Short Communication

Cost implication of irrational prescribing of chloroquine in Lagos State general hospitals

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Abstract
Background: A major share of the hospital budget is spent on drugs. Irrational use of these drugs is a waste of financial and human resources that could have been deployed for another use within the hospital setting especially in cases where such drugs are provided free to patients. Also there is increased morbidity and progression of severity with irrational use. The objective of this study was to determine the irrational use of chloroquine and the subsequent cost implications in Lagos State general hospitals.
Methodology: A retrospective study period of one year (January to December, 2000) was selected. A total of 18,781 prescription forms of "Free Eko Malaria" were sampled for children and adults from all the Lagos State general hospitals. Drug costs in each prescription form were identified. Cost effectiveness analysis of chloroquine tablet and intramuscular injection was undertaken.
Results: The average cost of medicine per prescription was ₦ 132.071 ($1.03) which should have been ₦ 94.22 ($0.73) if prescribed rationally. The total cost of prescriptions for malaria under study was ₦ 2,480,425.00 ($19,348.09). About 68% {(₦ 1,679,444.00) ($13,100.19)} of the total cost was lost to irrational prescribing. This is a waste of scarce resources. When the prescriptions were differentiated into the different dosage forms prescribed, the prescriptions containing intramuscular injections only had over 90% of the cost lost to irrational prescribing. Cost effectiveness analysis showed that chloroquine tablet was 17 times more cost effective than chloroquine injection (intramuscular) from a health care system perspective while it was 14 times more cost effective from a patient perspective.
Conclusion: There is waste of scarce resources with irrational dispensing of drugs and these resources could have been deployed to other uses or areas within the hospitals. The tablet chloroquine was more cost effective than injection chloroquine (intramuscular). Increasing the cost of tablets, decreasing effectiveness of tablets, decreasing the cost of injections and increasing the effectiveness of injections did not change the cost effectiveness conclusion.
Key Words: Rational use, Irrational use, Cost, Cost effectiveness, Malaria, Chloroquine.

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Introduction

Rational use of medicines 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" [1]. This definition was formulated at the Conference of Experts on the Rational Use of Drugs held in Nairobi in 1985.

Treatment with medicines is one of the most cost-effective medical interventions known, and the proportion of national health budgets spent on medicines ranges between 10% and 20% in developed countries and between 20% and 40% in developing countries.

Rational use of medicines for all medical conditions is fundamental to the provision of universal access to adequate health care, satisfying health-related human rights and attaining health-related Millennium Development Goals. The World Health Organization (WHO) has thus been working to ensure that medicines are used in a therapeutically sound and cost-effective way by health professionals and consumers in order to maximize the potential of medicines in the provision of health care [2]. Thus, the scope of rational or good quality use of medicines covers the elimination of their overuse and underuse and lack of adherence to treatment.

Irrational or non-rational use is the use of medicines in a way that is not compliant with

rational use as defined above. Worldwide more than 50% of all medicines are prescribed, dispensed, or sold inappropriately, while 50% of patients fail to take them correctly. Irrational use of medicines is a very serious global public health problem [http://mednet2.who.int/tbs/tbs2006/tbs_programme06.htm]. Irrational use of medicines not only causes serious harm to patients through suboptimal treatment outcomes and unnecessary side effects, admissions to hospital and death, but also wastes huge amounts of scarce resources [http://www.who.int/gb/ e/e_eb118.html.]

Common types of irrational medicine use include the use of too many medicines per patient (polypharmacy); inappropriate use of antimicrobials, often in inadequate dosage, for non-bacterial infections; over-use of injections when oral formulations would be more appropriate; failure to prescribe in accordance with clinical guidelines; inappropriate self-medication, often of prescription only medicines.

Inappropriate use and over-use of medicines waste resources—often out-of-pocket payments by patients—and result in significant patient harm in terms of poor patient outcomes and adverse drug reactions. Furthermore, over-use of antimicrobials is leading to increased antimicrobial resistance and non-sterile injections are increasing the transmission of hepatitis, HIV/AIDS and other blood-borne diseases. Finally, irrational over-use of medicines can stimulate inappropriate patient demand, and lead to reduced access and attendance rates due to medicine stock-outs and loss of patient confidence in the health system [http://www.who.int/medicines]. The review by Hardon and Le Grand reports the medical effects of inappropriate use of drugs [3].

Malaria is a curable and preventable disease and it is a major public health problem in Nigeria. 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 [4]. It exists as both uncomplicated and severe forms. If the uncomplicated case is not managed promptly and effectively then it can progress to severe malaria which is a more serious problem that can lead to death. At the time of this study chloroquine was the first-line drug for uncomplicated malaria in Nigeria though recently the first-line drug has been changed to Artemisinin based Combination Therapy [4,5] but there is the possibility that chloroquine may still come back on the scene 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 from use [6]. 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 [7,8].

This aim of this study was to determine the irrational use of chloroquine and the subsequent cost implications in Lagos State general hospitals, Lagos State, Nigeria, where malaria is treated free under the “Free Eko Malaria” program.

Materials and Methods

Study area and population

The study was carried out in Lagos State which has twenty local governments. Population of the state is projected to be about 10 million based on the 1991 census using a 6% incremental rate. All ten general hospitals in Lagos State were studied.

Data collection

A retrospective study period of one year (January to December, 2000) was selected. A total of 18,781 prescription forms of “Free Eko Malaria” were sampled for children and adults from Lagos State general hospitals. The prescription forms were sampled using a systematic sampling method [9]. Cost of drugs in each prescription form were determined using the prices obtained from the hospitals except for drugs that were donated, prices of which were obtained from wholesalers. Cost of needles and syringes and cotton swabs were incorporated in prescriptions containing injections (intramuscular).

Total cost of prescriptions and average drug cost per prescription were calculated. Rational and irrational prescribing was determined by calculating the dosage of chloroquine prescribed using the formula: $F = T / R$, where, F = Fraction of total dosage recommended in relation to age; T = Total dosage prescribed in relation to age; and, 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). Incorrect dosage is $F < 0.80$ (classified as underdose) and $F > 1.20$ (classified as overdose).

Cost effectiveness analysis of chloroquine tablet and injection

Cost effectiveness analysis was conducted using a decision table [10]. The criteria used were spectrum of activity (parasite clearance), pharmacokinetics (bioavailability), frequency of administration, safety on administration, and adverse drug reaction/side effect. Cost effectiveness analysis of chloroquine tablet and intramuscular injection was calculated using bioavailability data from literature [11], frequency of administration [12], and by making some assumptions to calculate the criterion rating (Table 1) and effectiveness rating (Table 2). The unit cost of drug and other items required to administer the drugs used in this study were employed to calculate medical costs (Appendix, Table 6). Annual salaries of pharmacist I, senior pharmacist, staff nurse and senior nursing officers in Lagos State were used to calculate personnel costs (Appendix, Table 7).

Table 1. Decision table.

Criterion	Tablet Chloroquine	Value (%)	Injection Chloroquine	Value (%)
1. Spectrum of Activity Assumption	Desired therapeutic outcome (Parasite Clearance)	100	Parasite Clearance	100
2. Pharmacokinetics*	Bioavailability,	90	Bioavailability	90
3. Frequency of Administration**	Frequency of once daily	100	Frequency of administration (8 hourly)	33
4. Safety on administration	Risk of infection 0} Risk of abscess 0} 0% Pain at site of injection 0} Tolerability of administration 100 – 0	100	Risk of infection 50} Risk of abscess 50} 60% Pain at site of injection 80} Tolerability of administration 100 – 60	40
5. Adverse Drug Reaction	Nausea and vomiting 10} Pruritus 10} 10% Tolerability = 100 –10	90	Pruritus 10} Hypotension 60} 50% Cardiac depression 80} Tolerability 100 - 50	50

Once daily frequency of administration=100%; twice daily frequency of administration= 50%; thrice daily (8 hourly) frequency of administration= 33%; four times daily frequency of administration=25%. *Ref 14; ** Ref 15.

Data Analysis

The data were analyzed using EPI Info Version 6 (EPI-6 Info) statistical software [13].

Results

Dosage of Chloroquine (CQ) in the Prescriptions

Over 50% of the prescriptions were irrational (Table 3). When the prescriptions were separated into different dosage forms prescribed, over 90% of prescriptions with intramuscular injection only were irrational while only about 11% of prescriptions with tablets only (Appendix, Table 8) were irrational. Chi square test showed that all the differences in proportion were statistically significant ($p< 0.0001$)

Cost of prescriptions

About 68% of the total cost of prescriptions was lost to irrational prescribing (Table 3). When the prescriptions were separated into different dosage forms prescribed, over 90% of the cost of prescriptions with injection only was lost to irrational prescribing while only about 11% was lost for prescriptions with tablet only (Table 4). Chi square test showed that all the differences in proportion were statistically significant ($p<0.0001$)

Table 2. Effectiveness rating.

	Criterion	Tablet Chloroquine			Injection Chloroquine		
		Value (%)	Assigned Weight	Criterion Rating	Value (%)	Assigned Weight	Criterion Rating
1	Spectrum of Activity	100	0.3	30	100	0.3	30
2	Bioavailability	90	0.2	18	90	0.2	18
3	Frequency of Administration	100	0.1	10	33	0.1	3.3
4	Safety on drug administration	100	0.2	20	40	0.2	8
5	Adverse Drug Reaction (Tolerability)	90	0.2	18	50	0.2	10
6	Sum of Criteria Rating		1.0	**96**		1.0	**69.3**

Criterion Rating = Criterion Value x Assigned Weight (%). Sum of Criteria Ratings = Measure of Effectiveness.

Table 3. Cost and dosage of prescriptions.

	PRESCRIPTIONS n (%)	COST in Naira (%)	Mean Cost in Naira ± SE
CORRECT	8,501 (45.26)	800,981 (32.29)	94.22 ± 0.661
OVERDOSE	3,414 (18.18)	445,825 (17.97)	130.587 ± 0.929
UNDERDOSE	6,866 (36.56)	123,3619 (49.76)	179.671 ± 0.742
TOTAL	18,781 (100)	2,480,425 (100)	132.071± 0.52

Table 4. Cost for correct and incorrect prescriptions in relation to dosage forms prescribed.

	INJ ONLY ₦ (%)	INJ + SYRUP ₦ (%)	INJ + TABLET ₦ (%)	SYRUP ₦ (%)	TABLET ₦ (%)
CORRECT	76,201 (6.6)	98,826 (33.00)	201,179 (58.55)	136,834 (38.46)	287,941 (88.58)
OVERDOSE	12,670 (1.1)	133,230 (44.49)	105,119 (30.60)	168,891 (47.48)	25,915 (7.97)
UNDERDOSE	1,067,717 (92.3)	67,426 (22.51)	37,271 (10.85)	50,004 (14.06)	11,201 (3.45)
TOTAL	1,156,588	299,482	343,569	355,729	325,057

₦ = sum in naira; (%) percentage of the total sum.

Cost effectiveness analysis

Tablet form was 17 times more cost effective than intramuscular injection from a health system perspective and 14 times more cost effective from a patient perspective (Table 5). Tablet form was more cost effective at all levels of sensitivity test both from health system and patient perspectives (Appendix, Tables 9 and 10).

Patient perspective

CEA = Cost / Effectiveness

Tablet CQ=₦41.33/ 96 = ₦ 0.430/Unit of effectiveness.

Injection CQ=₦416.184/ 69.3 = ₦ 6.006/Unit of effectiveness.

Tablet Chloroquine was found to be 14 times more cost-effective than Injection Chloroquine.

Health care system perspective

CEA = Cost / Effectiveness

Tablet CQ=₦ 21.33/ 96 = ₦ 0.222/Unit of effectiveness.

Injection CQ=₦ 256.184/ 69.3 = ₦ 3.697/Unit of effectiveness.

Table 5. Cost per unit effectiveness for tablet and injection.

PERSPECTIVE	TABLET	INJECTION	INJECTION/TABLET
HEALTH SYSTEM	₦0.222	₦3.697	17 times
PATIENT	₦0.430	₦6.006	14 times

Tablet Chloroquine was found to be 17 times more cost-effective than Injection Chloroquine (intramuscular).

Discussion

From the prescriptions surveyed it was discovered that the lowest percentage of correct dose 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.

Underdosage was a major problem when injection chloroquine only is prescribed. Reports in the literature indicate that underdosage is implicated in chloroquine resistant malaria [7,8]. 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 are about 7 to 8 which have to be given every 6 or 8 hours [12]; 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 [11,12]. 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 [14,15]. From the cost effectiveness analysis chloroquine tablet was found to be more cost effective than the injection and this remained valid even with the sensitivity tests whether from a patient perspective or a health system perspective.

The cost of giving tablets was low; furthermore, adverse effects are minimal with tablet dosage form and the possibility of completing the dose is high. For these reasons, injection should be discouraged and tablet chloroquine encouraged.

Consequences of irrational drug use may even include deaths from resistant organisms. Expenditure that could be used more cost effectively allowing patients greater access to drugs and other healthcare benefits and to produce greater benefits for patients under rational use of drug is being wasted. In conclusion, correct dosage was obtained more when tablet chloroquine only was prescribed than any other dosage form. Under-dosage was a major problem when intramuscular injection chloroquine only was prescribed than any other dosage form.

From the results of the cost-effectiveness analysis the tablet chloroquine was more cost effective than the injection chloroquine. Increasing the costs of tablets, decreasing effectiveness of tablets, decreasing the costs of injections and increasing the effectiveness of injections did not change the cost effectiveness conclusion.

It is suggested that tablet chloroquine should be used to treat uncomplicated malaria in our hospitals and where injection cannot be avoided, in case of vomiting patients, the injection should be followed by tablet as soon as the vomiting stops to complete the dose. This study provides evidence that irrational use wastes resources.

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References

1. World Health Organization (WHO) 1985 The Rational Use of Drugs. Report of the Conference of Experts. Geneva: WHO. Resolution WHA54.11
2. Hardon AP and le Grand A. Pharmaceuticals in communities. Practices, public health consequences and intervention strategies. Bulletin 330. Royal Tropical Institute, The Netherlands, 1993.
3. Federal Ministry of Health (FMOH). National Malaria and Vector Control Division. Federal Republic of Nigeria National Antimalarial Treatment Policy. November 2004.
4. Federal Ministry of Health (FMOH). National Malaria and Vector Control Division. Federal Republic of Nigeria National Antimalarial Treatment Guidelines. 2005.

5. Laufer MK, Thesing PC, Eddington ND, Masonga R, Dzinjalamala FK, Takala SL, Taylor TE and Plowe CV (2006) Return of Chloroquine Antimalarial Efficacy in Malawi. New England Journal of Medicine 355: 1959-1966.
6. Bjorkman A and Phillip-Howard PA (1990) Drug resistant malaria: mechanisms of development and inferences for malaria control. Transactions of the Royal Society of Tropical Medicine and Hygiene 84(3): 323-324.
7. Hellgreen U, Ericsson O, Kihamia CM and Rombo L (1994) Malaria parasites and chloroquine concentration in Tanzania school children. Tropical Medicine and Parasitology 45: 293-297.
8. World Health Organisation/Action Programme on Essential Drugs WHO/DAP. How to investigate drug use in Health Facilities. Selected drug use indicators. Geneva. WHO/DAP/93.1. 1993.
9. Cano SB and Fujita NK (1988) Formulary evaluation of third-generation cephalosporins using decision analysis. Am Journal of Hospital Pharmacy 45: 566-569.
10. Tracy JW and Webster LT (Jnr) Drugs used in the Chemotherapy of Protozoal Infections in Goodman and Gilman's The Pharmacological Basis of Therapeutics 10th Edition. (Editors: Hardman JG and Limbird LE) 2001, 1069 – 1095.
11. White NJ The treatment of malaria. The New England Journal of Medicine, 1996, 335: 800-806.
12. Dean AG, Dean JA, Colonbier D, Bredel KA, Smith DC, Burton AH, Dicker RC, Sullivan K, Fagan RF, Arner TG (1995) Epi Info, Version 6: A Word-Processing, Database, and Statistsics Program for Public Health on IBM-compatible Microcomputers. Centers for Disease Control and Prevention, Atlanta, Georgia, USA.
13. Simonsen L, Kane A, Lloyd J, Zaffran M and Kane M (1997) Unsafe injections in the developing world and transmission of blood borne pathogens. Bulletin of the World Health Organization 77: 789-800.
14. Frank C, Mohamed MK, Strickland GT, Lavanchy D, Arthur RR and Magder LS (2000) The role of parenteral antischistosomal therapy in the spread of hepatitis C virus in Egypt. Lancet 355: 887-891.
15. Khan AJ, Luby SP, Fikree FF, Karim A, Obaid S and Dellawala S. (2000) Unsafe injections and the transmission of hepatitis B and C in a periurban community in Pakistan. Bull of the WHO 78: 956-963.

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Conflict of interest: No conflict of interest is declared.

Appendix

Table 6. Calculation of costs.

	Direct Medical Cost	Tablet Chloroquine	Injection Chloroquine
1	Acquisition Cost	10 Tablets x ₦2 = **₦20**	8 Amps of 200mg x ₦15 = ₦120 8 Needles and Syringe x ₦10 = ₦80 8 Cotton wool and Spirit x ₦5 = ₦40 **₦240**
2	Costs Associated with preparation and administration of drug	Pharmacist ₦0.0256 x 52 sec = **₦1.33**	Nurse ₦0.0238 x 85 sec per injection ₦2.023 x 8 doses = **₦16.184**
3	Travel Cost (to patient) assuming ₦20/trip	₦20 x 1 (1 visit) = **₦20**	₦20 x 8 (8 hourly injection) = **₦160**
	Total	**₦41.33**	**₦416.184**

Time for dispensing tablet by the pharmacist = 52 sec. Time for administering the injection by the nurse = 85 sec. The cost here is based on the patient perspective. If only the health care system perspective is considered then the total cost for chloroquine tablet is N21.33 and for injection is ₦256.184.

Table 7. Health care personnel cost.

Personnel	Salary Per Annum	Hours/Week	Number of Weeks/Annum	Mean Salary (₦)/Sec
Pharmacist I	₦176,850	40	52	.0236
Senior Pharmacist	₦206,772	40	52	+.0276 **.0512** **2** **= .0256**
Staff Nurse	₦149,922	40	52	.0200
Senior Nursing Officer	₦206,772	40	52	+.0276 **.0476** **2** **=.0238**

Mean Salary/Second = Annual Salary/(Hours/Week x Weeks/Annum x 3600s).

Table 8. Correct and incorrect prescriptions in relation to dosage forms prescribed.

	INJ ONLY n (%)	INJ + SYRUP n (%)	INJ+TABLET n (%)	SYRUP n (%)	TABLET n (%)
CORRECT	377 (6.37)	587 (34.27)	1,534 (57.95)	1,257 (40.11)	4,746 (88.46)
OVERDOSE	69 (1.16)	707 (41.27)	773 (29.20)	1,421 (45.34)	444 (8.28)
UNDERDOSE	5,476 (92.47)	419 (24.46)	340 (12.84)	456 (14.55)	175 (3.26)
TOTAL	5,922	1,713	2,647	3,134	5,365

INCORRECT (Irrational) = OVERDOSE + UNDERDOSE; n = number of prescriptions; INJ = Injection.

Table 9. Cost per unit of effectiveness for different sensitivity tests using health system perspective.

SENSITIVITY TEST	TABLET	INJECTION	INJECTION/TABLET
Increasing the cost of tablet by 100%	₦ 0.444	₦3.697	8.33 times
Increasing the cost of tablet by 500%	₦1.110	₦3.697	3.33 times
Decreasing effectiveness of tablet to 69.3	₦ 0.308	₦3.697	12.00 times
Increasing the effectiveness of Injection to 96	₦0.222	₦2.669	12.02 times
Decreasing the cost injection by 50%	₦0.222	₦1.848	8.32 times
Decreasing the nursing time to 40 sec per injection	₦0.222	₦3.573	16.09times

Table 10. Cost per unit of effectiveness for different sensitivity tests using patient perspective.

SENSITIVITY TEST	TABLET	INJECTION	INJECTION/TABLET
Increasing the cost of tablet by 100%	₦0.861	₦6.006	6.98 times
Increasing the cost of tablet by 500%	₦2.153	₦6.006	2.79 times
Decreasing effectiveness of tablet to 69.3	₦0.5964	₦6.006	10.07 times
Increasing the effectiveness of Injection to 96	₦0.430	₦4.335	10.08 times
Decreasing the cost injection by 50%	₦0.430	₦3.003	6.98 times
Decreasing the nursing time to 40 sec/injection	₦0.430	₦5.882	13.68 times