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Compliance with malaria chemoprophylaxis programmes in Zimbabwe

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Summary

Compliance with malaria chemoprophylaxis programmes was studied in the National Railways and two large commercial farm labour forces in Zimbabwe. Prophylaxis was primarily conducted using pyrimethamine/dapsone and the study measured compliance rates through interview and the detection of drug in the urine. Compliance rates as indicated from registers or questioning were not always reliable and were found from urine examination to be in the range of 50–60% for the farm labour force. Annual drug utilization figures also indicated that complete coverage was not being achieved. – The results are discussed in relation to the difficulties involved in implementing malaria prophylaxis programmes. The limited use of large scale chemoprophylaxis is stressed, particularly in the light of increasing drug resistance.

Key words: malaria; prophylaxis programmes; pyrimethamine; dapsone.

Introduction

Mass distribution of drugs for the prevention or suppression of malaria in whole communities or in selected groups has received varying support over the years. Early chemoprophylaxis programmes in Africa and elsewhere using pyrimethamine rapidly met with the problem of drug resistance (Ricosse et al., 1969; Black, 1973; Laing, 1984) which was overcome for a period by the use of various drug combinations or by the use of 4-aminoquinolines alone. However, as the development of insecticide resistance, coupled with other technical and administrative problems, resulted in a failure to meet malaria control programme objectives mass drug administration became relatively widespread (Jeffrey, 1984; Beausoleil, 1984). Laing (1984) mentions the "sad story of the

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virtual failure of chemoprophylaxis as a major method of controlling malaria in Africa" and this is seen in some of the reports of mass drug administration programmes (Ricosse et al., 1969; Clyde, 1966; Najera et al., 1973; MacCormack and Lwihula, 1983; Laing, 1984).

Successful drug prophylaxis against malaria is difficult to achieve for many reasons (WHO, 1967) chief amongst which is the difficulty in achieving the required frequency of administration at the right dosage (WHO, 1967; Grammicia, 1981; MacCormack and Lwihula, 1983; Jeffrey, 1984). Nevertheless large scale malaria chemosuppression or prophylaxis has been seen by many countries as the only realistic intervention method available.

Whilst many countries continue to view prophylaxis of special groups as necessary and to have a significant health impact the development of *Plasmodium falciparum* resistance to chloroquine in south-east Asia, South America and more recently Africa (Kihamia and Gill, 1982) has been linked to drug pressure from prophylactic programmes (Onori, 1982; Jeffrey, 1984; Draper et al., 1985). This has resulted in a change in expert opinion such that mass chemoprophylaxis for children under 5 years of age in malarious areas is now not recommended (WHO, 1984a, b) and the termination of mass drug administration programmes that are not time limited and targetted at high risk groups or the control of epidemics is recommended (WHO, 1984a, b).

The high cost of providing chemoprophylactic protection to most groups would be more advantageously used in improving the access of the general population to treatment through an improved health care or primary health care system (WHO, 1984a; Beausoleil, 1984).

Zimbabwe has recently experienced its first cases of chloroquine resistant *P. falciparum* malaria in the north of the country (Mutambu et al., 1986) and it was against this background that an evaluation of the existing malaria chemoprophylaxis programmes was carried out as part of an overall reassessment of malaria drug availability and utilization.

Materials and Methods

The investigation covered the major malaria prophylaxis programmes in operation in Zimbabwe during the malaria season of 1984/85.

Hippo Valley Estates Ltd. and Triangle Ltd. are two companies farming 30,000 ha of irrigated sugar. Situated in south-east Zimbabwe (21° 5′S, 31° 30′E) in a region of meso-hyperendemic malaria, there is a population under prophylaxis of approximately 76,000 staff and dependants. The population is grouped into compact villages (Triangle 48 villages, Hippo Valley 45 villages) of about 1000 residents and there is a community health worker (CHW) with a small clinic in each village who has the responsibility of delivering the prophylactic drugs. Five villages on each estate were randomly selected for investigation.

National Railways of Zimbabwe (NRZ) has approximately 21,000 staff and dependants which are included in the malaria prophylaxis programme. Staff are distributed along all the lines of rail from hyper- to hypoendemic malaria in numerous settlements of various sizes.

Information on the prohylactic programme under study was collected by interviewing the medical officer in charge as well as drug distributors and by the examination of urines for dapsone

(Lignin test) and chloroquine (Lelijveld and Kortmann test, Bruce-Chwatt, 1981). Preliminary screening in the laboratory confirmed the Lignin test to be 100% sensitive for three days after ingestion of pyrimethamine 12.5 mg/dapsone 100 mg. There were no false positives in the control negative group, however, the test is not specific for dapsone and will be positive in the presence of other sulpha drugs. Urines were collected within two days of prophylactic distribution.

No warning was given of an intended visit to irrigation scheme villages and on arrival all people present in the village were asked to provide urine samples and were checked against the C.H.W. register. For the National Railways only the place of work was visited and samples were taken from all employees present.

Data of the incidence of malaria on the irrigation schemes was available from the two hospitals serving the population. Incidence of malaria in the surrounding area was calculated from blood slides submitted to Blair Research Laboratory as part of a routine diagnostic service (Taylor and Mutambu, 1986) compared with the 1982 population census figure of 31,000.

Results

Hippo Valley and Triangle

Both estates have a prophylaxis programme for malaria which involves the distribution of pyrimethamine/dapsone on a fixed day each week throughout the year to all staff and their dependants living in villages on the estate. All of these official residents, some 76,000 people, are registered with the community health worker. Alternative drugs (chloroquine) are only used by about 300 people with severe side effects from pyrimethamine/dapsone. Missing people are usually followed up and people leaving the village for any length of time are given sufficient tablets for self medication while absent. There are no positive measures to ensure compliance with the prophylactic programme on Hippo Valley, however, on Triangle estate workers who contract malaria are not given sick leave and have to pay a small hospital fee.

A total of ten villages were visited, five on each estate. One village on each estate could not be investigated further as, in the first the CHW was absent on urgent personal business and so no drug was distributed, and in the second, the CHW had no usable records of drug distribution.

Apart from the one example mentioned above, all CHW's had a register with each individual in the community identified. Drug consumption each week was recorded although there was variability in the number of uncompleted entries. Unregistered people were found and included casual workers and visitors all of whom were given antimalarials by the CHW on request.

The results of investigation of compliance with the malaria prophylaxis programme in Triangle and Hippo Valley are shown in Table 1. Urines were only tested for the presence of sulpha drugs as all CHW's claimed that a negligible amount of chloroquine was distributed.

There was considerable variability in the results from village to village and to provide an overall assessment of the success of the prophylactic programme on each estate the village data have been pooled in Table 1 although ranges are also presented.

Table 1. Summary of investigations into compliance with the malaria prophylactic programme for four villages in Hippo Valley and four villages in Triangle from a total of 93 villages

	Triangle			Hippo Valley			Total	
	n	%	range	n	%	range	n	%
A) No. registered	213			211			424	
B) No. unregistered residents (over 1 week)	50			74			124	
C) Total examined	280			297			577	
D) No. registered recorded as taking prophylaxis	144	68	50–96	183	87	80–94	327	77
E) No. registered not recorded as taking prophylaxis	69			28			97	
F) No. of D) with positive sulpha test	101	70	64–77	97	53	49–63	198	61
G) No. of E) with positive sulpha test	24	35	0–50	7	25	13–33	31	32
H) No. of registered with positive sulpha test	125	59	40–67	104	49	45–58	229	54
I) No. of unregistered residents (over 1 week) with positive sulpha test	20	40	31–50	34	46	18–60	54	44
J) No. children under 15 years	83			76			159	
K) No. children registered	63	76	61–91	55	72	43–81	118	74
L) No. unregistered children with positive sulpha test	7	35	20–100	9	43	20–75	16	39
M) No. registered children with positive sulpha test	37	59	22–76	26	47	0–71	63	53

Children under 15 years made up 27.5% of the population examined. It is not known how this compares to the actual age structure of the population. Over 90% of employees examined were adult males.

The majority of unregistered residents had been present for several months or several years. Overall 43.5% of unregistered residents were found to have taken antimalaria drugs as compared to 54% of registered residents and they made up 21% of the population examined (Table 1). Of the employees on the malaria register who were examined, 85.7% (range 60–100%) were recorded as having taken their prophylaxis on the due date but urine examination showed this to be only 58.4% (range 44–75%). Of the registered dependants examined, 68.1% (range 32–94%) were recorded as taking prophylaxis on the due date whereas urine examination showed only 49.8% (range 20–61%) had actually done this.

The total number of residents proved from urine examination to be taking malaria prophylaxis was 51.6% and was higher at Triangle (55.1%) than at Hippo Valley (48.4%). Registered children had higher compliance rates than unregistered children (Table 1) but there was no significant trend of higher or lower compliance rates in registered child dependants than in registered adult dependants.

The total amounts of pyrimethamine/dapsone used annually from 1981–83

Table 2. Annual usage of pyrimethamine/dapsone by Hippo Valley Estates Ltd. (population 36,000) and Triangle Ltd. (population 40,000) 1981–1983

		No. of tablets	Tablets/person
Hippo Valley	1981	896,000	25
	1982	864,000	24
	1983	960,000	27
Triangle	1981	2,000,000	50
	1982	1,472,000	37
	1983	1,336,000	33

and the number of tablets per protected person is shown in Table 2. Triangle used in excess of 50% more drugs than Hippo Valley whilst the target population is only 11.1% higher at 40,000 people. On average 2.5 m tablets are used annually by the estates which was calculated to only be sufficient to provide a 75% coverage of the population. The present investigation shows that a 51.6% coverage is being achieved and this difference is probably due to drug wastage by non-compliers and drug usage on the unknown number of unregistered residents.

The incidence of malaria from hospital records maintained by the two estates was 8.3 cases/1000 population in 1982. This compares with 21.3 cases/1000 people reported from the adjacent subsistence farming area with a population of 31,000 people.

National Railways

Three stations were visited in malarious areas. The official policy of NRZ is that malaria prophylactic drugs are taken once weekly throughout the year but there were a variety of distribution methods in operation and no records were kept at any station. All stations visited used pyrimethamine/dapsone for prophylaxis and had a supply of the drug. Drugs are ordered whenever supplies run low from a central store but all three stations had no order books or forms for malaria drugs. Such being the case it was difficult to say how many tablets were consumed by what proportion of the target population in any given year. Drug consumption was not supervised.

Due to variable information received on the type of drug used for prophylaxis, urines were examined for both dapsone and chloroquine. The results of both tests are combined in Table 3. No dependants were tested for compliance with the prophylactic programme and all employees found were adult males.

Overall 276 employees were screened and tested for sulphonamides and chloroquine at the three stations and only 20 gave a positive test, 7 for sulpha drugs and 13 for chloroquine. Of the 18 (6.5%) who claimed to have taken prophylaxis only 4 (22.2%) gave a positive test. Of 258 (93.5%) employees who

Table 3. Results of urine examination of malaria prophylactic drugs in employees from 3 settlements of the National Railways of Zimbabwe

	Chiredzi	Kadoma	Mutare	Total	(%)
A) No. tested	44	31	201	276	
B) No. +ve test	5	4	11	20	(7)
C) No. claiming no pill taken	36	29	193	258	(94)
D) No. claiming taken the pill	8	2	8	18	(7)
E) No. C) –ve test	34	25	183	242	(94)
F) No. D) +ve test	3	0	1	4	(22)

claimed not to have taken the tablets, 242 (93.8%) were also negative for the test. The difficulty of timing urine examinations for prophylactic drugs to close after administration may have resulted in an underestimate of the number actually on prophylaxis. However, the high proportion of employees claiming they were not taking prophylaxis is in itself a strong support for the examination results (Table 3).

Discussion

The evaluation of mass drug administration programmes has usually relied upon measurement of malaria prevalence and incidence (Ricosse et al., 1969; Najera et al., 1973; Black, 1973) or questionnaires (MacCormack and Lwihula, 1983) to assess successful coverage. In Zimbabwe most of the chemoprophylaxis programmes for the prevention of malaria in special groups are based on the pyrimethamine/dapsone combination. This provided the opportunity to evaluate the success of these programmes by specific reference to individual compliance by examination of urine specimens for dapsone. The frequency and severity of side effects to pyrimethamine/dapsone are being evaluated in a separate study.

The lignin test for dapsone may have overestimated the number of people on prophylaxis due to the positive reaction with other sulpha drugs. Whilst this could not be excluded it is not believed to be very significant in the present study nor to alter the general conclusions. The Lelijveld and Kortmann test for chloroquine gave a less clear end point and any questionable result was given the benefit of the doubt and recorded as positive. This test is reliable and only effective for one to two days after drug consumption at 5 mg/kg (Bruce-Chwatt, 1981; Rombo et al., 1986). The test for chloroquine was only used for the Railways staff and presented a problem in that there had been no consistent day of drug consumption for this group.

The prophylaxis programme at Hippo Valley and Triangle were in most senses ideal programmes with the advantages of:

a) a fully implemented Primary Health Care approach with CHW's in each village;
b) a register of all or most residents;
c) a motivated senior medical management;
d) a parallel residual spraying programme;
e) motivation of individuals through health talks and penalties;
f) supervised administration of drugs.

Negative aspects, however, were related to a failure to carry out the above to the necessary degree of excellence for full prophylactic coverage, for example, the absence of the health worker on the drug distribution day, the failure to keep the register up to date or to register all people, inadequate supervision of drug distribution and possibly not enough health education. Overall the programme was excellently planned and executed and the above comments relate to only small infringements, however, the impact is such that they are probably responsible for the overall coverage rate of 51.6%. Compliance rates for the labour force (58.4%) was higher than for their dependents (49.8%) which may be expected as employees are more likely to identify with programmes initiated by the management than are their dependents. This compliance was relatively high considering the all year round nature of the programme and the constraints to any programme as outlined by Grammicia (1981). Even a well motivated manager, who has other wide ranging responsibilities, may after some time fail to see that the annual drug usage is not enough for the target population and that something must be wrong. The register was only a better than average guide to drug consumption as only 61% of those recorded as having taken prophylaxis were actually shown to have done so (Table 1). Of those recorded as not having taken prophylaxis the register was 68% correct (Table 1) and many of the discrepancies were probably people who had been given tablets for journeys away from home and were on self medication with extra tablets. The reason for many of the registered consumers being negative is probably due to the failure to supervise drug consumption adequately as either the CHW allowed tablets to be taken away for consumption elsewhere or in practice she is busy with the register or elsewhere while the tablet is supposed to be consumed. The programmes were having a significant impact on the number of malaria cases per 1000 population which were significantly lower in the irrigation schemes in 1982 than reported for the adjacent, and drier, subsistence farming areas which also have a programme of residual spraying for malaria control. When it is taken into account that the malaria reporting from the subsistence farming areas is probably only 10–20% of the actual number of cases (Taylor and Mutambu, 1986) then the significance of the reduction is made even more apparent.

The results of the investigation into the programme of the NRZ indicates the difficulties of effecting malaria chemoprophylaxis programmes under anything but strict supervison. The scattered nature of railways settlements

with no specific health or health trained personnel, coupled with an apparent reliance on self motivation had a consequence of very poor compliance rate with the programme (7.2%) (Table 3). As there was no register, individuals were asked whether or not they had taken their tablets on the due day and railways personnel who answered "no" were 90% correct as shown by urine examination.

Whilst special groups can obtain significant benefit from protection against malaria it would clearly appear that chemoprophylactic programmes are not likely to succeed when dealing with small scattered groups of labour without an unduly high standard of commitment and organization which is unlikely to be achieved and much less sustained. That a concentrated labour force can be successfully protected given motivated programme managers is seen from the Triangle and Hippo Valley results which despite some failings still achieved a satisfactory reduction in malaria cases.

Pyrimethamine/dapsone for prevention of malaria in special groups has been used for over 10 years in Zimbabwe. It was chosen to minimize the risk of selecting for chloroquine resistant strains of *P. falciparum* and now that these strains have been detected in the north of the country it becomes even more important to reduce improper use of chloroquine. The existence of *P. falciparum* cross resistance between pyrimethamine/dapsone and pyrimethamine/sulphadoxine drugs is not known and is a risk of using dapsone as a prophylactic drug. However, resistance to sulphadoxine is already present in Africa (Timmermans et al., 1982) and as chloroquine is the most valuable drug for the therapy of malaria priority must be given to its protection.

The present study shows once again the difficulty of achieving effective chemoprophylactic protection against malaria even under the most favourable circumstances. First priority must be given to ensuring adequate access to therapy for all sectors of the population before embarking on preventive or suppressive therapy. There must be real doubt whether effective chemoprophylactic protection through the normal health services, even with a fully implemented primary health care programme, can be achieved for either pregnant women or infants in the majority of the malaria endemic regions of Africa.

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