Lessons from the field

Intermittent preventive treatment of malaria during pregnancy in central Mozambique

Paula E Brentlinger,^a Martinho Dgedge,^b Maria Ana Chadreque Correia,^c Ana Judith Blanco Rojas,^d Francisco Saúte,^e Kenneth H Gimbel-Sherr,^d Benjamin A Stubbs,^f Mary Anne Mercer^a & Stephen Gloyd^a

Problem New WHO strategies for control of malaria in pregnancy (MiP) recommend intermittent preventive treatment (IPTp), bednet use and improved case management.

Approach A pilot MiP programme in Mozambique was designed to determine requirements for scale-up.

Local setting The Ministry of Health worked with a nongovernmental organization and an academic institution to establish and monitor a pilot programme in two impoverished malaria-endemic districts.

Relevant changes Implementing the pilot programme required provision of additional sulfadoxine-pyrimethamine (SP), materials for directly observed SP administration, bednets and a modified antenatal card. National-level formulary restrictions on SP needed to be waived. The original protocol required modification because imprecision in estimation of gestational age led to missed SP doses. Multiple incompatibilities with other health initiatives (including programmes for control of syphilis, anaemia and HIV) were discovered and overcome. Key outputs and impacts were measured; 92.5% of 7911 women received at least 1 dose of SP, with the mean number of SP doses received being 2.2. At the second antenatal visit, 13.5% of women used bednets. In subgroups (1167 for laboratory analyses; 2600 births), SP use was significantly associated with higher haemoglobin levels (10.9 g/dL if 3 doses, 10.3 if none), less malaria parasitaemia (prevalence 7.5% if 3 doses, 39.3% if none), and fewer low-birth-weight infants (7.3% if 3 doses, 12.5% if none).

Lessons learned National-level scale-up will require attention to staffing, supplies, bednet availability, drug policy, gestational-age estimation and harmonization of vertical initiatives.

Bulletin of the World Health Organization 2007;85:873-879.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. التجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Background

The magnitude and burden of malaria infection during pregnancy (MiP) have been well documented.^{1,2}

The need for action has been recognized by WHO, which now recommends that sub-Saharan African countries with stable malaria transmission address MiP through intermittent preventive treatment with sulfadoxine-pyrimethamine (SP) during pregnancy (IPTp), maternal use of insecticide-treated bednets (ITNs) and good case management of maternal malaria and anaemia.^{3,4}

Context

In 2003, the Mozambican health ministry piloted an MiP programme containing all principal elements of the new WHO strategy to determine the best mechanisms for national-level scale-up.

The ministry designed and implemented the pilot programme with technical, logistical and financial assistance from two partner institutions: a nongovernmental organization (NGO) and an academic institution.

The ministry selected Nhamatanda and Gondola districts from 10 districts in Manica Province and 13 in Sofala Province, based on high malaria burdens (31-41 cases/100 persons/year, according to ministry estimates), low socioeconomic status (72-93% of population living in poverty)⁵ and accessibility. Within each district, the five health units (out of eight in Gondola, six in Nhamatanda) with the largest antenatal caseloads (30-400 new patients/month) were chosen. Between 80% and 90% of local pregnant women are thought to attend antenatal care.⁶ All women presenting for initial antenatal visits between October 2003 and June 2004 were invited to enrol in an observational study. Women who declined could still

(Submitted: 22 May 2006 – Final revised version received: 22 April 2007 – Accepted: 30 April 2007)

^a Department of Health Services, School of Public Health and Community Medicine, PO Box 357660, University of Washington, Seattle, Washington 98195, USA. Correspondence to Paula E Brentlinger (e-mail: brentp2@u.washington.edu).

^b Ministry of Health, Maputo, Mozambique.

^c Health Alliance International, Chimoio, Mozambique.

^d Health Alliance International, Seattle, Washington, USA.

^e National Malaria Control Programme, Ministry of Health, Maputo, Mozambique.

^f Department of Epidemiology, School of Public Health and Community Medicine, University of Washington, Seattle, Washington, USA. doi: 10.2471/BLT.06.033381

receive IPTp. Follow-up continued until

The protocol for collection of patient and programme data was approved by the Mozambican National Bioethics Committee and the University of Washington; informed consent was procured from all participants.

Pilot protocol

Antenatal nurses explained IPTp and demonstrated bednet use at each clinic session. Because of high HIV prevalence, 3 preventive SP doses (directly observed by nurses) were recommended.7 Dose 1 could be given at 16 weeks or after quickening (contraindications: adverse reaction to SP or co-trimoxazole [CTX], last SP dose within 1 month, current CTX use). Subsequent doses were indicated at intervals of 1 month or more. SP was not co-administered with CTX due to concerns about toxicity and crossresistance.2,8,9

Nurse supervisors visited each site weekly to collect data, answer questions and solicit suggestions. The authors and nurse supervisors (who did not engage in direct patient care) also conducted quarterly semi-structured interviews with clinic staff at each site. Subsequent adjustments to the pilot programme were made after discussion with ministry officials.

Observed problems and solutions

The set-up process, regular supervisory visits and quarterly site meetings yielded information on pertinent operational issues.

SP availability

SP was Mozambique's second-line antimalarial; first-level health units were not authorized to stock it. The national formulary declared SP to be contraindicated in pregnancy. Provincial stocks of SP were inadequate for IPTp. We obtained additional SP and formulary restrictions were waived.

Directly observed SP

Only two sites had water consistently. Most had few or no drinking cups. We provided reusable plastic cups, spoons, jugs, buckets, trays, basins and hand towels (mean cost US \$144.30 per health unit).

Gestational age estimation

There were marked differences among

clinics in the proportion of women given SP at the first visit (range 47.7-88.5%).

We redefined SP eligibility to include audible fetal heart tones, quickening or estimated gestational age of 16 weeks or more barring contraindications, and the proportion of women given SP during the first antenatal visit rose significantly; for example, from 47.7% to 71.6% (P = 0.005). Using our new criteria, 85.9% of women were eligible for SP at the first visit, versus 74.7% when using quickening as the only criterion.

Uncertainty about gestational ages seemed well-founded due to poor maternal recall of menstrual periods and the absence of pregnancy tests and ultrasound. The eventual date of delivery was more than 28 days different than the estimated date in 31.8% of liveborn singleton deliveries.

Programmatic incompatibilities

We encountered multiple actual or potential incompatibilities (Table 1) between MiP interventions and other health initiatives. Frequent absences and staffing changes mandated on-thejob IPTp training for four new nurses in three sites. Because the standard antenatal card was created before the introduction of IPTp, we created an addendum for recording of preventive SP doses, ITN use and medication allergies. We were unable to devise a system for informing antenatal clinics of antimalarial treatment given elsewhere.

ITNs were only available for purchase at three sites. Elsewhere, we worked with local shopkeepers to establish sales posts. Highly subsidized nets were unavailable. Clinic nurses reported that the most common reason for not using ITNs was cost. We supplied ITNs for all antepartum and postpartum units, and for patient education. We recommended that symptomatic malaria occurring less than 1 month after preventive SP be treated with quinine. We maintained this policy when Mozambique changed its first and second-line drugs to SP + amodiaquine and artemether-lumefantrine.

Impact and outputs

Following WHO guidelines, we measured proportions of women with severe anaemia (hemoglobin 7 g/dL or less) or peripheral parasitaemia and the proportion of low-birth-weight infants, each stratified by SP exposure. We also

measured the proportion of women who received one, 2 or 3 doses of SP, and the proportion reporting bednet use on the night preceding the first or second antenatal visit.

Antenatal nurses recorded SP administration and self-reported bednet use at each visit. Data were available for 7911 women; they comprised 90.2% of the 8767 new prenatal patients the ministry recorded during the pilot period.

Overall, 92.5% of women received 1 dose or more of SP. Of the 4988 women who had completed their pregnancies or reached term before July 2004, 22.1% received 1 dose, 30.4% received 2 doses, and 43.6% received 3 doses (mean: 2.2 doses). Of women with at least three antenatal visits, 78.6% received all 3 doses. However, 47.6% had less than three visits (Fig. 1). Of the 591 women who received no SP, 527 (89.2%) had only one visit, and 56.6% presented too early to be eligible.

Most SP administration errors were of omission. Only 45 women (0.6%) received SP in spite of having no fetal movements and a gestational age of 15 weeks or less. Rarely (0.5% of women), 4 doses were given.

At the first and second antenatal visits, 4.5% and 13.5% of women reported having used nets the night before. Women first reported using bednets at a mean estimated gestational age of 25.8 weeks (95% confidence interval, CI: 25.4-26.2).

For logistical and financial reasons, impact data were available only for subsets of women. In April and May 2004, a cross-sectional study of maternal haemoglobins (measured by HemoCue) and peripheral parasitaemia (Giemsastained peripheral blood smears, asexual P. falciparum parasites counted against 500 leukocytes, readings confirmed by two microscopists) was conducted in the two health facilities with laboratories. Study participants presenting for antenatal care at those facilities during this period were eligible, and we collected haemoglobin and/or parasitaemia data on 1167 women.

The prevalence of severe anaemia (haemoglobin 7.0 g/dL or less) was 3.4% in women who had not yet received SP and 0.8% in women who had received 2 doses or more of SP (P = 0.036). Maternal peripheral malaria parasitemia was present in 39.3% of women who had not yet received SP, and 7.5% in

Table 1. Operational interactions between IPTp and other antenatal care initiatives

Health initiative	Problem	Solution	Comments
Provision of ferrous sulfate to prevent maternal anaemia	Some nurses asked patients to schedule follow-up visits at 35–day intervals (instead of the usual 28 days) to avoid giving second and third SP doses at intervals of less than a full calendar month. Ferrous sulfate was prepackaged in 30-tablet lots; the nurses repackaged it in 35-tablet lots.	Redefine the minimum interval between SP doses as 28 days, rather than 1 month.	-
Treatment of syphilis	Some clinics used the genital ulcer arm of an algorithm for syndromic treatment of STIs to guide treatment for asymptomatic pregnant women with positive serologic tests for syphilis, because the syndromic algorithm contained no arm for treatment of asymptomatic persons. Patients were treated with a 3-day course of CTX and 3 injections of penicillin.	Advise nurses to give the first dose of SP at the time of the second dose of penicillin (usually one week after first dose) to avoid concurrent therapy with SP and CTX.	We brought this issue to the attention of WHO and the health ministry's reproductive health division. The STI algorithm was in the process of revision during the study period.
Prophylaxis of AIDS-related opportunistic infections ^{8,9}	Elevated risk of adverse reactions in HIV-infected persons treated with both CTX and SP. Concern about elevated risk of SP resistance in persons taking preventive CTX. Redundancy of giving preventive SP to persons on preventive CTX, which also prevents malaria infection.	Because AIDS treatment was not yet available in the pilot districts, this problem did not materialize during the study period.	We defined daily CTX treatment as a contraindication to SP prophylaxis. New Mozambican antenatal cards will include space for recording daily CTX use.
Highly active antiretroviral treatment (HAART) ^{22,23}	Elevated risk of myelosuppression in women receiving both zidovudine and SP. Risk of diagnostic confusion should a patient develop severe cutaneous adverse reactions or hepatotoxicity after receiving both SP and daily nevirapine.	Because AIDS treatment was not yet available in the pilot districts, this problem did not materialize during the study period.	The health ministry has defined HIV-positive persons as a high-priority group for receipt of subsidized ITNs. New Mozambican antenatal cards will include space for recording antiretroviral treatment. Discussions are continuing regarding ideal IPTp regimen for women on HAART, and mechanisms of collaboration between antenatal and HIV clinics.
Treatment of symptomatic malaria in pregnancy	First-line malaria regimen at end of study was SP and amodiaquine. Pregnant women with symptomatic malaria were often treated outside the antenatal clinic by clinicians who did not ask when the most recent dose of SP had been given.	Provincial health officials circulated a letter advising local clinicians to check antenatal card for date of most recent SP dose, and to proceed to third-line treatment (quinine) in women who had recently been given preventive SP.	Revision of Mozambican prenatal card is in progress, and will allow easier charting of SP doses. Future IPTp trainings will include local physicians and health technicians as well as antenatal nurses.
Management of pregnant women with seizures and/or coma	Local written guidelines called for immediate treatment for eclampsia or pre-eclampsia, with antimalarial treatment to be considered only if symptoms failed to resolve in 24 hours.	Our discussions with local physicians revealed that their practice was to treat for both malaria and pregnancy-induced hypertension because of the clinical difficulty of distinguishing between the syndromes.	Future IPTp guidelines may recommend urgent treatment for both malaria and pregnancy-induced hypertension in case of seizures or coma.
Recording and reporting	Abbreviation "SP" used to denote sulfadoxine-pyrimethamine by malaria programme <i>and</i> to denote "seropositive for HIV" by HIV/AIDS programme.	Common local practice is to call sulfadoxine-pyrimethamine by its common trade name, Fansidar.	Future revisions of antenatal card may or may not use SP abbreviation to record HIV serostatus. Discussions in progress.

CTX, co-trimoxazole; HAART, highly active antiretroviral therapy; IPTp, intermittent preventive treatment of malaria in pregnancy; ITN, insecticide-treated bednet; SP, sulfadoxine-pyrimethamine; STI, sexually transmitted infection.

women who had received all 3 doses (P < 0.001). Haemoglobin levels and parasitaemia prevalence are described by gravidity and SP use in Table 2. SP use was associated with significantly higher haemoglobin levels and lower parasitaemia prevalence even when stratified by parity. We have reported elsewhere that ITNs and SP appeared to contribute independently to the reduction of maternal malaria parasitemia, and that SP appeared to be effective even in HIV-infected study participants. 10

Birth weight data were only available for pregnancies terminating in an institutional delivery by July 2004. We acquired birth weight data on 2529 liveborn singleton infants and 71 pairs of liveborn twins. Low birth weight was noted in 12.5% of liveborn singleton infants delivered by women who had received no SP and 7.3% in women who had received 3 doses (P = 0.019 for trend; data not shown). A similar but non-significant pattern was observed in twins.

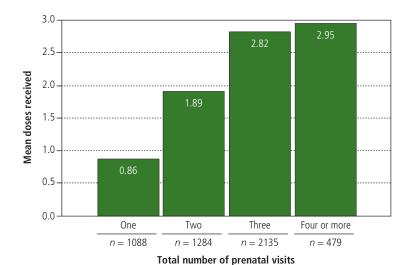
Discussion

In this pilot IPTp programme, antenatal nurses successfully administered at least 1 dose of preventive SP to over 90% of women. Although this level of performance is substantially higher than that reported elsewhere^{11,12} fewer than half (43.6%) received the full 3-dose course, largely because of infrequent antenatal attendance. Adjusting for antenatal care utilization patterns, the estimated population-level coverage of the full 3-dose regimen was 37.6%. Had we not revised our criteria for SP eligibility, our coverage would have been even lower.

Promotion of ITNs was far less successful than SP prophylaxis, apparently because local prices exceeded purchasing power. This, like our difficulties with drinking water and cups, is consistent with other reports. ^{13–15}

Statistically significant associations between reported SP administration and three indicators of impact suggest that the pilot data accurately reflect actual clinical practice, that the reduction in adverse outcomes was unlikely to be caused by chance and that local *Plasmodium falciparum* resistance to SP had not yet rendered SP-based IPTp ineffective. ¹⁶ Our maternal parasitaemia data also confirmed the health ministry's indirect evidence that MiP was highly prevalent in the pilot region.

Fig. 1. Total number of preventive SP doses received, compared to total number of antenatal visits



SP, sulfadoxine-pyrimethamine.

The majority of women who had three or more antenatal visits before delivery received the full course of 3 preventive doses of sulfadoxine-pyrimethamine; however, 48% of subjects had made only one or two visits.

We believe that Mozambique's approach was unique because of the attention given to real or potential conflicts between MiP-related interventions and other vertical initiatives affecting pregnant women, and because of its attention to the effect of imprecise gestational age estimation on SP uptake.

The difficulties encountered with SP supply, materials for directly observed SP administration, staff turnover, bednet availability and pricing, gestational age estimation and incompatibilities with other health initiatives are unlikely to be unique to Mozambique. However, details are likely to vary substantially by site, thus limiting generalizability of our findings.

The observed level of success would not have been possible without the intensive support of the study supervisors, funds with which to complement the core health ministry budget and the enthusiastic participation of health authorities at all levels. These conditions may not be replicable elsewhere. Measurement of output and impact indicators was particularly labour-intensive. However, lessons learned from the pilot should enable scale-up to occur with less intensive supervision and support than was required for the pilot programme.

Lessons learned

The pilot IPTp programme merits replication at the national level in Mozambique. Mozambique's modifications of

standard WHO protocols (e.g. definition of contraindications to SP, redefinition of eligibility criteria for first dose) should be preserved. Pilot programme procedures for estimating SP need, providing materials for directly observed SP and expanding the antenatal card should be adopted nationally. Increased communication and cooperation among stakeholders will be required to eliminate programmatic incompatibilities. Attention to the provision of ferrous sulfate, folic acid and/or multivitamins, with particular attention to HIV-infected women, should also be enhanced. 17,18 Donor support may be required for population-level provision of ITNs. The support of the scientific community will be required for pharmacovigilance, monitoring of long-term effectiveness of SP, definition of safe and effective alternatives to SP (including acquisition of data on pharmacodynamics of antimalarials in pregnant women with and without HIV infection, including those on antiretroviral therapy), and malaria-related operations research. 19-21 Frequent supportive supervision at the health-clinic level is indispensable in our experience.

With adequate political will, however, we believe that all of this is feasible, even in the resource-constrained setting we describe. Indeed, in the aftermath of this pilot programme, IPTp was successfully implemented throughout Sofala and Manica provinces based on the lessons we have learned and described.

52 (43.7%)

3 (9.4%)

1 (4.8%)

2 (12.5%)

< 0.001

Table 2. Maternal peripheral malaria parasitaemia and maternal haemoglobin levels in cross-sectional evaluation

	Mean h	naemoglobin levels (95%	CI)	
	All women (n=1167)	Primigravidae (n=269)	Secundigravidae (n=203)	Gravida ≥ 3 (<i>n</i> =696)
All levels of SP	10.5 (10.4–10.6)	10.1 (9.9–10.3)	10.7 (10.5–10.9)	10.6 (10.4–10.7)
Number of SP doses				
0 (n=712)	10.3 (10.2–10.5)	10.0 (9.7-10.2)	10.6 (10.3–10.9)	10.4 (10.2–10.6)
1 (n=214)	10.6 (10.4-10.8)	10.2 (9.7–10.7)	10.7 (10.0–11.3)	10.8 (10.5–11.0)
2 (n = 175)	10.8 (10.6-11.0)	10.5 (10.0-11.0)	11.3 (10.5–12.0)	10.8 (10.6–11.1)
3 (n=66)	10.9 (10.5–11.2)	11.0 (9.9–12.1)	10.9 (10.2–11.6)	10.8 (10.4–11.3)
P-value (linear regression)	< 0.001	0.009	0.173	0.003
	Malaria	parasitaemia prevalence	2 (%)	
	All women (n=1078)	Primigravidae (n=248)	Secundigravidae (n=188)	Gravida ≥ 3 (<i>n</i> =641)
All levels of SP exposure	277 (25.7%)	106 (42.7%)	58 (30.9%)	113 (17.6%)

99 (63.1%)

4 (9.3%)

2 (5.7%)

1 (7.7%)

< 0.001

CI, confidence interval; SP, sulfadoxine-pyrimethamine.

255 (39.3%)

10 (5.0%)

7 (4.3%)

5 (7.5%)

< 0.001

Acknowledgments

Number of SP doses 0 (n=649)

1 (n = 199)

2(n=163)

3(n=67)

P-value (χ^2)

This project was supported under a cooperative agreement from the US Centers for Disease Control and Prevention through the Association of Schools of Public Health (Grant Number U36/CCU300430–20). We also received financial and/or technical support from Health Alliance International, Popula-

tion Services International in Mozambique, WHO in Mozambique and the African Region, and the United Nations Children's Fund in Mozambique. We are grateful to the study nurses and participants, the Provincial Health Directorates of Sofala and Manica provinces, and the District Health Directorates of Nhamatanda and Gondola for their

enthusiastic participation. The contributions of study supervisors Fernanda Toalha and Maria Felicidade Faria and of bednet coordinator Fungai Chimbé Chinhacata were indispensable.

104 (28.0%)

3 (2.4%)

4 (3.7%)

2 (5.3%)

< 0.001

Competing interests: None declared.

Résumé

Traitement préventif intermittent contre le paludisme des femmes enceintes dans le centre du Mozambique

Problématique Les nouvelles stratégies de l'OMS pour la lutte contre le paludisme pendant la grossesse préconisent un traitement antipaludique préventif intermittent, l'utilisation de moustiquaires de lit et une amélioration de la prise en charge des cas.

Démarche Un programme pilote pour la Mozambique de lutte contre le paludisme pendant la grossesse a été conçu pour déterminer les besoins liés au passage à l'échelle supérieure.

Contexte local Le ministère de la santé a collaboré avec une organisation non gouvernementale et un établissement d'enseignement supérieur dans la mise au point et le suivi d'un programme pilote appliqué dans deux districts appauvris d'endémie du paludisme.

Modifications pertinentes Pour la mise en œuvre du programme pilote, il a fallu fournir une quantité supplémentaire de sulfadoxine-pyriméthamine (SP), du matériel pour l'administration sous surveillance directe de ce médicament et des moustiquaires. Il a également fallu modifier la fiche anténatale et obtenir une dérogation au guide national de prescription concernant la

SP. Le protocole de départ a dû être modifié car l'imprécision dans l'évaluation de l'âge gestationnel conduisait à une prise incomplète des doses de SP. Plusieurs incompatibilités avec d'autres initiatives sanitaires (y compris des programmes de lutte contre la syphilis, l'anémie et le VIH) ont été découvertes et surmontées. Les principaux résultats et effets ont été mesurés : 92,5 % des 7911 femmes enceintes ont reçu au moins une dose de SP, le nombre moyen de doses de SP reçues étant de 2,2. Lors de la deuxième visite anténatale, 13,5 % des femmes utilisaient une moustiquaire de lit. Parmi les sous-groupes (1167 personnes pour les analyses en laboratoire, 2600 naissances), on a relevé une association significative entre l'utilisation de SP et une élévation du taux d'hémoglobine (10,9 g/dl pour la prise de 3 doses de SP contre 10,3 g/dl en l'absence de toute dose de SP), une baisse de la prévalence des parasites du paludisme (7,5 % pour la prise de 3 doses contre 39,3 % en l'absence de toute prise de SP) et une baisse de la proportion d'enfants de petit poids à la naissance (7,3 % pour la prise de 3 doses contre 12,5 % en cas l'absence de toute prise de SP).

Enseignements tirés Le passage à l'échelle nationale du programme imposera de s'intéresser aux besoins en personnel, en fournitures et en moustiquaires, à la politique en matière de médicaments, à l'estimation de l'âge gestationnel et à l'harmonisation des initiatives verticales.

Resumen

Tratamiento preventivo intermitente de la malaria durante el embarazo en el centro de Mozambigue

Problema En las nuevas estrategias de la OMS para combatir la malaria durante el embarazo se recomienda el tratamiento preventivo intermitente, el uso de mosquiteros y una mejor gestión de los casos.

Enfoque Se diseñó un programa piloto de control de la malaria en el embarazo en Mozambique a fin de determinar las condiciones necesarias para emprender una expansión masiva.

Entorno local El Ministerio de Salud colaboró con una organización no gubernamental y una institución académica para establecer y seguir de cerca un programa piloto en dos distritos pobres con malaria endémica.

Cambios relevantes La aplicación del programa piloto se basó en el suministro de sulfadoxina-pirimetamina (SP), material para la administración de SP bajo observación directa, mosquiteros y una tarjeta prenatal modificada. Fue necesario levantar las restricciones formales aplicables a nivel nacional a la SP, y hubo que modificar el protocolo original porque la imprecisión de las estimaciones de la edad gestacional conllevaba la omisión de dosis de SP. Se descubrieron y resolvieron numerosas incompatibilidades con otras iniciativas de salud (incluidos programas de control de la sífilis, la anemia y el VIH), y se midieron diversos resultados e impactos: el 92,5% de 7911 mujeres recibieron al menos una dosis de SP, y el número medio de dosis de SP recibidas fue de 2,2. En la segunda visita prenatal, el 13,5% de las mujeres usaban mosquiteros. Por subgrupos (1167 para análisis de laboratorio; 2600 nacimientos), el uso de SP se asoció de forma significativa a concentraciones de hemoglobina mayores (10,9 g/dl en caso de 3 dosis; 10,3 si no se había recibido ninguna dosis), una menor parasitemia malárica (prevalencia del 7,5% en caso de 3 dosis; 39,3% si no se había recibido ninguna dosis) y un menor número de lactantes con bajo peso al nacer (7,3% frente a 12,5% en caso de 3 o cero dosis, respectivamente).

Enseñanzas extraídas Para extender masivamente las medidas de control a nivel nacional habrá que prestar atención al personal necesario, los suministros, la disponibilidad de mosquiteros, la política farmacéutica, la estimación de la edad gestacional y la armonización de las iniciativas verticales.

ملخص

المعالجة الوقائية المتقطعة للملاريا أثناء الحمل في وسط موزمبيق

المشكلة: توصى الاستراتيجيات الجديدة لمنظمة الصحة العالمية بشأن مكافحة الملاريا أثناء الحمل بإجراء معالجة وقائية متقطعة، واستخدام الناموسيات وتحسن التدبير العلاجي للحالات.

النهج: أعدُّ برنامج ارتيادي للمعالجة الوقائية المتقطعة للملاريا أثناء الحمل في موزمبيق بغرض تحديد المتطلبات اللازمة للنهوض بهذه المعالجة.

الإطار المحلى: عملت وزارة الصحة مع إحدى المنظمات غير الحكومية وأحد المعاهد الأكاديمية على إنشاء ورصد برنامج ارتيادي في مقاطعتَيْن فقيرتَيْن تتوطن فيهما الملاريا.

تغبُّرات ذات علاقة: تطلُّب تنفيذ البرنامج الارتيادي توفير كميات إضافية من عقار سلفادوكسين - ببرعيثامين، ومواد لإعطاء هذا العقار تحت المراقبة المباشرة، وناموسيات، وبطاقة معدَّلة للرعاية أثناء الحمل، مع الحاجة إلى التخلِّي عن قيود كتيِّب الوصفات الوطني حول السلفادوكسين - بيريميثامين. وتطلُّب البروتوكول الأصلى إجراء تعديل عليه بسبب مايؤديه عدم الدقة في تقدير العمر الحملي من تفويت لجرعات من هذا العقار. واكتُشف العديد من جوانب عدم التوافق مع مبادرات صحية أخرى (ما يشمل برامج مكافحة

الزهري، وفقر الدم وفيروس العوز المناعي البشري) وأمكن التغلُّب عليها. وقيست النواتج والتأثيرات الأساسية، حيث تلقّى 92.5% من 7911 سيدة جرعة واحدة على الأقل من سلفادوكسين - بيرعيثامين، مع كون متوسط عدد الحرعات المتلقاة 2.2 جرعة. وفي الزيارة الثانية أثناء الحمل، استخدم 3.5% من هؤلاء السيدات الناموسيات. وفي مجموعات فرعية (1167 سيدة خضعن للتحليلات المخترية، 2600 ولادة) ارتبط استخدام السلفادوكسين - برعيثامن ارتباطاً يعتد به إحصائياً بوجود معدلات هيموغلوبن أعلى (10.9 غ/دل إذا أخذت 3 جرعات و10.3 إذا لم تؤخذ أي جرعة) وانخفاض طفيليات الملاريا في الدم (معدل انتشار 7.5% إذا أخذت 3 جرعات و39.38% إذا لم تؤخذ أي جرعة) وعدد أقل من حالات انخفاض وزن الوليد عند ولادته (7.3% إذا أخذت 3 جرعات و12.5% إذا لم تؤخذ أي جرعة).

الدروس المستفادة: يتطلّب النهوض بهذه المعالجة على المستوى الوطني مزيداً من الاهتمام نحو توفير العاملين والإمدادات والناموسيات، ووجود سياسة دوائية، وتقدير للعمر الحملي، وتحقيق الانسجام بن المبادرات العمودية.

References

- 1. Desai M, ter Kuile FO, Nosten F, McGready R, Asamoa K, Brabin B, et al. Epidemiology and burden of malaria in pregnancy. Lancet Infect Dis 2007;
- 2. ter Kuile FO, Parise ME, Verhoeff FH, Udhayakumar V, Newman RD, van Eijk AM, et al. The burden of co-infection with human immunodeficiency virus type 1 and malaria in pregnant women in sub-saharan Africa. Am J *Trop Med Hyg* 2004;71:41-54.
- 3. A strategic framework for malaria prevention and control during pregnancy in the African Region. Brazzaville: WHO Regional Office for Africa; 2004.
- 4. Menéndez C, D'Alessandro U, ter Kuile F. Reducing the burden of malaria in pregnancy by preventive strategies. Lancet Infect Dis 2007;7:126-35.
- 5. Mapeamento de vulnerabilidade. Maputo: Ministério de Plano e Finanças;
- 6. A statistical profile of disparities in Mozambique: an overview of the situation of children and women based on findings from the 2003 Demographic and Health Survey. Maputo: UNICEF; 2005.

Preventing malaria during pregnancy in Mozambique

Paula E Brentlinger et al.

- Parise ME, Ayisi JG, Nahlen BL, Schultz LJ, Roberts JM, Misore A, et al. Efficacy of sulfadoxine-pyrimethamine for prevention of placental malaria in an area of Kenya with a high prevalence of malaria and human immunodeficiency virus infection. Am J Trop Med Hyg 1998;59:813-22.
- Iyer JK, Milhous WK, Cortese JF, Kublin JG, Plowe CV. Plasmodium falciparum cross-resistance between trimethoprim and pyrimethamine. Lancet 2001; 358:1066-7.
- Kobbe R, Marks F, May J, Meyer C. Editorial: Antifolates in prevention of HIV-associated opportunistic infections and in intermittent preventive treatment of malaria in Africa. *Trop Med Int Health* 2005;10:293-4.
- Brentlinger PE, Montoya P, Blanco Rojas AJ, Correia MA, Dgedge M, Saúte F, et al. Prevalence and predictors of maternal peripheral malaria parasitemia in central Mozambique. Am J Trop Med Hyg 2007;77:228-34.
- Rogerson S, Chaluluka E, Kanjala M, Mkundika P, Mhango C, Molyneux M. Intermittent sulfadoxine-pyrimethamine in pregnancy: effectiveness against malaria morbidity in Blantyre, Malawi, in 1997-99. *Trans R Soc Trop Med Hyg* 2000;94:549-53.
- van Eijk A, Ayisi J, ter Kuile F, Slutsker L, Otieno J, Misora A, et al. Implementation of intermittent preventive treatment with sulphadoxinepyrimethamine for control of malaria in pregnancy in Kisumu, western Kenya. *Trop Med Int Health* 2004;9:630-7.
- Barat L, Palmer N, Basu S, Worrall E, Hanson K, Mills A. Do malaria control interventions reach the poor? A view through the equity lens. Am J Trop Med Hyg 2004;71:174-8.
- Assessment of MIPESA country experiences in the adoption and implementation of malaria in pregnancy policies, including best practices and lessons learned. Kampala: Malaria in Pregnancy East and Southern Africa (MIPESA) Coalition; 2006.

- Worrall E, Morel C, Yeung S, Borghi J, Webster J, Hill J, et al. The economics of malaria in pregnancy: a review of the evidence and research priorities. Lancet Infect Dis 2007;7:156-68.
- Roll Back Malaria. Sulfadoxine-pyrimethamine (SP) for intermittent preventive treatment of malaria during pregnancy in areas of moderate to high-level SP resistance. Geneva: WHO; 2005.
- Van Eijk AM, Ayisi JG, Slutsker L, ter Kuile FO, Rosen DH, Otieno JA, et al. Effect of haematinic supplementation and malaria prevention on maternal anemia and malaria in western Kenya. *Trop Med Int Health* 2007;12:342-52.
- 18. Friis H. Micronutrient interventions and HIV infection: a review of current evidence. *Trop Med Int Health* 2006;11:1849-57.
- Greenwood B, Alonso P, ter Kuile FO, Hill J, Steketee RW. Malaria in pregnancy: priorities for research. *Lancet Infect Dis* 2007;7:169-74.
- Ward SA, Sevene EP, Hastings IM, Nosten F, McGready R. Antimalarial drugs and pregnancy: safety, pharmacokinetics, and pharmacovigilance. *Lancet Infect Dis* 2007;7:136-44.
- Fernandes N, Figueiredo P, do Rosário VE, Cravo P. Analysis of sulphadoxinepyrimethamine resistance-conferring mutations of *Plasmodium falciparum* from Mozambique reveals the absence of the dihydrofolate reductase 164L mutant. *Malar J* 2007;6:35.
- Brentlinger PE, Behrens CB, Micek MA. Challenges in the concurrent management of malaria and HIV in pregnancy in sub-Saharan Africa. *Lancet Infect Dis* 2006;6:100-11.
- Jamisse L, Balkus J, Hitti J, Gloyd S, Manuel R, Osman N, et al. Antiretroviralassociated toxicity among HIV-1-seropositive pregnant women in Mozambique receiving nevirapine-based regimens. *J Acquir Immune Defic* Syndr 2007;44:371-6.