COMMUNITY-BASED PROGRAM FOR MALARIA CASE MANAGEMENT IN THE BRAZILIAN AMAZON

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Abstract. In areas of drug-resistant malaria, control programs may restrict chemotherapy until malaria has been confirmed via microscopy to contain costs and toxicity. In Brazil, patients travel to centralized laboratory posts (FNS) at great cost for diagnosis and treatment. A program was established through the bars of a mining town offering free dipstick diagnosis and mefloquine treatment on a 24-hr basis; falciparum malaria dipstick tests are accurate and easy to use. Outcomes were compared with historical data and results of a neighboring non-intervention village. Guidelines for dipstick use and treatment were followed for 98% of visits. The number of FNS visits was reduced from 2,316 (expected) to 1,097 (observed) with 626 dipstick tests applied. Ninety-five percent of those who visited the FNS experienced onset of malaria symptoms in the town where the FNS was located. There was an unexpected doubling of the malaria hospital admission rate. We demonstrate that dipstick testing can be used in a sustainable, community-based program that should be applicable in a wide variety of settings.

INTRODUCTION

Ideally, malaria treatment should be initiated during the early stages of illness at the peripheral community level to minimize morbidity and mortality. In these settings, clinical diagnosis is usually all that is available; because this diagnosis is so inaccurate, there is a tendency to be cautious, which leads to overdiagnosis and overtreatment. Another reason for overtreatment may be the financial incentives of drug vendors to sell antimalarial drugs. This overtreatment may be reinforced in the majority of cases because patients have self-limiting, nonmalarial illnesses that improve after (but not due to) antimalarial therapy.

When cheap and safe drugs, such as chloroquine, were still effective, this may have been the preferred method of patient management. However, we have now learned that even with such attractive characteristics, limiting a drug’s use should be considered in order to delay the development of resistance. The majority of malarious areas outside of Africa are now chloroquine resistant; effective, alternate regimens are expensive and sometimes toxic. For these reasons, many have recommended restricting chemotherapy to microscopically diagnosed cases. In this scenario, the feasibility of microscopy is the limiting factor determining the extent to which case management will be available in the periphery.

Brazil’s malaria is largely restricted to the Amazon region where the vivax to falciparum ratio is ~ 2:1, with variations depending on the specific locale.1–2 Falciparum malaria is resistant to chloroquine, and Fansidar (pyrimethamine + sulfadoxine), with quinine + tetracycline or mefloquine3–4 are effective alternatives. The malaria control program is largely dependent on centralized government laboratory posts (FNS) that provide microscopic diagnosis and treatment at no cost to patients. In areas where microscopy was unavailable, an attempt was made to continue with clinical diagnosis and therapy with chloroquine, but these efforts were quickly abandoned when patients experienced a high number of falciparum malaria treatment failures. Despite the large number of FNS laboratories, such facilities are still far from large segments of target populations, and patients spend much time and money traveling to them. This scenario in Brazil is typical of many countries where governments are trying to restrict antimalarial use to microscopically confirmed cases.

Recognizing the need for laboratory diagnosis at the village level, Etting and others5,6 evaluated the use of mobile clinics for microscopy and treatment on a semiweekly basis. Although this method did reach otherwise neglected groups (women and children), half of the subjects requesting slides were not ill, and ~ 84% did not have symptoms that would have led to central clinic visits. As might be expected, the slide positivity rate fell from ~ 20% in the central clinics to 5% at the mobile clinics. Along these lines, other studies to improve peripheral management resulted in no reduction in the number of visits to central clinics.7 Clearly, the diagnostic arm of peripheral programs is vulnerable to gross overuse and abuse. But it is not clear if making services more accessible in place and time will worsen or improve this problem.

An antigen-detecting dipstick test (ParaSight-F, Becton Dickinson, Franklin Lakes, NJ) has been shown to be accurate in symptomatic patients for falciparum diagnosis when used by minimally trained personnel.8–10 The specificity and sensitivity for detecting falciparum malaria in a Brazilian clinic was 97 and 91%, respectively.11 Regarding effective therapy, a hospital-based study in the same area in 1995–1996 showed a mefloquine cure rate of 99% in 94 subjects.4

Our objective was to set up and evaluate a community-based program in the Brazilian Amazon for malaria management that used dipstick diagnosis and mefloquine treatment. Once the program was introduced, our intent was to interfere as little as possible in the operational aspects except to monitor results and ensure that supplies were always available to health care providers. An economic analysis of this project will be presented elsewhere.

MATERIALS AND METHODS

Study design. The results of the intervention, applied to Baixão (the test village) for 1 year, were compared with data from Baixão from the previous year (historical control). In addition, a similar, nearby village (Mutum) was designated as a concurrent control and monitored during the 2 years to...
assess the year-to-year variation in outcome variables. The principal outcome was Baixa˜o’s change in the number of patient visits to the FNS laboratory and the number of hospitalizations of patients with malaria. Besides this, we examined the number of dipstick diagnoses performed, adherence to indications for dipstick test use, the proportion with positive results, and the reasons why some patients continued to use the FNS system.

**Site and population.** The study was conducted in Apiacas municipality (population ~ 7,800), a gold-mining area of Brazil’s southern Amazon. The rural areas surrounding Apiacas are divided in 2 major mining villages, Baixa˜o and Mutum. The Apiacas hospital serves all the surrounding mining villages (including Baixa˜o and Mutum). There are no paved roads, and dirt roads are often impassable during the 5-month rainy season. The climate is tropical and humid, with marked wet and dry seasons. Malaria is by far the greatest cause of morbidity and hospital admissions. A government-sponsored FNS clinic (providing microscopy) and a 32-bed hospital is located in Apiacas. Diagnosis and treatment at the Apiacas FNS clinic is provided at no cost to patients. Private pharmacists are also available, but their services are seldom used because of the high costs. First- and second-line falciparum malaria treatment are composed of a 7-day regimen of quinine plus tetracycline, and mefloquine (1,000-mg single dose), respectively. For many years, falciparum malaria has been highly resistant to chloroquine and Fansidar.

Baixa˜o is an isolated gold-mining area with ~ 2-km radius and a population of 750, the majority of which are adult migrant workers whose history of malaria exposure and immunitv varies widely. Baixa˜o is 32 km from the town of Apiacas, whose FNS clinic performs nearly all of the malaria diagnosis (microscopic evaluation) and treatment for Baixa˜o’s patients. A population-based cross-sectional survey at the start of the study showed that ~ 5% of the Baixa˜o population had asymptomatic *Plasmodium falciparum* parasitemia (carriage). Power is limited to a few portable generators and gas operated mining sluices. Although the trip between Baixa˜o and Apiacas takes only a few hours in the dry season, transportation is difficult to arrange, especially during the rainy season and at night. The average time for arranging and round trip travel to Apiacas is estimated to be 1.5 days and costs an average of US$40. Miners earn an average of US$10 per day.

Mutum, the adjacent mining village with malaria ecological factors very similar to Baixa˜o’s, is located 35 km from Apiacas in the other direction. There is very little interchange between the 2 villages regarding malaria management. Mutum itself has an FNS malaria clinic (with microscopy services) located within the village, but patients also go to Apiacas to visit the FNS clinic and hospital. Otherwise, conditions are similar to those of Baixa˜o.

**Intervention.** Six of Baixa˜o’s 15 bars were chosen to perform malaria diagnosis and treatment. Locations were selected to ensure that all inhabitants would be within a 20-min walk from a participating bar. In addition, bars needed to have enough staff members (2–3 people) so that 24-hr service 7 days a week was possible. Each bar’s staff participated in a 2-day training session that covered malaria epidemiology, biology, clinical aspects, indications for diagnostic tests, and procedures for treatment and referral. It is noteworthy that only 2 hr were needed to adequately train personnel specifically on the use and interpretation of dipsticks. We instructed providers to do the following:

1. Refer all subjects with severe symptoms (including vomiting) to Apiacas hospital regardless of malaria diagnostic test results.
2. Perform dipstick diagnosis on those presenting with at least one of the following: fever, headache, backache, generalized myalgia, or a history of one of these symptoms within the past day. We discouraged, but permitted (as long as symptoms were recorded), dipstick tests on anyone not fulfilling the symptom criteria.
3. Repeat any initially negative dipstick within 12–24 hr at the patients’ request. If the second result was still negative, they were to refer the patient to Apiacas for persistent or worsening symptoms.
4. Record the number who presented but did not meet criteria for dipstick test use. For those getting a dipstick test, record the patient’s, name, age, sex, presenting symptoms, test result, and treatment or referral. Keep all dipsticks for collection and reexamination by FNS staff.
5. Prescribe chloroquine treatment for dipstick-negative cases of malaria. Observe mefloquine treatment (1,000-mg single dose) for dipstick-positive cases. And redose if vomiting occurred within an hour.
6. Work voluntarily, without compensation from patients or the government.
7. Educate those in their respective village areas about all aspects of the program. Periodic population-based interviews would be conducted by the study investigators to assess the level of community education.

Ethical approval was obtained from the National Health Program, and subjects gave oral informed consent to participate.

**Monitoring.** At the Apiacas and Mutum FNS clinics, data routinely collected were not affected by the study. Data collected included patients’ demographic data, residence, site of acquisition of malaria, results of microscopic diagnosis, and treatment administered. During the intervention, all patients who lived in Baixa˜o and who presented to the Apiacas FNS were asked their reason for the visit and if they had previously sought diagnosis and treatment through Baixa˜o’s bars. At the 30-bed Apiacas hospital, admission criteria and recording of data were not affected by the study, with illness diagnosed as malaria only when there was smear confirmation. Near the beginning of the second year, there was a change in hospital staff that may have affected admission criteria and rates. The FNS staff of Apiacas was instructed to visit the staff of the 6 participating bars on a monthly basis to ensure that records were being kept, to replenish dipstick and mefloquine supplies, and to collect dipstick tests.

In Baixa˜o, the population’s acceptance of our intervention was evaluated through 2 cross-sectional surveys (randomly selecting households for interviews) during the second month and at the end of the intervention. During both interviews, patients were asked about knowledge and use of the new program as well as hospitalizations for malaria during the previous year. During the second interview, subjects
were also asked about their willingness to pay for dipstick tests.

**Data collection and analysis.** The principal outcomes were the number of Apiacas FNS visits and malaria hospitalizations from Baixa˜o during the study intervention. By use of historical data from the year immediately preceding our study intervention (yr1) and adjustments for the year-to-year variation (on the basis of Mutum’s data for the 2 study years), we calculated the expected (exp) number of visits that would have occurred from Baixa˜o under the old program for the second year (yr2). This was compared with the observed (obs) number of visits from Baixa˜o during the second year:

\[
\text{Baixa}_\text{exp}\text{yr2} = \text{Baixa}_\text{obs}\text{yr1} \times \left(\frac{\text{Mutum}_\text{obs}\text{yr2}}{\text{Mutum}_\text{obs}\text{yr1}}\right)
\]

The same method (observed versus expected) was used to study the change in hospitalizations from Baixa˜o, where the year-to-year adjustment was based on Mutum’s hospitalization rates (from examination of hospital records), and the Baixa˜o rates were based on community-based cross-sectional interviews. The number of malaria deaths (~ 1 per year) from Baixa˜o was considered too low to monitor as an outcome.

A multiplier effect was defined as the number of FNS visits prevented (expected minus observed) divided by the number of dipstick tests applied. One would expect one dipstick test to prevent one visit, resulting in a multiplier effect of 1. This multiplier effect can also represent overuse when the ratio is much less than 1. For example, in the results of Ettling and others\(^6\) cited above, the multiplier effect of mobile clinic diagnosis would be 16%. For our study, the multiplier effect was also calculated by month to see if there was a trend with duration of the program (learning curve) or if there was a correlation with dipstick positivity ratio. Statistical conclusions were based on chi-square tests, confidence intervals of incidence density ratios, and confidence intervals of the difference of these ratios.

**RESULTS**

In general, the new system was easily implemented, easily sustained, and well received by the inhabitants of Baixa˜o. The quality of record-keeping and information obtained by the participating bars of Baixa˜o, the cross-sectional interviews, and the Apiacas and Mutum FNS clinics were complete and meticulous. Volunteers were easily taught to use and accurately read the dipstick tests. The hospital records were adequate regarding the number of patients, admissions, and diagnosis, but the patients’ place of residence was often not detailed enough. The populations of the 2 mines remained constant throughout the study period, and no new malaria control interventions were initiated. The number of FNS clinic visits, the number of dipstick tests used, and the dipstick test results are given in Table 1 for Baixo˜o and Mutum.

Of the 1,097 patients who continued to use the Apiacas FNS clinic during the second study year, 1,042 (95%) reported that they did so because symptoms began in Apiacas. In Baixo˜o, all patients presenting for diagnosis had symptoms that met the criteria for use of dipstick tests. Only 9 patients with initial negative dipstick test findings returned for a second dipstick test after 24 hr because of continuing symptoms.

The overall multiplier effect was 1,219 \(\div 626, \sim 2\), significantly greater than 1 (\(P < 0.0001\)), implying that 2 visits were prevented for each dipstick test applied. There was no correlation by month of the multiplier effect with study duration, but there was a significant inverse correlation with the proportion of dipstick tests that were positive (\(P < 0.005\); data not shown). Table 2, shows Baixo˜o’s and Mutum’s malaria hospitalization rates for the years before and during the dipstick intervention. For Mutum, the results are based on a sample of hospital records and the ratio between years are intended to be used as an adjustor for the year-to-year variation.

There were 75 and 196 villagers in the 2 cross-sectional surveys, which were performed in July 1996 (3 months after the start of dipstick test intervention) and August 1997 (6 weeks after the end of the intervention), respectively. In the first interview, 85% knew of the new program, and 32% had already used it. In the second interview, 87% knew about the system and 65% had already used it. Of those who had not used dipstick tests, only 12% (~30 people) did not trust this diagnostic method. This number is compatible with the 55 visits (at 2 visits per resident) by those who used the
Apiacas FNS clinic even though their symptoms began in Baixão. In the second survey, many who denied the knowl-
edge of the system had recently arrived to work in the mines. Of those who had used dipstick tests, 98% said they were
satisfied with the system and would use it again instead of
going to the Apiacas FNS. The average amount users were
willing to pay for the dipstick was US$5.60 (we did not ask
about willingness to pay for mefloquine). Almost all the par-
ticipants considered this new program a great advantage for
the community. The program still continues (and has begun
in neighboring communities), although the study officially
closed in the summer of 1997.

**DISCUSSION**

This project represents an effort to establish a new strat-
ogy for malaria control in the Amazon, targeting those who
had the poorest access to diagnosis and treatment. There are
many such areas in the Amazon, typically gold-mining and
agricultural areas, with populations too small or malaria at-
tack rates too low to warrant a government clinic with mi-
croscopy services. These are also the remote frontier areas
where population migration makes establishing and main-
taining such clinics very difficult. Compared with the exist-
ing program and literature reports of attempts to extend to
the community other strategies for malaria case manage-
ment, our program was an unprecedented success. In general
terms, success was measured by the frequent, appropriate
use of the new system and a corresponding reduction in re-
liance on the old.

This project’s design is really that of an ecological study
with the intent to look at individual behavior, rather than
ecological effects. There is an inherent danger in concluding
that the changes in behavior we observed were caused by
our intervention because there could be confounding vari-
ables present during our intervention but not in our historical
or concurrent controls. The most obvious confounder is a
difference in malaria transmission or a difference in the in-
cidence of other diseases that cause malaria like symptoms.

Despite these shortcomings, our study can be used to de-
scribe the way in which dipstick tests were used by this
community-based program. A significant ( > 0) number were
used with a high proportion positive. There was little change
in this pattern over a 1-year period. A significant number
continued to use the old system because of convenience,
with only a small fraction not trusting the results of dipstick
tests. Interviews indicated that the community coverage (i.e.,
average and use) of the intervention was high. Despite the
intervention, there continued to be a significant ( > 0) num-
ber of malaria hospitalizations. A more definitive study
would have required a large number of villages randomized
to intervention and control groups in an attempt to adjust for
confounding effects. These descriptive results can be viewed
as a pilot effort to describe the use of dipstick tests in such
communities.

For the reasons cited above, further analysis comparing
observed results to expected outcomes are questionable and
prone to confounding effects. However, with this caveat, if
one considers the calculated number of expected clinic visits
and hospital malaria admissions, there was a reduction in the
number of clinic visits, with about half of these patients not
being assessed by a dipstick test. The number of hospital
malaria admission doubled. All of these results are statisti-
cally significant. It is possible that these observations are
related through the following mechanism. When diagnosis
and treatment are reliable and easily accessed, a significant
number of patients who would normally have traveled to
central clinics would delay diagnosis at the community level.
Those with nonmalaria illness ( ~ 70%) would experience
spontaneous cure, whereas those with malaria become suf-
ciently ill because of this delay to require hospitalization.
The high number without malaria who spontaneously cure
without diagnosis contributes to our observed multiplier ef-
fect and high dipstick test positivity rate, whereas those with
malaria (say 30%) may be the reason for the increase in
malaria hospitalizations.

Regarding this point, for malaria cases diagnosed in Baix-
ão during the second year, we expected ~ 120 more malaria
cases than observed, which is a number similar to the in-
creased number of malaria hospitalizations (100) from Baix-
ão. Unfortunately, our study of hospitalized patients was not
detailed enough to determine the exact reasons for the in-
crease—only that it did occur and should be monitored
closely in future studies.

We did not feel it necessary to compare dipstick tests to
microscopy during our study because studies have shown
that the majority of errors result from specific laboratory
workers who misread tests. These types of errors can be
avoided by careful training and, as in our study, periodic
collection and reexamination and confirmation of readings
themselves. On the basis of the results of a recent study in
a similar population of the same area, we expect, compared
with microscopy, our positive predictive value and negative
predictive value to be 90 and 97%, respectively. We consider
the “over-treatment” of the 10% of patients with false-pos-
itive findings to be negligible compared to the treatment of
patients with asymptomatic parasitemia (related to the car-
riage rate of 5% of the entire population). To minimize the
effects of the 3% false-negative (one minus the negative pre-
dictive value) results, providers were trained to repeat neg-
ative tests within 24 hr for patients who remained symptom-
atic.

There are 2 main reasons to consider our study only a
pilot study. First, as mentioned above, a larger number of
randomized villages needs to be studied comparing dipstick
tests and existing program for malaria management. Second,
we are uncertain exactly how the new program changes be-
avior and how each change is related to outcome. For ex-
ample, for the number of FNS visits prevented, one could
stratify the results into those seeking diagnosis via dipstick
test and those who do not. In both groups, there are other
levels of stratification based on the presence or absence of
falciparum malaria infection and having a correct or incor-
correct diagnosis. How much each of these contributes to the
outcomes of visits prevented and excess hospitalizations has
yet to be determined.

Furthermore, beyond stratification of the study by sub-
populations, the underlying cause of each effect is still not
clear. For example, although it is tempting to think that those
with falciparum malaria who are diagnosed and treated in
the periphery are benefiting from early diagnosis and treat-
ment, they may actually be worse off if they waited longer
(than under the old program) before seeking diagnosis for reasons described above. Are these the types of patients contributing to higher malaria hospitalization rates, or is it another group for another reason? These underlying reasons need to be identified in future studies to see if and how the program can be improved.

There are effects that we have not attempted to measure that others may consider important. This program may have affected transmission, duration of patient suffering, and appropriate antimalaria drug use, leading to a slower development of resistance. Health authorities in multidrug-resistant areas may find some of these reasons compelling arguments for program implementation. Worldwide, many community settings exist that are similar to ours, but there are also many areas with equally important but different outcome variables. For example, in such communities, it may be more important to reduce mortality or the indiscriminate use of antimalarial drugs by the private sector. However, we do feel that following the principles used in our program would give the best results (whatever the outcomes) in almost all situations. Easy access to effective diagnosis and treatment, community education and responsibility, and periodic government monitoring should apply to all malaria control programs. If these criteria are not established and sustained, the private sector will quickly fill and capitalize on this new niche.

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