Research

Impact of prepackaging antimalarial drugs on cost to patients and compliance with treatment

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Objective To examine the extent to which district health teams could reduce the burden of malaria, a continuing major cause of mortality and morbidity, in a situation where severe resource constraints existed and integrated care was provided.

Methods Antimalarial drugs were prepackaged into unit doses in an attempt to improve compliance with full courses of chemotherapy.

Findings Compliance improved by approximately 20% in both adults and children. There were 50% reductions in cost to patients, waiting time at dispensaries and drug wastage at facilities. The intervention, which tended to improve both case and drug management at facilities, was well accepted by health staff and did not involve them in additional working time.

Conclusion The prepackaging of antimalarials at the district level offers the prospect of improved compliance and a reduction in the spread of resistance.

Keywords Antimalarials/administration and dosage; Drug packaging; Patient compliance; Drug costs; Prescriptions, Drug; Ghana (*source: MeSH*).

Mots clés Antipaludique/administration et posologie; Emballage médicaments; Observance prescription; Coût médicament; Ordonnance médicale médicament; Ghana (*source: INSERM*).

Palabras clave Antimaláricos/administración y dosificación; Embalaje de medicamentos; Cooperación del paciente; Costos en drogas; Prescripción de medicamentos; Ghana (*fuente: BIREME*).

Introduction

Malaria is a public health problem in more than 90 countries inhabited by 40% of the world's population. It is responsible for up to 500 million clinical episodes and 2.7 million deaths a year, predominantly among young children in sub-Saharan Africa (*1*). In tropical Africa the total cost of malaria in terms of health care, treatment and lost productivity is estimated to be over US$ 1800 million a year (*2*). In Ghana, malaria is the principal cause of lost days of healthy life (*3*). Chloroquine is still effective against the disease and remains the first-line drug of choice for treatment (*4*).

As in many other countries of sub-Saharan Africa, Ghana has a decentralization policy allowing districts to decide how to organize their health services. Vertical programmes no longer exist and districts are required to provide integrated health care. District health management teams are expected to plan and implement health services on the basis of perceived needs and to explore financing mechanisms with a view to supplementing the resources received from central government. They also have to explore innovations and carry out operational research in order to ensure that the services are acceptable and affordable to the people (*5*).

In 1995 a meeting of district officers in Ghana considered the problems posed by malaria. The officers each undertook preliminary situation analyses of the status of malaria and its control, and it emerged that the cost of treatment to patients was high, largely because of the dispensing of excessive volumes of chloroquine and the prescribing of chloroquine injections for uncomplicated malaria. Attention was also drawn to long waiting times at dispensaries and poor compliance with recommended treatment regimens (*6*). The district health management teams decided to implement their own interventions with a view to improving matters. The present paper describes a study conducted in Wenchi

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District, which was designed primarily to assess the effect of prepackaging antimalarials on compliance. It also examined the efficiency of malarial management at the facility level, costs to patients, waiting times and acceptance by district health staff. Approval for the study was given by the Ethics Committee of the Ministry of Health through its Health Research Unit, and by the Brong Ahafo Regional Health Administration and the Wenchi District Assembly.

Methods

Study area
Wenchi District is in Brong Ahafo Region and lies within two of the ecoepidemiological areas of malaria transmission (7). The northern part falls within the northern savanna area, while the southern part falls within the tropical rain forest. Malaria transmission is intense, stable and perennial, with slight seasonal variations. Peak transmission occurs shortly after the rains. The prevalence of parasitaemia is estimated to be between 45.9% and 46.8%. The commonest species is *Plasmodium falciparum* and the principal vector is *Anopheles gambiense* (8). Malaria continues to be the main cause of morbidity and mortality. Severe and complicated cases account for nearly 40% of the cases seen at the district hospital (9). Chloroquine is the only antimalarial drug allowed to be used at health centres, health posts and rural clinics (10).

Intervention
The six health facilities selected for the study were randomly allocated to an intervention group of three and a control group of three. In the intervention facilities, patients diagnosed as having uncomplicated malaria were treated with prepackaged antimalarials, while in the control group the routine way of prescribing drugs continued. Malaria was diagnosed clinically since microscopy was not available. The prepackaged drugs, chloroquine and paracetamol, were available in seven treatment regimens based on the weights of the patients in accordance with a modified WHO protocol (Table 1). Tablets were prepackaged at the district level by means of a simple instrument for cutting and sealing polythene bags. The packs of chloroquine tablets were divided into three compartments, each containing a daily dose. Half-tablet doses were obtained by breaking the tablets manually. Syrups were prepackaged at the facility in plastic bottles purchased by the district health management team. Cost recovery being a feature of the Ghanaian health system, no attempt was made to vary government policy in this respect. Patients were charged the standard rates for the pharmaceutical products. Patients receiving tablets at the intervention facilities paid for the prepackaging, the cost of which was almost the same as that of prescribing envelopes in the control facilities, and those requiring chloroquine syrup were charged a small fee to cover the cost of the bottles.

The staff in both groups of facilities were aware of the intervention.

Data collection
Patients were observed at the dispensaries in both groups and a checklist was used to record waiting times and the type of advice given by dispensers. Waiting time was defined as the time elapsing between the presentation of a prescription by a patient and the receipt of the prescribed drug. With the help of a structured questionnaire, patients were interviewed to obtain information on the number of drugs given, the amount paid, and the patients' views on whether the cost was too high. The outpatient cards of interviewed patients were examined to confirm the numbers, types and dosages of drugs prescribed, the clinical features presented, the examinations conducted and the diagnoses made. Consulting room registers and the daily drugs issue books were reviewed to determine the total numbers of malaria cases seen, the ages of patients, and the types and quantities of antimalarials dispensed. This information was used to determine excess consumption, a measure of consumption at the facility level.

Patients diagnosed as having malaria and treated with chloroquine were interviewed in their homes on the fourth day after attending the clinic. Compliance was deemed to have occurred if the drug had been taken on the three intervening days as prescribed. No prior notice of follow-up visits was given, although their likelihood was mentioned to patients when informed consent for participation in the study was obtained. Again with the help of a questionnaire, patients were interviewed in order to determine whether medication was taken according to the advice of the prescriber or dispenser, and to obtain information on the method of taking the medicine, the duration of treatment, and reasons for non-compliance. In addition, the interviewers asked to see any tablets or syrup that had not been taken. Focus group discussions were held with patients and staff on their perception and acceptance of the prepackaging.

Analysis
Mean waiting times were determined for both groups and other variables were summarized as proportions. Excess consumption for a period was calculated as:

$$\frac{(\text{actual consumption} - \text{estimated ideal consumption}) \times 100}{\text{estimated ideal consumption}}.$$

The estimated ideal consumption was based on age groups. All patients who were diagnosed as having malaria on the day of data collection were included in the sample. The differences in outcome between the intervention and control groups were evaluated by means of χ^2 tests; P values below 0.05 were considered significant. Qualitative data were analysed by collating all themes that emerged in responses during focus group discussions and observations.

Table 1. **Prepackaging regime**

Group	Age range	Weight range (kg)	Chloroquine			Paracetamol
			Day 1	Day 2	Day 3	
1	0–6 months	3.4–7.4	5 ml	5 ml	2.5 ml	5 ml three times a day
2	7–11 months	7.5–9.9	7.5 ml	7.5 ml	2.5 ml	5 ml three times a day
3	1–3 years	10.0–14.4	10 ml	10 ml	5 ml	10 ml three times a day
4	4–6 years	14.5–18.4	15 ml	15 ml	7.5 ml	10 ml three times a day
5	7–11 years	18.5–34.9	2½ tablets	2½ tablets	1 tablet	2 tablets when necessary
6	12–15 years	35.0–59.9	3 tablets	3 tablets	1½ tablets	2 tablets when necessary
7	16 years and above	60.0 and above	4 tablets	4 tablets	2 tablets	2 tablets when necessary

Results

Observations were made on 654 patients, 314 and 340 of whom visited the intervention and control facilities respectively. They were interviewed and their outpatient cards were reviewed. For the compliance aspect of the study, 509 patients were followed up and interviewed, 262 and 247 of whom were treated at the intervention and control facilities respectively. In both phases there were no significant differences in basic characteristics between the groups (Table 2).

The mean waiting time at dispensaries was 5.3 minutes in the intervention facilities and 13.8 minutes in the control facilities (Table 3). The 50% reduction was statistically significant ($P < 0.001$). One patient spent 270 minutes in a control facility because she had to find a bottle in which to put the prescribed syrup. The same counselling was given in both groups.

There was a 50% reduction in the total cost. The average cost was $ 0.72 in the intervention facilities and $ 1.38 in the control facilities, a significant difference ($P < 0.001$). Patients from the control facilities perceived the amount paid as high. The average numbers of drugs prescribed at the intervention and control facilities were 2.9 and 3.7 respectively. The smaller volumes of syrup and fewer tablets prescribed at the intervention facilities resulted in reduced excess consumption.

Of the patients in the intervention group, 98.3% were weighed, whereas in the control group only 26.1% were weighed, even though functioning scales were available in both groups. Prescribing was more correct in the intervention facilities than in the control facilities. As the prepackaged drugs were dispensed according to the weights of the patients, the prescribers in the intervention facilities were compelled to weigh the patients. A substantial number of adults weighed far less than 60 kg and therefore received 1125 mg chloroquine base instead of the usual adult dose of 1500 mg.

Compliance was over 20% higher in the intervention group than in the control group. For patients who were prescribed tablets, compliance in the intervention group was 82.0%, whereas in the control group it was 60.5% (Table 4). For those prescribed the syrup, compliance was 54.3% in the intervention group and 32.5% in the control group. These differences were significant ($P < 0.001$). A high proportion of the patients in the control group who did not comply said that this happened either because they did not understand the instructions given or because they forgot them. For the intervention group, non-compliance was largely attributable to side-effects (Table 5). The difference was statistically significant ($P < 0.001$).

In neither group was compliance related to educational status.

Of the non-compliant patients on tablets, 85.5% took less than the required amount of chloroquine, while 59.0% of those on syrup took more than the required amount.

During focus group discussions the staff at the intervention facilities felt that prepackaging was a good idea and they were very enthusiastic about the intervention. The medical assistants said that prepackaging made it easier for them to manage the drug supplies and that the monitoring of drugs issued to the dispensaries was easier and less time-consuming. They agreed that prepackaging had an indirect influence on their prescribing habits in that they tended to prescribe what they had prepackaged. It did not add to their workload, and improved teamwork since most of them came together to do the prepackaging. They suggested that other commonly used drugs should be prepackaged.

The patients approved because prepackaging made it easier for them to remember how to take the prescribed medicine. Some women commented that they no longer needed anybody to read instructions for them because looking at the packs was enough. The patients greatly appreciated being given syrups in cleaner bottles and tablets in polythene. They no longer had to look for bottles, which previously had not always been properly washed because of pressures of time. They were, however, unhappy about reduced volumes of syrup. Most patients would have preferred to have excess drugs, especially syrups, for use in the event of another episode of malaria. They were particularly happy that their children were being weighed.

Discussion

This study has demonstrated that prepackaging reduces waiting time. The 50% reduction in waiting time at dispensaries was achieved because time was not spent on counting tablets and pouring syrup while patients were waiting and, most importantly, because no time was wasted in looking for bottles to hold syrup. This was significant because long waiting times have been perceived as a reflection of poor quality of service and identified as one of the causes of poor utilization (11). Hence any measure that reduces waiting times is likely to increase utilization, which has traditionally been at relatively low levels in Ghana. Furthermore, reduced delays in starting treatment could, in some cases, improve outcomes (12).

This study has demonstrated that prepackaging reduces the cost of treatment to the patient because smaller volumes of syrup and fewer tablets are dispensed. Prepackaging per se may not directly reduce polypharmacy and the prescription of injection, but in this case it did indirectly influence prescribing habits. The medical assistants in charge, having supervised the prepackaging of oral chloroquine and paracetamol, and having arranged the drugs for easy dispensing, were motivated to prescribe what they had packed. The prescribers were all aware of the study and therefore the possible influence of being observed on their prescribing habits was probably similar in both groups. In Ghana, as in most developing countries, the cost of treatment is inversely related to utilization (13, 14). There is also growing evidence that the high cost of treatment makes people delay longer than they would otherwise before seeking care (12). Both policy-makers and the general public would welcome any intervention that reduced cost without compromising effectiveness or quality.

Furthermore, prepackaging can improve the utilization of public health services by reducing temporary shortages through the elimination of excess consumption. Such shortages of drugs were observed in the control facilities, one of which used up its ten-week stock of drugs in eight weeks. Drug shortages at health facilities can also contribute to poor utilization of public health services (11).

With regard to long-term malaria control, the most important result of the present study is the demonstration that prepackaging improves compliance. A similar study in China's Hunan Province showed that blister packaging of antimalarials improved compliance by approximately 20% (15). The use of interviews with patients and counts of tablets may lead to the overestimation of compliance (16), as there is scope for manipulation by patients. Yet this approach remains the most frequently recommended and most widely used for measuring compliance, because it is cheap, uncomplicated and rapid, and does not require highly skilled personnel and sophisticated equipment (17). Since the method used for measuring compliance was the same in both the intervention group and the control group, bias

was probably obviated. The prepackaging not only made it easier for the dispensers to give instructions to patients but also made it easier for the patients to

Table 2. Basic characteristics of study groups

	Intervention ($n = 262$)	Control ($n = 247$)	P-value
Age group (years)			
Under 1	37 (14.1)[a]	32 (13.0)	
1–3	50 (19.1)	45 (18.2)	
4–6	26 (9.9)	20 (8.1)	0.910
7–15	39 (14.9)	38 (15.4)	
≥ 16	110 (42.0)	112 (45.3)	
Sex			
Male	100 (38.2)	97 (39.3)	0.798
Female	162 (61.8)	150 (60.7)	
Education			
None	165 (63.0)	144 (58.3)	
Primary	82 (31.3)	88 (35.7)	0.549
Other	15 (5.7)	15 (6.0)	

[a] Figures in parentheses are percentages.

Table 3. Comparison of main variables in phase 1 between intervention and control groups

Variables	Intervention ($n = 314$)	Control ($n = 340$)	P-value
Waiting time			
Mean waiting time	5.3 minutes	13.8 minutes	<0.001
Maximum waiting time	22 minutes	270 minutes	
Cost of treatment			
Average cost	US$ 0.72	US$ 1.38	<0.001
Maximum cost	US$ 2.00	US$ 6.50	
Amount paid considered high	22 (7.0)[a]	48 (14.1)	<0.001
Prescription			
Mean number of drugs prescribed	2.9	3.7	<0.001
Injections prescribed	6 (1.9)	34 (10.0)	<0.001
Correct prescription	293 (93.3)	250 (73.5)	<0.001
Consumption	−3.1%	71.2%	<0.001

[a] Figures in parentheses are percentages.

Table 4. Compliance in intervention and control groups

	Intervention	Control	P-value
Tablets	$n = 167$	$n = 152$	
Yes	137 (82.0)[a]	92 (60.5)	<0.001
No	30 (18.0)	60 (39.5)	
Syrup	$n = 95$	$n = 95$	
Yes	52 (54.7)	31 (32.6)	<0.001
No	43 (45.3)	64 (67.4)	
Total	$n = 262$	$n = 247$	
Yes	189 (72.1)	123 (49.8)	<0.001
No	73 (27.9)	124 (50.2)	

[a] Figures in parentheses are percentages.

Table 5. **Reasons given for non-compliance by patients in intervention and control groups**

Reasons	Intervention group (numbers of patients)	Control group (numbers of patients)
Message unclear	33	74
Forgot instructions	0	14
Side-effects	35	31
Felt better	5	2
Lost/spoilt	0	3
Total	**73**	**124**

understand what was said by the dispensers and remember how to take the treatment. The prepackaging served to remind patients how to take the medication and to protect it so that they had the opportunity to complete the treatment regimen. This is important in Ghana, where chloroquine, the cheapest antimalarial, is still effective. Studies in southern Ghana indicate that resistance to chloroquine in *P. falciparum* is still generally low (*18*). The prepackaging of drugs can be expected to result in more patients taking the full treatment regimen, thereby preventing the development of resistance and extending the time before it will be necessary to switch to a more expensive drug for first-line treatment. The prepackaging also improved stock control at the intervention facilities. It became easier and less time-consuming for the managers of health facilities to conduct regular monitoring of the drugs issued to the dispensaries and prevented wastage.

This intervention is potentially sustainable because the materials used are readily available and cheap, and, more importantly, acceptable to both general populace and health workers. The cost of prepackaging is recovered from patients. The health services (district health management teams and health institutions) only need seed capital for the purchase of a sealing machine and polythene bags. The results of the study suggest that the investment would be worthwhile.

Some patients were happy to receive excess quantities of drugs so that they could use them for subsequent episodes of illness in their households. These patients were dissatisfied with the reductions in quantities prescribed in the intervention group, despite the lower costs. Although this group was a minority, there was evidently a need to inform households that chloroquine was unstable and should not be kept for long periods in the home. Furthermore, chloroquine tablets packed in polythene bags may disintegrate within a month, especially if not stored in a dry, dark place (*19*). When the intervention is introduced on a wider scale, therefore, it is proposed to ensure that all prepackaged tablets be dispensed within a month after packaging and that syrups be dispensed within two weeks.

However, the findings of the study are overwhelmingly positive, showing that the intervention is workable at the district level with the use of low-level technology; that it is easy to implement, and that it has many other advantages. Currently, the system is being expanded to the regional level in order to establish whether it can be sustained on an increased scale.

Several studies have shown that a large proportion of malaria cases are treated outside the public sector with over-the-counter drugs used at inadequate doses (*20–24*). Consequently, there are grounds for recognizing the role of home treatment and drug shops in the management of malaria and for incorporating them into existing control strategies (*24*). Prepackaging could be one of the strategies for making chloroquine available to communities for home management. This would go a long way towards reducing costs, including direct costs and the opportunity costs of travelling and waiting time (*25*), and would help to provide children with prompt and adequate treatment of presumptive episodes of clinical malaria (*26*). ∎

Résumé

Impact du préconditionnement des antipaludiques sur le coût pour le patient et l'observance du traitement

Objectif Examiner dans quelle mesure les équipes sanitaires de district ont pu réduire la charge du paludisme, une cause majeure de morbidité et de mortalité, dans une situation où les ressources étaient sévèrement limitées et où les établissements dispensaient des soins de santé intégrés.

Méthodes Les antipaludiques étaient préconditionnés en doses unitaires pour tenter d'améliorer l'observance de la chimiothérapie sur une cure complète.

Résultats L'observance a été améliorée d'environ 20 % chez l'adulte comme chez l'enfant. On a observé une réduction de 50 % du coût pour les patients, de l'attente au dispensaire et du gaspillage de médicaments sur place. L'intervention, qui tendait à améliorer à la fois la prise en charge des cas et la gestion des médicaments au niveau du dispensaire, a été bien acceptée par le personnel soignant et n'a pas entraîné d'augmentation du temps de travail.

Conclusion Le préconditionnement des antipaludiques au niveau du district permet d'envisager une amélioration de l'observance et une diminution de la propagation de la résistance.

Resumen

Repercusión del preenvasado de los medicamentos antipalúdicos en el costo para los pacientes y la observancia del tratamiento

Objetivo Analizar en qué medida los equipos de salud de distrito podrían reducir la carga de paludismo, una causa importante y persistente de mortalidad y morbilidad, en una situación de grave escasez de recursos en la que se proporcionaba atención integrada.

Métodos Se procedió a preenvasar los medicamentos antipalúdicos en dosis únicas con objeto de mejorar la observancia de los regímenes completos de quimioterapia.

Resultados La observancia mejoró aproximadamente en un 20% tanto en los adultos como en los niños. Se registraron reducciones del 50% del costo para los pacientes, de los tiempos de espera en los dispensarios y de la cantidad de medicamentos desperdiciada en los centros. La intervención, destinada a mejorar el manejo tanto de los casos como de los medicamentos en los establecimientos, fue bien acogida por el personal sanitario, para el que no supuso trabajo adicional.

Conclusión El preenvasado de antipalúdicos a nivel de distrito permitiría mejorar la observancia y reducir la propagación de la resistencia.

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