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Community-based distribution of sulfadoxine-pyrimethamine for intermittent preventive treatment of malaria during pregnancy improved coverage but reduced antenatal attendance in southern Malawi

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Summary

OBJECTIVE To evaluate the impact of a 2-year programme for community-based delivery of sulfadoxine-pyremethamine (SP) on intermittent preventive treatment during pregnancy coverage, antenatal clinic attendance and pregnancy outcome.

METHODS Fourteen intervention and 12 control villages in the catchment areas of Chikwawa and Ngabu Government Hospitals, southern Malawi, were selected. Village-based community health workers were trained in information, education and counselling on malaria control in pregnancy and the importance of attending antenatal clinics and promoted these messages to pregnant women. In the intervention group community health workers also distributed SP to pregnant women.

RESULTS In the control area, coverage of intermittent preventive treatment during pregnancy (>2 doses) was low before (44.1%) and during the intervention (46.1%). In the intervention area, coverage increased from 41.5% to 82.9% ($P < 0.01$). Antenatal clinic attendance (>2 visits) was maintained in control villages at above 90%, but fell in intervention villages from 87.3% to 51.5% ($P < 0.01$). Postnatal malaria parasitaemia prevalence fell in women from both study areas during the intervention phase ($P < 0.05$). Increasing the coverage of intermittent preventive treatment during pregnancy to >40% did not significantly improve maternal haemoglobin or reduce low birthweight prevalence.

CONCLUSIONS Better coverage of community-based intermittent preventive treatment during pregnancy can lower attendance at antenatal clinics; thus its effect on pregnancy outcome and antenatal attendance need to be monitored.

keywords malaria, pregnancy, birthweight, anaemia, sulfadoxine-pyrimethamine, antenatal attendance, Malawi

Introduction

Despite high antenatal clinic (ANC) attendance in many African countries, relatively few pregnant women receive intermittent preventive treatment (IPTp) with sulfadoxine-pyrimethamine (SP) (World Health Organization 2005). Coverage remains below the Abuja target of at least 60% coverage and the more recent Roll Back Malaria goal of 80% (Hill & Kazembe 2006). In view of this, different approaches to IPTp delivery have been evaluated (Mbonye *et al.* 2007a,b). In Malawi, the effectiveness of IPTp with SP in preventing placental malaria is high (Filler *et al.* 2006), even when SP efficacy in pregnant women is falling (Msyamboza *et al.* 2007), although less than half of eligible women attending ANC received the recommended two doses of IPTp (Holtz *et al.* 2004; Roll Back Malaria Monitoring and Evaluation Report 2005). This low coverage relates to shortage of trained health workers, absence of safe drinking water for ingestion, late ANC attendance, staff misunderstanding and drug shortages (Ashwood-Smith *et al.* 2002; van Eijk *et al.* 2004).

Community-based distribution of IPTp could supplement ANC delivery and this approach requires appropriate evaluation. There are few previous studies of

community-based delivery of anti-malarials to pregnant women. A chloroquine chemoprophylaxis programme in Kenya achieved only 29% coverage, deemed to be due to lack of awareness and the drug's side effect of itching (Kaseje *et al.* 1987). In rural Gambia traditional birth attendants have been successfully used to deliver dapsone-pyrimethamine fortnightly, to both primigravidae and multigravidae (Greenwood *et al.* 1989). It is also important to consider potential negative effects of community based distribution and its potential influence on antenatal attendance.

Our aim was to assess the uptake of IPTp in a rural area of southern Malawi through a community-based distribution programme with village volunteers, some of whom had attended a rural literacy training programme whose curriculum included teaching on malaria control in pregnancy (Hogg *et al.* 2005).

Materials and methods

Study population

The study was conducted in Chikwawa District, southern Malawi between June 2002 and November 2004. This is a hot, dry and low-lying rural area whose population is mainly engaged in subsistence farming. The main crops are maize, sorghum, sugar cane and cotton. The rainy season is between December and March. There are two government hospitals in the district, Chikwawa and Ngabu, about 60 km apart, which offer free antenatal and delivery services. An Adolescent Girls Literacy Project (AGLIT) has been operating in Chikwawa District since 1997. AGLIT is a community-based education project for illiterate adolescent girls which aims to improve their health seeking behaviour through combined literacy and health education (Hogg *et al.* 2005).

Study intervention

Community-based distribution of IPTp SP was linked to the AGLIT project as a means of improving awareness and understanding of this intervention in these rural communities. Villages which participated in the AGLIT programme in the catchment areas of Chikwawa and Ngabu Hospitals were selected. Fourteen villages were selected in the Chikwawa Hospital catchment area as the control group, and 12 in the Ngabu Hospital catchment area as the intervention group. In the intervention population, village meetings informed people about malaria during pregnancy, the importance of antenatal care and IPTp made available through a community health worker (CHW) based in each village as well as at ANCs. The meetings held in the control population varied slightly from those of the intervention villages and the emphasis was placed on providing postnatal health care in an attempt not to alter the women's current antenatal practices. In the control area women were asked to enrol with the CHW so that their baby could be weighed at birth and the mother tested for anaemia and malaria after delivery. The fact that SP was available through the antenatal clinic was mentioned only if brought up in the course of the discussions. SP for IPTp in Malawi at the time of the study was only available at health facilities; anti-malarials were not sold in grocery stores and there were no private pharmacies in these rural areas.

Community health workers gave three SP tablets under direct observation at the first contact only if women had felt baby movements or if the fundus was 18 weeks or more (fundal height mid-way between symphysis pubis and umbilicus). Women with a history of allergy to SP or cotrimoxazole (Bactrim) or taking SP within the previous month were not given IPTp SP. A second or third dose of IPTp SP was provided at least 1 month after the first or second dose if these doses had not been obtained already at the ANC. Health staff at the hospital ANCs recorded all SP doses they provided on the women's antenatal card. CHWs also recorded village-based SP that was administered by placing a sticker on the same card in order to avoid multiple dosing. The pre-intervention phase was completed between June and November 2002; the intervention took place between December 2002 and November 2004, in order to cover two wet and two dry seasons.

Selection and training of community health workers

Women who had taught the AGLIT curriculum in the selected villages acted as CHWs in their respective villages. If there was no female teacher, another literate woman was chosen by the village. Each village had one CHW. In both control and intervention villages CHWs were trained to collect socio-demographic and obstetric factors and information on malaria and bed net use using a semi-structured questionnaire. They were trained to encourage pregnant women in their villages to attend the ANC at their respective hospitals. They were also trained to measure birth weight (nearest 100 g) using a hanging dial scale (Chasmor, London, UK). It was necessary to train CHWs in intervention villages to measure fundal height by tape measure in order to avoid SP prescription to women in the first trimester.

Community awareness and enrolment of participants

At the beginning of the intervention, community awareness meetings were held in all selected villages; later, village meetings were conducted every 3 months in each village to discuss challenges and issues which had arisen. Pregnant women either voluntarily approached CHWs for

enrolment in the study or in some cases were actively sought out by the CHW. At the time of enrolment informed consent was requested. The intention was to enrol all pregnant women in the selected AGLIT villages. In control and intervention groups, women were advised to start or continue hospital antenatal attendance. In the intervention villages, they were also advised to return to the CHW if they did not receive SP at the antenatal clinic. All women were advised to inform their CHW within 2 days of their home delivery, or if there was pregnancy loss. Hospital deliveries were monitored by research staff in both intervention and control areas. Birth weight at hospital deliveries was measured by midwives, while CHWs collected this information at home deliveries. The hanging scales used in the village were compared to the hospital scales using standard weights between 1 and 4 kg. Scales were calibrated using standard weights before each weighing.

Laboratory tests

A post-natal finger prick blood sample for malaria microscopy and haemoglobin assessment was obtained by mobile health workers within 1 week of delivery and at the same time as birth weight was measured. Haemoglobin (Hb) was assessed by HaemoCue (Angelholm, Sweden). A thick blood smear was made for malaria parasitaemia and stained with Field's stain. A slide was considered negative if no asexual parasites were seen after counting 200 white blood cells (Trape 1985). Parasite density was computed assuming a mean WBC count of 8000/μl. Women who were severely anaemic (Hb <8 g/dl) were referred to the hospital and SP treatment was provided for those with positive malaria smears.

Data analysis

Data were analysed using SPSS for Windows (SPSS, Chicago, IL, USA) and Epi-Info 2004 (Centres for Disease Control and Prevention, Atlanta, GA, USA). Analysis was based on intention-to-treat, defined by pregnancy enrolment through a CHW in either study area. Chi-square test or Fisher's exact test were used for categorical and student's *t*-test or Mann–Whitney test for continuous variables. Women under 20 years of age were considered adolescents. Anaemia was defined as haemoglobin <11.0 g/dl for moderate and <8.0 g/dl for severe. Low birthweight (LBW) was defined as <2500 g. For all births, weight and maternal haemoglobin were plotted by day of weighing after delivery (days 1–7). These were adjusted to correct for the average daily change by stratified analysis for day of weighing in the first week. Prevalence risk ratios and 95% CI were estimated for LBW or anaemia prevalence in primigravidae compared to multigravidae as these indicatiors have been shown to relate to malaria exposure in pregnancy (Brabin 1991; Savage *et al.* 2007). This was performed in Stata 8.0 (Stata Corporation 2003) using the generalised estimating equations algorithm by multiple regression with an independent correlation matrix to account for clustering. Only singleton pregnancies were included in the analysis.

The study was carried out in 14 intervention villages and 12 control group villages. The average village size was about 500 people. The total population covered was approximately 14 000 people, with about 750 expected pregnancies per year, with approximately 250 primi- and secundigravidae. ANC attendance and SP coverage was assessed after delivery, with any visit or administration of IPTp-SP counted irrespective of whether it occurred before or after enrolment within the study.

The Malawi College of Medicine Research Ethical Committee and the Liverpool School of Tropical Medicine Ethical Committee granted ethical approval.

Results

Educational and pregnancy characteristics before the intervention were comparable between the two groups (Table 1), although women in the intervention area

Table 1 Antenatal and delivery characteristics for the two study areas before the intervention

Characteristic	Control area *n* = 107 (%)	Intervention area *n* = 87 (%)
Socio demographic		
Primigravidae	28 (26.2)	22 (25.3)
Adolescent	20 (18.8)	17 (19.5)
School attendance*	28 (83.3)	68 (78.0)
AGLIT attendance	32 (29.9)	27 (31.0)
Married	99 (93.0)	78 (89.7)
Subsistence farming	103 (96.5)	79 (90.8)
Malaria related		
Bed net ownership	13 (12.2)	2 (2.3)
≥2 ANC visits	103 (96.3)	76 (87.3)
≥2 SP doses	47 (43.9)	36 (41.4)
Iron supplements	95 (88.8)	81 (93.1)
Malaria prevalence†	9 (8.4)	9 (10.3)
Anaemia (<11.0 g/dll)†	82 (76.6)	71 (81.6)
Anaemia (<8.0 g/dl)†	28 (26.1)	20 (22.9)
Low birthweight	6 (5.6)	8 (9.2)

AGLIT, Adolescent Girls Literacy Project; ANC, antenatal clinic; SP, sulfadoxine-pyrimethamine.
*>3 years.
†Post-natal values between 1–7 days.

attended ANC less often ($P = 0.041$) and owned fewer bed nets ($P = 0.022$). Post-natal malaria prevalence was low in both study areas (<10.5%). Pre-intervention mean birth weight was 3191 g (±379) in the control and 3,121 g (±492) in the intervention area.

In the intervention phase, 878 women in the control (240 primigravidae) and 874 in the intervention area (244 primigravidae) were enrolled and followed to delivery. Coverage estimates during the intervention phase for two or more SP doses, or two or more ANC visits, are shown in Table 2 in 6-month intervals. In control villages, the overall coverage of two or more SP doses (45.9%) did not differ from that in the pre-intervention phase (43.9%), with the lowest coverage observed in the last 6-month period (30.1%). ANC attendance for all pregnant women remained high and uniform throughout the 2 years (96.3% pre and 92.9% post-intervention). In the intervention villages, uptake of two or more SP doses increased from 41.4% in the pre-intervention to an average of 72.7% during the intervention phase. There was a significant linear trend for this change in the intervention villages, with the highest uptake in the last 6-month period (82.1%), (chi square trend, $P < 0.001$). This was paralleled by a sequential decrease in ANC attendance which averaged 66.0% during the intervention against 87.3% before and with the lowest ANC attendance in the last 6-month interval (51.5%). No differences between primigravidae and multigravidae were found. The reduced ANC attendance in the intervention group was associated with a lower uptake of iron supplementation, based on number of iron tablets distributed, than in the control group (45.2% *vs.* 51.2%, $P < 0.01$). Among women who visited the ANC, SP coverage was higher in the control than in intervention villages although there was no difference in the gestational time of starting ANC between the two groups; 43–46% of deliveries occurred in health facilities in both arms.

Table 3 shows that post-natal moderate or severe anaemia prevalence was higher in primiparae and multiparae from the intervention area than in women from the control area. This difference was not significant for severe anaemia. For malaria and LBW outcomes prevalence estimates were also higher in women from the intervention

Table 2 Coverage (%) with ≥2 SP doses or ≥2ANC visits during the intervention

	Control area		Intervention area	
Period	≥2 SP doses	≥2 ANC visits	≥2 SP doses	≥2 ANC visits
Pre-intervention	43.9 (107)	96.3 (107)	41.4 (87)	87.3 (87)
December 2002 to May 2003	61.5 (135)	91.8 (134)	51.6 (219)	78.7 (202)
June 2003 to November 2003	55.5 (173)	93.6 (173)	72.4 (181)	75.3 (174)
December 2003 to May 2004	50.9 (267)	96.6 (266)	81.5 (238)	65.1 (238)
June 2004 to November 2004	30.1 (322)	89.8 (322)	82.1 (274)	51.5 (274)
All post-intervention	45.9 (897)	92.9 (895)*	72.7 (912)	66.0 (888)*

ANC, antenatal clinic; SP, sulfadoxine-pyrimethamine.
Brackets: sample size.
*Data on numbers of ANC visits not available for two women in the control area and 24women in the intervention area.

Table 3 Malaria-related outcomes

	Primiparae				Multiparae			
Outcome %	Control area (236)	Intervention area (242)	Prevalence risk ratio (95% CI)	*P*-value	Control Area (637)	Intervention area (618)	Prevalence risk ratio (95% CI)	*P*-value
Hb <11.0 g/dl	78.4	86.8	1.78 (1.12–2.85)	0.016	72.7	80.1	1.45 (1.13–1.86)	0.004
Hb <8.0 g/dl	13.1	15.3	1.10 (0.68–1.77)	0.695	10.3	16.0	1.33 (0.97–1.78)	0.061
Malaria prevalence	1.7	7.0	3.56 (1.41–9.02)	0.007	4.2	4.3	1.06 (0.65–1.74)	0.806
Low birthweight	12.6	18.4	1.77 (1.09–2.89)	0.022	10.3	13.8	1.60 (1.15–2.22)	0.005

area, except for malaria prevalence in multiparae (Table 3).

In intervention villages, LBW prevalence was 18.4% in primiparae and 13.8% in multiparae; in control villages the corresponding values were 12.6% and 10.3%. The relative risk for excess LBW in primiparae compared to multiparae was 1.35 (0.97–1.88, $P = 0.07$) in the intervention area and 1.23 (0.82–1.84, $P = 0.32$) in the control area. The risk estimates for excess post-natal anaemia (Hb <8.0 g/dl) in primiparae compared to multiparae were 0.95 (0.6–1.4, $P = 0.79$) in intervention groups and 1.27 (0.8–1.9, $P = 0.25$) in control groups. There were three still births and one perinatal death in the intervention area, one stillbirth and four perinatal deaths in the control area.

Discussion

This community-based intervention study showed that it was feasible and acceptable to train female volunteers to distribute IPTp-SP to pregnant women in a poor rural area of southern Malawi. This approach significantly improved coverage (>80%) with two intermittent treatments. However, the intervention was also associated with significantly lower ANC attendance, which by the end of the observation period resulted in almost half of enrolled mothers failing to attend at least two ANC. This pattern was observed for both primigravidae and multigravidae. Reluctance to attend ANC could relate to efficiency and professionalisation of this care with a preference to opt out provided IPTp – SP was made available elsewhere through the community. In The Gambia reluctance of women to attend for ANC has been recently described and issues of acceptability warrant greater consideration (Stokes *et al.* 2008). Cross-over attendance between the two study hospitals is considered unlikely in view of the distance separating them and the transport costs required, which are considerable for these poor rural communities. Results from a community IPTp distribution study from Uganda reported higher ANC attendance (4+ visits, 76.1%) in women accessing Health Units compared to those accessing IPTp through CHWs, traditional birth attendants or drug shop vendors (56.8%) (Mbonye *et al.* 2007a,b), which supports the findings in Malawi that ANC decreases with these alternative delivery approaches for IPTp.

The negative effect on ANC attendance in Malawi was sufficiently large to seriously reduce the uptake of haematinic supplementation routinely available at the ANC. The higher IPTp coverage in the intervention villages should have resulted in improved anaemia and birth weight outcomes. Instead, pregnancy outcomes were poorer in terms of post-natal anaemia, low birth weight and malaria prevalence in intervention than in control villages. In both study groups post-natal malaria prevalence was low (<10%), and lower than in previous studies which reported estimates of 33.3% for primiparae and 18.1% for multiparae who had received two doses of SP (Verhoeff *et al.* 1998). Reduced malaria transmission over the 2-year study period may explain such low prevalence, although bed net usage was universally rare and likely to have only a small influence on the prevalence of infection. Post-natal malaria prevalence was measured which may lead to a lower prevalence due to rapid parasite clearance from peripheral blood with the absence of the placenta after delivery. In Burkina Faso in primi- and secundiparae malaria prevalence was 23.2% at delivery and 5.8% during the week after delivery (S. Gies, unpublished data).

Post-natal prevalence of severe anaemia (Hb <8.0 g/dl) was lower in the intervention phase compared to pre-intervention estimates. This reduction was observed in both study groups, despite their difference in SP coverage. There was almost no difference in moderate anaemia (Hb <11.0 g/dl) prevalence in either group comparing pre- and post-intervention phases. The time of the pre-intervention phase corresponded mostly to the dry season, whereas the intervention period covered two rainy and two dry seasons and this difference could be reflected in differences in malaria exposure risk and study outcomes between the study phases. This is a limitation of this study and a 12-month pre-intervention covering both wet and dry seasons would have been preferable. The excess risk for severe anaemia in primiparae compared to multiparae was higher in the control than in the intervention area (1.27 *vs.* 0.95), suggesting a greater reduction in this risk in the intervention area, although it did not reach statistical significance. Previous estimates comparing this excess risk used antenatal haemoglobin values which are preferable to post-natal estimates because of dilutional changes occuring after delivery due to maternal blood loss and possible dehydration.

It is uncertain what the increased IPTp coverage from a pre-intervention average of 45.9–72.7% was able to achieve in terms of pregnancy outcome. The prevalence ratios for the excess risk estimates for low birth weight or maternal anaemia in primiparae compared to multiparae when plotted on reference nomograms (Brabin *et al.* 1999; Savage *et al.* 2007) for each study area would indicate that continued malaria exposure was occurring despite the large difference in SP coverage between the areas. Any deterioration in pregnancy outcomes related to the poorer ANC attendance in the group with high SP coverage may have been limited by this high coverage. Nevertheless pregnancy outcomes did not improve in these women compared to the control group despite their high SP coverage, suggesting that to observe a major impact at population level even

higher coverage is needed. There is good evidence that at an individual level IPTp is effective (ter Kuile *et al.* 2007), although we still have little evidence demonstrating the community effectiveness of the intervention, or how this relates to coverage levels or pregnancy outcomes. This information is required in order to assess the relative benefits of high SP coverage. These studies are complex, require large sample sizes, cluster randomisation and need to take into account changing access patterns to ANC services which may be influenced by availability of SP, as well as bed net use, climatic influences on malaria transmission (Uddenfeldt-Wort *et al.* 2006) and the proportion of adolescent pregnancies (Uddenfeldt-Wort *et al.* 2008). A recent large community effectiveness trial from Burkina Faso has assessed the effectiveness of a community health promotion campaign with IPTp SP (Gies *et al.* 2008). Despite higher coverage with two doses of SP in the intervention villages, this did not translate into a significant difference in pregnancy outcomes, indicating that a major impact of IPTp-SP at community level can be detected only with extremely high coverage, possibly above the current Roll Back Malaria goal of 80% by 2010 (WHO Global Strategy 2005). New intervention approaches to improve SP coverage have been assessed in Uganda which improved coverage, although there was more anaemia in the new approaches arm and no differences in birth weight prevalence were demonstrated (Mbonye *et al.* 2007a,b, 2008).

With SP resistance increasing, the duration of its use for IPTp is limited and alternative anti-malarial combinations are being evaluated. With the expected future changes in drug selection, we need to establish community-based approaches for evaluation and monitoring as these will provide effectiveness estimates with different drug delivery choices and strategies. Other delivery strategies should be linked to ANC health services, so that pregnant women do not have to make conflicting decisions.

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