + tetracycline group. This was, however, no longer found to be statistically significant.

The overall results showed that the cure rate of the artesunate regimen ranges from 79.2% to 100%, compared with 68.3% to 77.4% for quinine + tetracycline, if assumptions on losses to follow-up are taken into account. The probability for cure was 13% to 32% higher for artesunate recipients.

Adverse reactions

The rate of occurrence of adverse reactions and the relative risks for their occurrence were significantly lower among those who received artesunate (49%), compared with quinine + tetracycline (80%) (aRR = 0.60 (95% C.I. = 0.44–0.83), referent: quinine + tetracycline). The specific adverse reactions reported by the study population included headache, vomiting, dizziness, diarrhoea, drowsiness, tinnitus and body ache. Among these, the adverse reactions which led to noncompliance were the following: tinnitus (50%), vomiting (16.7%), severe diarrhoea (17%), and "could not tolerate" (16.7%).

Discussion

This is the first study to quantify and compare the compliance rates as well as the relative risks (or more aptly the probability) of compliance with the two antimalarial regimens in Thailand. The observed higher compliance with artesunate bespeaks well of its potential for preventing drug pressure from intake of subtherapeutic doses of the drug and underscores its advantage over quinine + tetracycline in preventing and delaying the spread of the prevailing multidrug resistance problem, particularly along the Thai–Cambodian and Thai–Myanmar borders. This, together with the observed higher curative effectiveness when it is used in the field, has accentuated its promising role as an alternative second-line drug to quinine + tetracycline for the control of multidrug-resistant falciparum malaria in these areas. The finding that more than half of the study subjects who were lost to follow-up were not residents of the study area reflects the mobile characteristics of this population and underscores the advantage of giving short-course drug regimens which would facilitate surveillance for resistance. Data on the ranges of compliance and cure rates of the two drug regimens established by the intention-to-treat method of analysis can be used by drug policy-makers to do sensitivity and cost-effectiveness analyses of various antimalarial regimens. Results of these could then guide the choice of antimalarial drug that will be employed for malaria control.

Although the balance of evidence suggests that the compliance rate and curative effectiveness were significantly higher in the artesunate group, the finding that there was no statistically significant difference between the two regimens in the "worst" case scenarios signals the need for a larger study to obviate any doubt of "no difference" between the two.

A major limitation of this study is the method used for measuring compliance. The returned pill count and/or patient interview method tends to overestimate compliance (*17*) since it relies on history (*18*), the veracity of the patient which is difficult to assess or prove, and the assumption that pills removed from the container were ingested (*19*). As such, it is open to ready manipulation by the patient. Despite this shortcoming it is still the most frequently recommended (*19, 20*) and most widely used method for measuring compliance, particularly for clinical trials (*18*), because it is cheap, not complicated, fast and does not require highly skilled personnel and sophisticated equipment. Moreover, to date there is still no documented, more reliable method (such as the use of a pharmacological marker, e.g. phenobarbital) to assess compliance with short-course regimens such as artesunate in the field. The finding that the probability of being compliant in the artesunate group was only 1.2–1.4-fold higher than that of the quinine + tetracycline group was, admittedly, of less magnitude than we expected. We, therefore, suspect that overestimation of the compliance with quinine + tetracycline (as gathered from patient interview/returned pill count) may well be the case here. Nevertheless, since the method used for measuring compliance was the same for both treatment groups, bias from the method used has been obviated.

The observation that even the patient who did not comply with artesunate was still cleared of the parasite by day 5 emphasizes the higher potential of artesunate for reducing mortality due to severe falciparum malaria or complications and strengthens its advantage over quinine + tetracycline.

The significance of the advice given by malaria clinic staff with regard to patient compliance was highlighted in this study. These efforts should be strengthened through more health education and better motivation of this category of health care provider. Provision of improved quality of advice and better patient–provider interaction should be encouraged. Up-to-date information on the effective-

ness and hazards of indiscriminate drug use or consequences of noncompliance must be disseminated to clinic staff so that they could pass on this information to the populations under their care.

Health education should also be targeted at the employers, particularly logging companies. They have served as the source of first treatment for some of our study populations, and have also been motivating employees towards better compliance with drug intake.

Since forgetting to take a drug has been put forward as a reason for noncompliance, efforts and strategies to improve the capacity to remember should be devised. One of these is for the delivery system of antimalarial drugs to use more informative packaging (e.g. blister packs with written instructions), particularly for patients who receive multidose treatment.

As reported in a previous study (*11*), the artesunate regimen used in this study was associated with fewer, milder and more tolerable adverse reactions than quinine + tetracycline. Only the adverse reactions related to quinine + tetracycline led to noncompliance (particularly, tinnitus which accounted for 50% of the reasons for failure to comply); none of the adverse reactions observed among the artesunate recipients was severe enough to result in noncompliance.

The finding that the curative effectiveness of artesunate was significantly higher than that of quinine + tetracycline was in contrast with the results of a hospital-based study (where compliance was complete), which compared these two regimens (*11*). This difference could probably be due to the lower compliance among the quinine + tetracycline recipients in the field.

In conclusion, this study has identified some of the reasons for compliance and noncompliance so that new interventions for improving compliance can be developed. We recommend a strategy which should integrate (1) the use of a simple, once-a-day, short-course drug regimen with minimal adverse reactions, but high curative effectiveness, (2) a better delivery system for antimalarial drugs, e.g. blister packs with written instructions, (3) improved health education, and (4) strengthening the advisory role of malaria clinic staff. Our findings can serve as the baseline for evaluating new interventions and for studying the compliance among migrant populations (*2*), which could be used as part of a surveillance-based early-warning system for monitoring drug resistance. The results also provide data for cost-effectiveness analysis studies, which are important for drug policy decision-making. The higher compliance rate and curative effectiveness of artesunate lead us to recommend its use instead of quinine + tetracycline for the treatment of uncomplicated falciparum malaria in clinics in Thailand.

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Résumé

Paludisme à falciparum non compliqué en Thaïlande: observance des traitements par l'artésunate et la quinine + tétracycline

Généralités. On pense que la principale cause de l'apparition et de la propagation de souches de *Plasmodium falciparum* multirésistantes est la pression médicamenteuse résultant de la non-observance des traitements et des traitements prescrits avec des doses infrathérapeutiques. Les efforts visant à empêcher que la multirésistance ne s'aggrave encore sont par conséquent actuellement dirigés vers la recherche d'interventions permettant d'améliorer l'observance des traitements multidoses par les antipaludiques actuellement employés. Cependant, la définition et l'évaluation de ces stratégies futures veulent que l'on connaisse l'observance de base de ces traitements sur le terrain et les raisons qui font qu'elle est bonne ou mauvaise. Jusqu'ici, on ne dispose pas encore de ce type de données.

Objectif. Comparer l'observance du traitement de 7 jours par la quinine + tétracycline à celle du traitement de 5 jours par 700 mg d'artésunate par voie orale en cas de paludisme à falciparum non compliqué, dans un dispensaire en Thaïlande.

Méthodes. Il s'agit d'un essai de terrain randomisé, contrôlé, effectué dans un dispensaire. Sur les 137 malades âgés de 15 à 60 ans ayant consulté le dispensaire de Chanthaburi en Thaïlande, 60 ont reçu un traitement par la quinine + tétracycline et 77 par l'artésunate. L'observance et les taux de guérison ont été évalués au 7e jour (quinine + tétracycline) et au 5e jour (artésunate), au moyen de l'approche visant à obtenir la guérison. L'observance a été évaluée en interrogeant les malades et en comptant les comprimés; les taux de guérison, par l'examen de gouttes épaisses. On a

noté les raisons invoquées pour l'observance et la non-observance.

Résultats. L'observance a été significativement plus élevée avec l'artésunate (98,4%) qu'avec la quinine + tétracycline (71,7%) (RRa = 1,39, intervalle de confiance à 95% = 1,15–1,68, en prenant comme référentiel la quinine + tétracycline). Le taux de guérison (100%) enregistré chez les malades ayant reçu de l'artésunate a été significativement plus élevé que celui enregistré chez ceux traités par la quinine + tétracycline (77,4%) (RRa = 1,32, intervalle de confiance à 95% = 1,12–1,55). Les raisons invoquées en faveur de l'observance ont été le désir de guérir et de suivre les conseils du personnel médical ou de l'employeur et la simplicité du schéma thérapeutique. La non-observance a été principalement due à des réactions indésirables ou à des oublis.

Conclusions/recommandations. Cette étude fournit des données qui peuvent servir de base à l'élaboration et à l'évaluation de nouvelles méthodes d'intervention pour améliorer l'observance. Nous recommandons une stratégie intégrant l'utilisation d'un schéma thérapeutique simple (avec un minimum de réactions indésirables, mais très efficace, par ex., l'artésunate), un meilleur système de fourniture des antipaludiques (par ex., des médicaments sous plaquettes thermoformées accompagnées d'instructions écrites), des efforts d'éducation sanitaire et le renforcement du rôle consultatif du personnel de santé s'occupant du paludisme. Ces résultats peuvent également être employés pour des études de coût/efficacité afin d'orienter la prise de décision en matière de politique pharmaceutique. La meilleure observance et l'efficacité curative de l'artésunate nous conduisent à recommander son utilisation, et non celle de l'association quinine + tétracycline, pour le traitement du paludisme à falciparum non compliqué dans les dispensaires de Thaïlande.

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