INTERVENTION STUDIES ON RATIONAL PRESCRIBING OF CHLOROQUINE IN LAGOS STATE GENERAL HOSPITALS

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ABSTRACT

Malaria is a curable and preventable disease and it is a major public health problem in Nigeria. Chloroquine was the first line drug in its treatment in Nigeria until recently where the Artemisinin Combination Therapies (ACTs) are being promoted and/or enforced. Inappropriate prescribing, the failure to prescribe drugs in accordance with guidelines based on scientific evidence to ensure safe, effective, and economic use, is an irrational drug use behavior which contributed to the change from chloroquine to ACTs as first line drug. The objective of the study was to determine the impact of two modes of educational intervention on the chloroquine prescribing pattern of prescribers in Lagos State General Hospitals. The design was a retrospective, longitudinal before and time-series after study with control group. The study was carried out in all the ten government General Hospitals under Lagos State Hospitals Management Board (now Lagos State Health Service Commission), using patient prescriptions.

Educational seminars were presented at 8 of the 10 general hospitals. Two hospitals served as controls. Among the 8 hospitals that had the seminars, 4 hospitals had educational posters describing correct doses of chloroquine left behind, whereas the other 4 had a plastic board printed with the correct doses.

Percentage of prescriptions with correct doses of chloroquine prescribed was determined before and after the intervention over a time-series (1 month, 3 months, 6 months and 12 months post-intervention). There was a significant increase in the percentage of prescriptions with a correct dosage of chloroquine post-intervention compared with pre-intervention ($p < 0.01$). There was no significant difference between the group with plastic box and the group with poster in percentage of correct prescriptions ($p > 0.05$).

In conclusion, educational intervention improved the prescribing of chloroquine in Lagos State General Hospitals

Key words: Chloroquine, Malaria, Rational Prescribing, Intervention

INTRODUCTION

Malaria is a disease caused by the parasite of the genus Plasmodium. The causative agents in humans are four species of Plasmodium protozoa: Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, and Plasmodium malariae. Of these, Plasmodium falciparum accounts for the majority of infections and is the most lethal.

Malaria is a common and serious tropical disease, which continues to be a huge public health problem throughout the world especially the developing countries. Worldwide prevalence of the disease is estimated to be in the order of 200 - 300 million clinical cases and over 1 million deaths each year[1]. In many developing countries especially in Africa, malaria exacts an enormous toll on lives, in medical costs, and days of labour lost. It reduces economic productivity and academic performance due to absenteeism from places of work and schools for up to one week during each attack. This is particularly disturbing because the countries concerned are economically poor and/or underdeveloped. In Nigeria, it is a major cause of morbidity and it is still one of the major causes of hospital attendance according to the Federal Ministry of Health[2].

Malaria is a curable disease if promptly and adequately treated and may present as uncomplicated (non-severe) or severe. Prompt and correct treatment of uncomplicated malaria is important to prevent progression to severe malaria, therapeutic failure and development of drug resistance. Also prompt access to early diagnosis and effective antimalarial treatments are major strategies for reducing morbidity ▶

and mortality from malaria[3,4].

Control involves vector control, protection from bites, chemoprophylaxis and treatment of any infection that develops as it is now recognized that for many countries, vector eradication is unrealistic[5].

Drug therapy has played an important role in the fight against malaria. Drugs can be used for prevention as well as to cure but the falciparum parasite is developing resistance to drugs used against it. Chloroquine was the first line drug in its treatment in Nigeria until recently where the Artemisinin-based Combination Therapies (ACTs) are being promoted due to resistance to chloroquine6 but there is the possibility that chloroquine may still become useful in Nigeria in the future as is the case in Malawi where chloroquine is again an efficacious treatment of malaria 12 years after it was withdrawn[7]. The change was necessitated by the fact that there is therapeutic failure to chloroquine which is due to a lot of factors including inappropriate dosage which is a form of irrational use. In addition, resistance to many insecticides used to prevent malaria has been reported[8].

Rational use of drugs (RUD), according to WHO requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost to them and their community[9]. RUD includes appropriate prescribing, appropriate drug, appropriate dispensing and appropriate use by patient. Irrational use of drugs is deviation from rational use of drugs which could be due to inappropriate prescribing, inappropriate dispensing or inappropriate use[10-11]. Irrational use of drugs has consequences for the health and wealth of the individual patients as well as the community. It can result in wasted resources leading to increased health care costs and reduced availability of other vital drugs. It can also lead to increased morbidity and mortality.

Inappropriate dosage is a form of irrational use of drug that could be due to both inappropriate prescribing and dispensing. Inappropriate prescribing is a manifestation of irrational drug use behaviour when drugs are not prescribed in accordance with guidelines based on scientific evidence to ensure safe, effective and economic use. Inappropriate dosage is one of the factors responsible for therapeutic failure of chloroquine [12-14].

The steps involved in improving prescribing practices or drug use are to

1. measure existing practices and identify specific problems (quantitative).
2. understand why they occur (qualitative)
3. suggest possible actions to correct the problems (intervention).
4. Assess resources available for action;
5. Choose an intervention or interventions to test;
6. Monitor the impact and restructure the intervention

Interventions implemented without gathering this information are likely to fail[10,15].

Intervention Strategies to Improve Drug Use

The three major strategies commonly used to change drug use are educational, managerial and regulatory interventions[15].

Educational Strategies

The basic objective here is to educate and persuade prescribers, dispensers and patients to prescribe, dispense and use drugs rationally. These strategies include lectures, seminars, workshops, continuing education, face to face contact, using printed materials, patient education, influencing opinion leaders, etc [16-19].

Managerial Strategies

These include using limited procurement lists, drug utilization review and feedback, supervision and monitoring, drug committees, cost information (selection, procurement and distribution), standard diagnostic and treatment guidelines, course-of-therapy packaging and price setting.[16,17,20].

Regulatory Strategies[21]

These include drug registration, limited drug lists, prescribing restrictions and dispensing restrictions. The strategies above may either be used singly or in combination. The selection of an appropriate intervention should consider its likely effectiveness, feasibility, cost, potential impact and unlimited effects.

An educational intervention is defined as any attempt to persuade physicians to modify their practice performance by communicating clinical information or guidelines. Educational strategies or interventions include educational materials, formal Continuing Education activities, outreach visits such as academic detailing, opinion leaders, audit with feedback, reminders and combination of these activities Research has shown that the most effective means of changing prescribing behaviour has been face-to-face contact [22-25]. A study in Indonesia showed that a small group on-site face-to-face education was more effective than large group seminars[10]. When interventions of different types are combined the impact is likely to be synergistically increased [26-31].

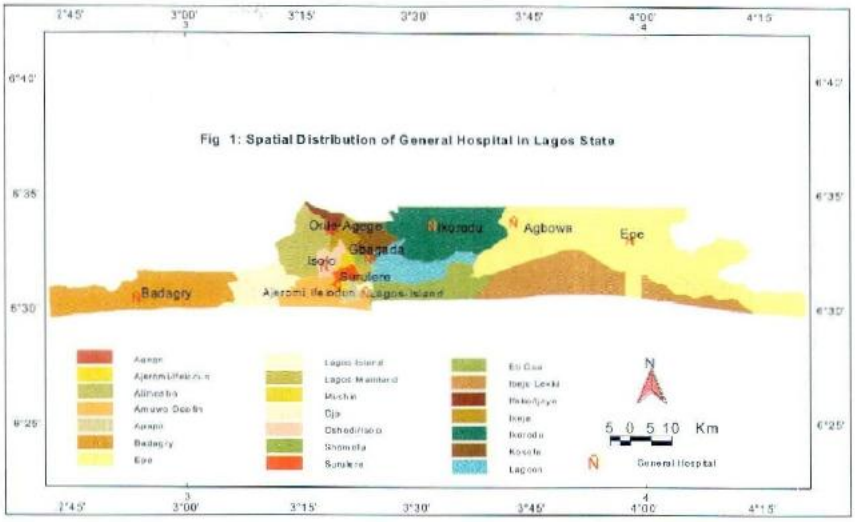
Objectives were to

1. Conduct a situation analysis of the prescribing pattern of chloroquine in the management of uncomplicated malaria in Lagos State General Hospitals (LSGH).
2. Conduct an intervention in order to improve prescribing pattern.
3. Compare the impact of two modes of educational intervention on chloroquine prescribing pattern of prescribers in LSGH.

Materials and Method

Study area

The study was carried out in Lagos State which has twenty local governments. Only nine of these local governments have General Hospitals, Epe has 2. (Fig 1). Population of the state is said to be above 11 million based on 2006 census.



Study Population

All the ten General Hospitals in Lagos State were studied. These were Agbowa General Hospital (Epe local govt.), Ajeromi General Hospital (Ajeromi-Ifelodun local govt.), Badagry General Hospital (Badagry local govt.), Epe General Hospital (Epe local govt.), Gbagada General Hospital (Kosofe local govt.), Ikorodu General Hospital (Ikorodu local govt.), Isolo General Hospital (Oshodi-Isolo local govt.), Lagos Island General Hospital (Lagos Island local govt.), Orile Agege General Hospital (Agege local govt.) and Surulere General Hospital (Surulere local govt.).

Research Design

A pre-test – post-test control group design was used for the intervention study. This study was conducted in three phases; the pre-intervention phase (phase1), intervention phase (phase 2) and post intervention phase (phase 3). The research methodology of this work is based on framework for formative and intervention studies[15].

Research Instruments/materials

"Free Eko Malaria" prescriptions were used for phase 1 or formative studies. Seminar method was used for phase 2 or intervention phase. "Free Eko Malaria" prescriptions were used for phase 3 or post intervention phase.

Procedure for data collection

Phase 1 (Pre-intervention phase) using "Free Eko Malaria" Prescriptions

A retrospective study period of one year (January – December, 2000) was selected. A total of 21,949 prescription forms of 'Free Eko Malaria' were sampled for children and adults from these General Hospitals. The prescription forms were sampled using systematic sampling method of WHO[32]. Drugs in each prescription form were costed using the prices obtained from the hospitals except for drugs that were donated, whose prices were obtained from wholesalers. Cost of needle and syringe and cotton swab were incorporated in prescriptions containing injections.

Core prescribing indicators and specific indicators of chloroquine were analyzed[32].

The core-prescribing indicators were:

1. Average number of drugs per encounter (prescription form)
2. Percentage of encounters with injections prescribed
3. Average number of injection per encounter

Complementary Drug Use Indicator:

3. Average drug cost per encounter
4. Percentage of encounters with dipyrone injection prescribed

Specific Chloroquine Indicators:

5. Percentage of encounters with chloroquine
6. Percentage of encounters with chloroquine tablets,
7. Percentage of encounters with chloroquine syrup,
8. Percentage of encounters with chloroquine injections,
9. Percentage of encounters with chloroquine injection + tablets,
10. Percentage of encounters with chloroquine injection + syrup
11. Average chloroquine fraction per encounter

Dosage of chloroquine prescribed

12. Percentage of encounters with correct dosage of chloroquine prescribed
13. Percentage of encounters with overdosage of chloroquine prescribed
14. Percentage of encounters with under-dosage of chloroquine prescribed

This was done for the different dosage forms prescribed, adults and children, each separate facility and all the facilities combined.

Dosage of chloroquine prescribed was calculated as:

$$F = \frac{T}{R} \text{----------Eq. 1}$$

where F = Fraction of total dosage recommended in relation to age
T = Total dosage prescribed in relation to age
R = Total dosage recommended in relation to age

Correct Dosage is $F = 1.0 \pm 0.2$ i.e. 0.8 to 1.20
(80 to 120 % of total recommended dose)

Phase 2 (Intervention phase)
Intervention was carried out between January and February 2002.

Educational intervention, a modification of Avon and Soumerai[22]; Schaffner et al.,[33]; Cohen et al.,[27]; Marton et al.,[34] and Dietrich[31], was carried out by means of seminars which were held in each hospital on their clinical meeting days with doctors, pharmacists, nurses and medical laboratory scientists in attendance. The following findings and their consequences were highlighted and how to avoid/prevent the pitfalls were discussed:

1. Prescribing pattern observed during the retrospective collection of baseline data, i.e. the pre-intervention phase
2. Results obtained from the questionnaire
3. Possible ways of improvement in the dosage of chloroquine prescribed such as prescribing tablets or syrups unless otherwise absolutely necessary e.g. vomiting
4. Avoidance or decrease in the prescribing of injections only unless when absolutely necessary e.g. vomiting
5. Prescribing of chloroquine injection followed by tablet or syrup to complete the recommended dose for the patient depending on the age or weight.
6. Reducing the number of drugs per encounter.

The ten General Hospitals were randomly divided into three (3) groups. Groups 1 and 2 were the experimental groups while group 3 was the control group.

Experimental Group 1
This group comprised of Agbowa, Ajeromi, Badagry and Orile Agege General Hospitals which received seminar presentation plus plastic boxes (semi + bpad). The plastic box was to recall the different chloroquine dosage regimens appropriate to the various ages, especially children and was filled with loose sheets. This is similar to gift items that are used by corporate bodies for publicising either their products or their organizations. The dosing schedules of chloroquine corresponding to different age groups were printed on the boxes (Table 1)[35]. They were placed on tables after the seminar and the prescribers were encouraged to refer to them while prescribing.

Experimental Group 2
This group comprised of Epe, Ikorodu, Isolo and Surulere General Hospitals which received seminar presentation plus poster (semi + post). The poster had pictures and appropriate doses for the corresponding age and weight. The poster was a modified one of Federal Ministry of Health[35].

Control Group 3
This comprised of Lagos Island and Gbagada General Hospitals which did not receive any intervention because they constitute the control group.

Phase 3 (Post -intervention phase)
Retrospective study of post-intervention prescribing patterns was carried out after 1, 3, 6 and 12 months to measure the impact of intervention. This was done to measure the short- (one and three months), medium- (six months) and long-term (one year) impacts. 2000 prescription forms were sampled each at 1, 3 and 12 months post intervention while 1934 were sampled 6 months post intervention from the hospitals. Core prescribing indicators and specific indicators of chloroquine were analyzed as was done during the pre-intervention study[32].

Data Analysis
The data collected were analyzed using EPI Info Version 6 (EPI-6 Info) statistical software36, Statistical Package for Social Sciences (SPSS) and Excel.

Continuous data are expressed as mean + SEM (Standard Error of Mean) while discontinuous or categorical data are expressed as percentages.

Chi-square distribution was used to determine whether or not there is an association between intervention time, intervention type, dosage form and dosage of chloroquine prescribed. Paired t tests and ANOVA were used to determine the significance of differences of arcsine-transformed percentages[31]. Tukey's honestly significant difference (HSD) was used for multiple comparisons to determine which means differ. Results were considered to be statistically significant if $p < 0.05$.

CQ TREATMENT OF NON – SEVERE MALARIA
1 Tablet = 150mg CQ base
Syrup 1 tsp (5ml) = 50mg CQ base
Injection: 3.5mg/kg 6 or 8 hourly until a total dose of 25mg/kg
(1 amp (5ml) = 200mg CQ base; 1 ml = 40 mg CQ base)

AGE (YRS)	WEIGHT (KG)	1ST DAY	2ND DAY	3RD DAY
		½ Tab 7.5ml(1½tsp)	½ Tab 7.5ml(1½tsp)	¼ Tab 3.75 ml(¾ tsp)
		1 Tab 15ml(3tsp)	1 Tab 15ml(3tsp)	½ Tab 7.5 ml(1½tsp)
		 1 ½ TABS	 1 ½ TABS	 1 TAB
		 2 TABS	 2 TABS	 1 TAB
		 4 TABS	 4 TABS	 2 TABS

Table I: Treatment of non-severe malaria with Chloroquine (Extracted from FMOH 2001 recommendation)[46]

RESULTS

PRESCRIBING PATTERN AT PRE, 1, 3, 6 AND 12 MONTHS POST INTERVENTIONS

The average number of drugs per prescription for each health facility are in Table 2. Average number of injections per prescription and average drug cost per prescription are presented in Table 2.

Percentage of prescriptions with at least one injection for each health facility are shown in Table 3. Percentage of prescriptions with dipyrone for each health facility are indicated in Table 3. Percentage of prescriptions with chloroquine are presented in Table 3.

Total percentage of prescriptions with correct dosage of chloroquine increased from 45.3% at pre-intervention to 72.4% at 1 month post intervention but reduced to 70.4%, 65.3% and 68.6% at 3, 6 and 12 months post intervention respectively (Figure 2).

In adults, percentage of prescriptions containing correct dosage of chloroquine increased from 56.5% at pre-intervention to 84.5% at 1 and 3 months post intervention but dropped to 77.5% and 81.5% at 6 and 12 months post intervention respectively (Figure 3). In children, the percentage of prescriptions containing correct dosage of chloroquine increased from 34.4% at pre-intervention to 61.2% at 1 month post- intervention but dropped to 56.7%, 54.3% and 56.6% at 3, 6 and 12 months post- intervention respectively (Figure 3). Percentage of correct dosage of chloroquine prescribed for each health facility at pre, 1, 3, 6 and 12 months post-intervention is as shown in Figure 6. Percentage of prescriptions containing injection chloroquine only, reduced from 31.2% at pre-intervention to 12.6% and 11.9% 1 and 3 months post-intervention respectively but later increased to 16% and 14.3% at 6 and 12 months post- intervention respectively (Figure 5). Percentage of prescriptions containing chloroquine tablets only, increased from 28.5% at pre-intervention to 47.7% and 50.1% at 1 and 3 months post-intervention respectively but this reduced to 45.5% and 40.9% 6 and 12 months post-intervention respectively.

The percentage of prescriptions with correct dosage of chloroquine for the control group increased from 60% at pre-intervention to 72.8%, 78.5%, 75.7% and 71.1 % at 1, 3, 6 and 12 months post-intervention respectively.

The percentage of prescriptions with correct dosage of chloroquine for the 'seminar + poster' group (semi+post) increased from 42.5% at pre-intervention to 71.5% at 1 month post-intervention but reduced to 69.9%, 62.2% and 67.3% at 3, 6 and 12 months post-intervention respectively.

The percentage of prescriptions with correct dosage of chloroquine for the 'seminar + plastic box' group (semi+bpad) increased from 40.75% at pre-intervention to 72.9% at 1 month post-intervention but reduced to 66.9%, 63% and 68.6% at 3,6 and 12 months post-intervention respectively (Figure 4).

The result of comparison of dosage of chloroquine in the different dosage forms prescribed at pre, 1, 3, 6 and 12 months post-intervention is as shown in Table 4.

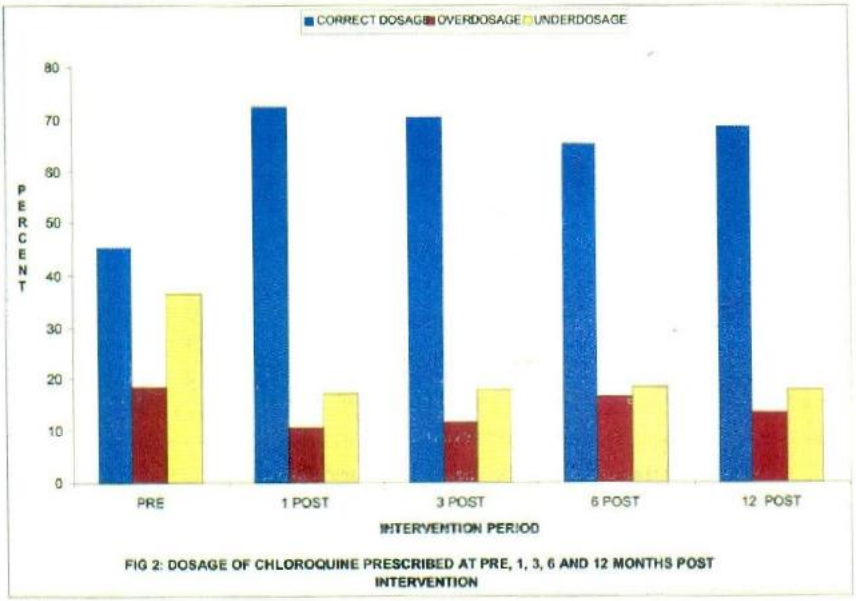


FIG 2: DOSAGE OF CHLOROQUINE PRESCRIBED AT PRE, 1, 3, 6 AND 12 MONTHS POST INTERVENTION

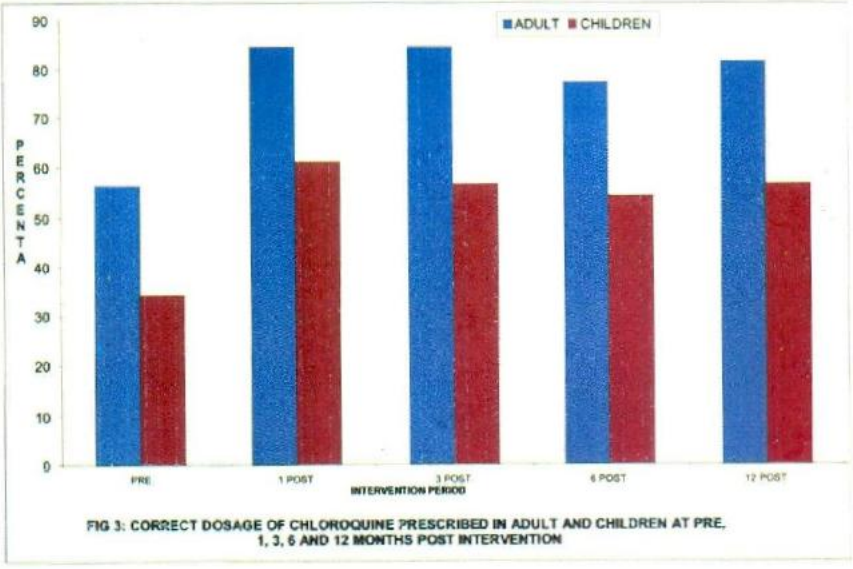


FIG 3: CORRECT DOSAGE OF CHLOROQUINE PRESCRIBED IN ADULT AND CHILDREN AT PRE, 1, 3, 6 AND 12 MONTHS POST INTERVENTION

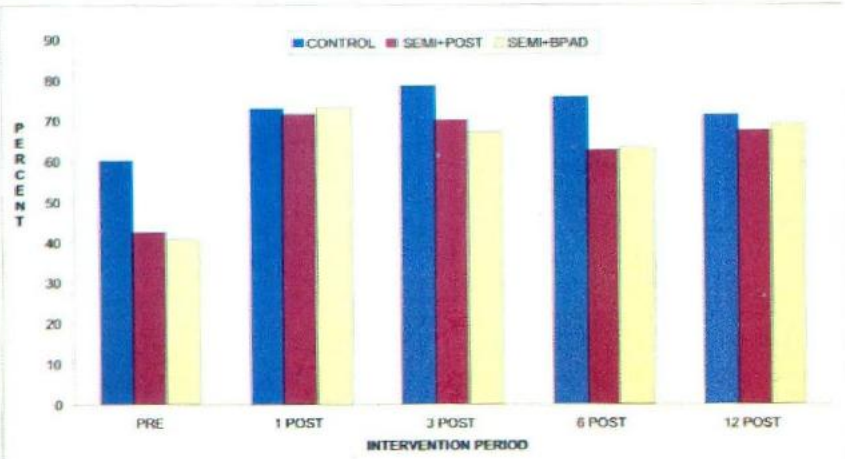


FIG 4: CORRECT DOSAGE OF CHLOROQUINE FOR THE DIFFERENT MODE OF INTERVENTION AT PRE, 1, 3, 6 AND 12 MONTHS POST INTERVENTION

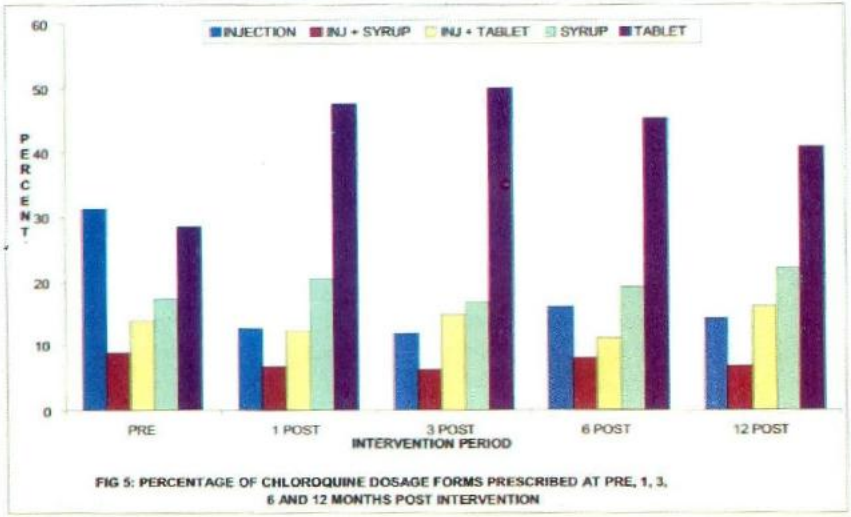


FIG 5: PERCENTAGE OF CHLOROQUINE DOSAGE FORMS PRESCRIBED AT PRE, 1, 3, 6 AND 12 MONTHS POST INTERVENTION

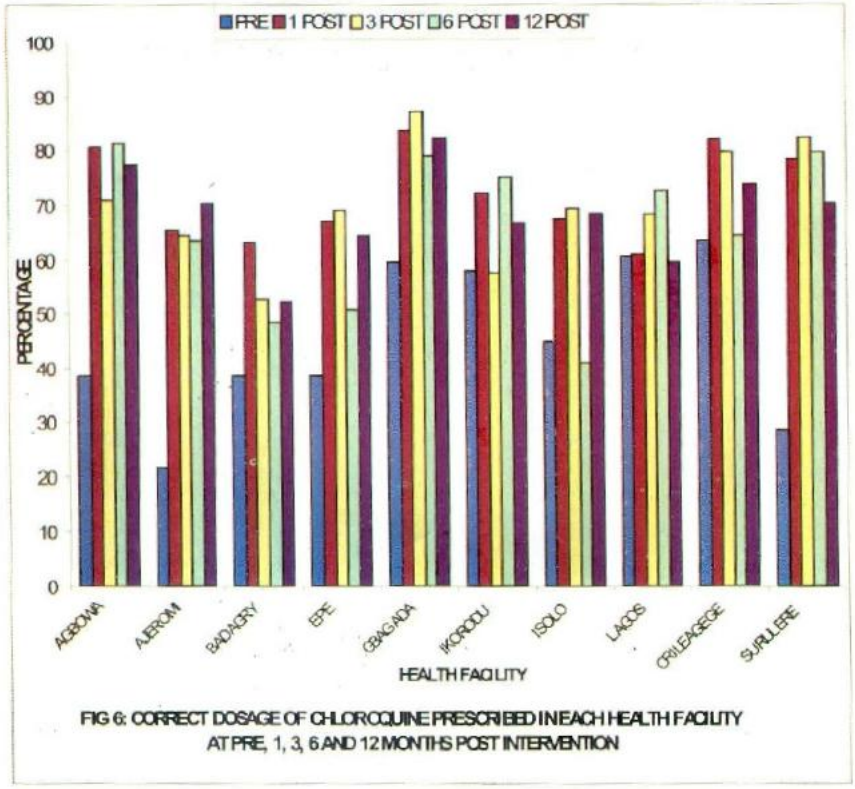


FIG 6: CORRECT DOSAGE OF CHLOROQUINE PRESCRIBED IN EACH HEALTH FACILITY AT PRE, 1, 3, 6 AND 12 MONTHS POST INTERVENTION

4.4 STATISTICAL ANALYSIS RESULTS

The percentage of prescriptions with correct dosage of chloroquine after the educational intervention was statistically different from before intervention ($p < 0.01$).

Using one way ANOVA the percentage of prescriptions with correct dosage of chloroquine in the plastic box intervention group was not statistically different from that in the poster intervention group ($p > 0.05$).

There was association between the dosage of chloroquine and the different dosage forms of chloroquine prescribed ($p < 0.001$)
There was association between intervention and dosage of chloroquine prescribed ($p < 0.001$).

There was association between the mode of intervention and dosage of chloroquine prescribed ($p < 0.001$)
Using Tukey HSD there was no statistically significant difference in percentage of correct prescriptions between 1 month, 3 months, 6 months and 12 months post intervention hence it is implied that the intervention was sustained.

5.1 DISCUSSION

From the prescriptions surveyed pre and post-intervention, some recurring results were observed. For example it was discovered that the highest percentage of underdose was observed where injection chloroquine only was prescribed while the highest percentage of correct dose of chloroquine was observed when tablet chloroquine only was prescribed whether considered per health facility, adult, children or overall in the total prescriptions studied. From literature underdosage is implicated in chloroquine resistant malaria[12-14]. Oral dosage form should be encouraged to be prescribed with injection in order to complete the dosage. The number of doses required to attain complete dosage for injection chloroquine only, in an adult is about 7 – 8 which have to be given every 6 or 8 hours; this is not convenient for ambulatory patients. Also the cost of injection and its administration was found to be higher than that of oral dosage form. In addition, side effects or adverse effects ►

to chloroquine injection are life threatening and these include hypotension, cardiac arrest, cardiac depression and cardiac arrhythmia[37]. The scourge of HIV/AIDS, hepatitis, poliomyelitis etc. in the country militates against use of injection because of cross infection and there is the possibility of injection abscess which results in additional costs to the patient[38-40]. From the cost effectiveness analysis and sensitivity analysis carried out chloroquine tablet was found to be more cost effective than the injection[41]. For these reasons, injection should be discouraged and tablet chloroquine encouraged.

The percentage of correct dosage was consistently higher in adults than in children (Fig 5). This may be attributed to the fact that tablets are mainly prescribed for adults. Also there are different age groups and different doses for the children. These doses may be cumbersome to remember by the prescribers hence the need to give them reminders, especially for the children doses. This was substantiated in the questionnaires where most of the prescribers filled 25mg/kg but could not fill the individual doses for the age groups. 64% of the prescribers filled the actual correct dose for adults while 6% just filled 25mg/kg whereas only 26 % of the prescribers filled the actual correct dose for children while 31% just filled 25mg/kg[42].

It was observed that injection dipyrone was prescribed frequently as antipyretic even when chloroquine tablet was prescribed. Although it is recommended in some literature that oral dipyrone should only be used when other analgesics have failed[43] it is unacceptable practice especially when this drug has been banned in many countries because it has been associated with irreversible agranulocytosis[44].

The average number of drugs per encounter in this study was fairly high with vitamin B complex been frequently prescribed on a thrice daily schedule for between 5 days to 2 weeks. It is documented that polypharmacy results in an increase risked for adverse drugs event[45]. One possible explanation for the identified polypharmacy is that patient usually complain of multiple problems which need to be managed/treated with drugs. A second reason is that many patients are often malnourished and so require vitamin supplementation to augment their diet. However, more emphasis should be placed on eating adequate and balance diet rather than relying on drugs.

Generally, it was observed that there was improvement in the indicators under consideration at 1 month post-intervention but the degree of the improvement was reduced at 3, 6 and 12 months post-intervention though the reduction was not statistically significant. This implies that the intervention was sustained but there may be need for a constant reminder and not just leaving educative materials like posters or plastic box with the prescribers. There is the tendency for people to revert to old behaviour after some time[10]. The pharmacist may serve as a reminder but there may be need to find out if pharmacists are ready for this or whether this will go well with the physicians. During the intervention seminars this issue was discussed and it was agreed that the pharmacist should call the attention of the physician to any unusual dose before correction. The marked increase in the percentage of prescriptions with correct dose of chloroquine 1 month post-intervention either overall or for the different mode of intervention shows that the intervention had impact on the prescribing habit. There was no visible pattern of prescribing peculiar to whether the hospital was in the rural or urban area. In this study it was not possible to determine whether the reason for irrational prescribing was culturally based but it was not economically based because the treatment was free as the state government bore the cost.

In Nigeria though, the first-line drug has been changed to Artemisinin based Combination Therapy [2,6] but there is the possibility that chloroquine may still re-emerge as is the case in Malawi where chloroquine is again an efficacious treatment for malaria [12] years after it was withdrawn[7].

CONCLUSION

From the results of this study it can be concluded that the intervention had significant effect on the correct dosage of chloroquine prescribed. The effect was more at 1 month post-intervention than other study times post intervention. Correct dosage was obtained more when tablet chloroquine only, was prescribed than any other dosage form. Under-dosage was obtained more when injection chloroquine only, was prescribed than any other dosage form. There should be a reminder of the appropriate dosage of chloroquine especially for the different age groups among the children at regular intervals.

There was no statistically significant difference in percentage of correct prescriptions between 1 month, 3 months, 6 months and 12 months post intervention hence it is implied that the intervention was sustained.

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TABLE 2: AVERAGE NUMBER OF DRUGS AND INJECTIONS AND AVERAGE COST PER PRESCRIPTION IN THE DIFFERENT HEALTH FACILITIES AT PRE, 1 MONTH, 3 MONTHS, 6 MONTHS AND 12 MONTHS POST INTERVENTION

PRE			1 MONTH POST			3 MONTHS POST			6 MONTH POST			12 MONTHS POST		
Av. No. of drugs ± SE	Av. No. of injec. ± SE	Av. cost of drugs ± SE ₦	Av. No. of drugs ± SE	Av. No. of injec. ± SE	Av. cost of drugs ± SE ₦	Av. No. of drugs ± SE	Av. No. of injec. ± SE	Av. cost of drugs ± SE ₦	Av. No. of drugs ± SE	Av. No. of injec. ± SE	Av. cost of drugs ± SE ₦	Av. No. of drugs ± SE	Av. No. of injec. ± SE	Av. cost of drugs ± SE ₦
4.360 ± 0.029	1.502 ± 0.027	135.389 ± 1.279	4.235 ± 0.107	0.940 ± 0.095	102.825 ± 5.026	4.025 ± 0.104	0.835 ± 0.090	86.725 ± 3.687	3.985 ± 0.122	0.746 ± 0.101	100.299 ± 5.132	4.520 ± 0.103	0.96 ± 0.093	104.175 ± 3.453
4.075 ± 0.024	1.869 ± 0.030	183.935 ± 3.022	4.345 ± 0.094	1.255 ± 0.095	158.375 ± 7.180	4.140 ± 0.098	0.975 ± 0.082	154.275 ± 11.637	4.955 ± 0.102	1.175 ± 0.094	141.875 ± 7.940	4.655 ± 0.097	0.915 ± 0.086	113.575 ± 6.562
4.186 ± 0.024	1.244 ± 0.028	139.547 ± 1.602	4.055 ± 0.059	0.990 ± 0.094	123.700 ± 5.621	4.340 ± 0.051	1.230 ± 0.101	136.825 ± 6.273	4.730 ± 0.069	1.620 ± 0.101	150.40 ± 6.128	4.090 ± 0.061	1.275 ± 0.099	133.100 ± 4.892
4.464 ± 0.028	1.808 ± 0.029	164.027 ± 2.685	4.310 ± 0.088	0.905 ± 0.095	120.890 ± 5.930	4.580 ± 0.107	1.120 ± 0.101	128.719 ± 7.487	4.915 ± 0.113	1.510 ± 0.108	141.90 ± 6.071	5.250 ± 0.129	1.820 ± 0.101	115.650 ± 4.310
3.216 ± 0.022	0.495 ± 0.020	96.992 ± 1.529	3.520 ± 0.057	0.165 ± 0.039	76.725 ± 4.039	3.740 ± 0.054	0.200 ± 0.101	84.125± 5.973	3.590 ± 0.057	0.315 ± 0.060	85.150 ± 2.835	3.705 ± 0.062	0.260 ± 0.050	95.985 ± 4.632
4.076 ± 0.026	1.054 ± 0.026	119.292 ± 1.535	4.065 ± 0.089	0.890 ± 0.088	102.800 ± 3.866	4.710 ± 0.098	1.295 ± 0.085	117.1 ± 5.460	4.525 ± 0.084	1.150 ± 0.082	110.25 ± 5.080	4.285 ± 0.094	1.240 ± 0.096	122.375 ± 6.601
5.250 ± 0.037	2.124 ± 0.029	147.710 ± 2.251	5.205 ± 0.125	1.910 ± 0.103	216.200 ± 25.825	5.080 ± 0.082	1.670 ± 0.078	224.400 ± 24.496	4.645 ± 0.092	1.350 ± 0.087	299.40 ± 35.423	5.080 ± 0.104	1.640 ± 0.091	198.100 ± 18.926
3 .487 ± 0.024	0.775 ± 0.024	117.222 ± 2.425	3.870 ± 0.096	0.935 ± 0.082	134.675 ± 13.321	4.195 ± 0.107	1.095 ± 0.088	136.200 ± 8.602	4.140 ± 0.099	0.820 ± 0.078	128.685 ± 7.751	4.390 ± 0.089	1.150 ± 0.096	118.360 ± 4.468
3.650 ± 0.025	0.533 ± 0.022	109.793 ± 1.394	3.935 ± 0.074	0.465 ± 0.073	92.400 ± 3.755	3.875 ± 0.069	0.605 ± 0.083	95.705 ± 4.48	4.525 ± 0.089	1.040 ± 0.096	121.325 ± 6.408	4.525 ± 0.089	1.040 ± 0.096	121.325 ± 6.408
4.970 ± 0.028	2.333 ± 0.028	207.747 ± 2.096	3.260 ± 0.089	0.275 ± 0.055	76.870 ± 3.567	3.445 ± 0.071	0.105 ± 0.033	64.275 ± 2.005	3.690 ± 0.082	0.220 ± 0.050	81.875 ± 3.564	4.265 ± 0.083	0.440 ± 0.062	154.100 ± 13.701
4.163 ± 0.009	1.352 ± 0.009	140.459 ± 0.678	4.080 ± 0.030	0.873 ± 0.029	118.546 ± 3.340	4.213 ± 0.029	0.913 ± 0.028	122.769 ± 3.313	4.383 ± 0.031	1.003 ± 0.029	137.338 ± 4.284	4.140 ± 0.031	1.030 ± 0.029	126.825 ± 2.871

KEY: AV – Average; NO – Number; SE – Standard Error; Injec - Injection

TABLE 3: PERCENTAGE OF PRESCRIPTIONS WITH AT LEAST ONE INJECTION, DIPYRONE AND CHLOROQUINE IN THE DIFFERENT HEALTH FACILITIES AT PRE, 1 MONTH, 3 MONTHS, 6 MONTHS AND 12 MONTHS POST INTERVENTION

PRE			1 MONTH POST			3 MONTHS POST			6 MONTH POST			12 MONTHS POST		
% with inj.	% with dipyrone	% with CQ	% with inj.	% with dipyrone	% with CQ	% with inj.	% with dipyrone	% with CQ	% with inj.	% with dipyrone	% with CQ	% with inj.	% with dipyrone	% with CQ
63.6	51.4	87.8	34.5	33.5	98	33.0	29.0	96.5	32.8	26.1	96.3	37.0	31.5	96.0
67.4	63.3	84.2	50	43	91	48.0	38.0	84.0	48.5	45.7	90.5	42.5	37.0	96.5
47.2	39.1	90	39	34.5	94.5	45.5	45.0	96.0	59.5	57.0	96	47.0	38.0	94.5
66.3	58.9	90.8	64	29.5	92.5	39.0	38.0	92.5	51.0	48.5	91.5	63.5	57.5	99.0
25.1	21.2	83.7	10	6.5	97.5	10.0	9.5	94.5	13.5	10.0	90	14.5	8.0	96.0
45.7	23.6	87.5	39	32.5	90.5	61.0	44.5	90.0	61	53.5	84	50.5	44.5	92.0
74.9	69.7	92.9	76.5	69	85	84.0	72.0	82.0	62	54.5	79	69.5	64.5	83.0
42.5	22.3	82.3	49	32.5	88.5	52.5	35.0	82.0	43	24	89	46.5	35.5	92.5
22.0	19.4	81.6	18	13.5	94.5	23.0	21.5	95.5	38.5	29.5	96	38.5	29.5	96.0
88.2	80.7	90.4	13.5	12.5	93.5	6.5	6.5	96.5	11.0	10	93.5	25.5	23.5	79.5
53.4	44.1	87.1	36.2	30.7	92.5	40.3	33.9	91.0	42.4	36.2	90.5	41.9	36.0	92.1

KEY: Av. No. of drugs : Average number of drugs; Av. No. of injec. : Average number of injections; Av. cost of drugs: Average cost of drug
SE: Standard Error of mean; Inj.: injection; CQ : chloroquine

TABLE 4: DOSAGE OF CHLOROQUINE IN THE DIFFERENT DOSAGE FORMS PRESCRIBED AT PRE,1 MONTH, 3 MONTHS, 6 MONTHS AND 12 MONTHS POST INTERVENTION

PRE			1 MONTH POST			3 MONTHS POST			6 MONTH POST			12 MONTHS POST		
% correct Dosage	% over dosage	% under dosage	% correct dosage	% over dosage	% under dosage	% correct dosage	% over dosage	% under dosage	% correct dosage	% over dosage	% under dosage	% correct dosage	% over dosage	% under dosage
6.6	1.2	92.2	14.6	2.6	82.8	8.4	0.9	90.7	10.8	2.2	87.0	17.0	0.8	82.2
34.3	41.2	24.5	54.7	28.9	16.4	44.4	31.6	23.9	44.4	43.0	12.6	63.2	28.0	8.8
58.0	29.1	12.9	72.7	18.5	8.8	75.1	15.6	9.3	54.1	38.8	7.1	62.0	31.2	6.8
40.5	45.1	14.3	71.3	10.0	18.7	62.3	18.7	19.0	65.4	23.0	11.6	64.7	18.8	16.5
88.0	8.7	3.3	90.5	8.2	1.4	89.6	8.0	2.4	90.8	8.3	0.9	92.3	5.8	1.9