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Electronic quality authentication-linked antimalarial drug survey in Sokoto metropolis, Nigeria

Ajibola M. Umarudeen*, Maxwell O. Egua

Department of Pharmacology & Therapeutics, University of Abuja, Abuja, Nigeria

ABSTRACT

Chemotherapy remains a key malaria control strategy but the emergence of resistance to antimalarial drugs by the malaria parasite poses a threat to sustained positive impact of this strategy. Circulation and use of fake/substandard antimalarial drugs are major contributory factors to the development of malaria resistance to chemotherapeutic agents. This antimalarial drug survey was carried out by covert visits to randomly selected commercial drug outlets in Sokoto metropolis, Nigeria, by the research team. The scope of the survey included determining the variety of registered antimalarial drug brands available at the commercial drug outlets in the study area and finding out which of these brands have the National Agency for Food and Drug Administration and Control (NAFDAC) registration numbers with or without the 12-digit (NAFDAC) PIN numbers for electronic drug quality authentication. A total of two thousand and two units of antimalarial drugs distributed across 78 brand names were sampled in this study. All the drugs sampled carried valid expiry dates and registration numbers but only 17 brands (21.79%) had the NAFDAC PIN numbers (and all of them were confirmed to be authentic). None of the syrup or suspension samples had the 12-digit PIN numbers. Sixty-one (78.21%) of the sampled brands spread across various formulations lacked the NAFDAC PIN numbers and their genuineness or sources could not be authenticated at the points of purchase.

Keywords: Antimalarial drug survey, electronic quality authentication

INTRODUCTION

Malaria is a public health front liner in Nigeria with virtually all of her population at risk of the infection and accounting for about two-thirds of all hospital visits. It is estimated that Nigeria loses about 132 billion naira to malaria annually in terms of cost of malaria prevention, treatment and lost man-hours (Carrington, 2001; Jimoh *et al.*, 2007). To combat the malaria menace, prompt malaria diagnosis and effective chemotherapy using Artemisinin – based antimalarial drug combinations was adopted in year 2005 as a key strategy in the National Malaria Control Programs (Eastman and Fidoc, 2009). However, the gains of this anti-malaria policy could be reversed by the emergence of malaria parasite's resistance to antimalarial chemotherapeutic agents (Breman, 2012). Use of fake and/or substandard anti-malarial drugs has been shown to contribute substantially to the development of malaria parasite's resistance to drugs (Tipke *et al.*, 2008; Newton *et al.*, 2010). Drug counterfeiting (antimalarial agents inclusive) is a global phenomenon (El-Duah and Ofori-Kwankye, 2012). In Nigeria, the counterfeit prevalence for all drugs was reported to be about 40% in 2001. Between then and now NAFDAC, the nation's anti- drug counterfeit agency, has stepped up its regulatory activities including the introduction of Mobile Authentication Service and Truscan device. Consequently, the high counterfeit prevalence reported in 2001 for all drugs in general, and the antimalarial drugs in particular, was said to have dropped significantly within a period of about ten years (WHO, 2011; Kelesidis and Falagas, 2015).

In Sokoto metropolis, as in most other Nigerian cities, anti-malarial medicines are sold on the counter to consumers often without prescription. But there is paucity of reports on the survey and quality assessment of anti-malarial medicines available in Sokoto using the NAFDAC-introduced mobile authentication service. This study was conducted to determine the variety of

***Corresponding Author:** Dr. Ajibola M. Umarudeen, Department of Pharmacology & Therapeutics, University of Abuja, Abuja, Nigeria.

E-mail: umarudeen.monisola@uniabuja.edu.ng

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antimalarial drug brands being sold to end users at the various retail outlets in Sokoto metropolis, Nigeria, and to confirm their authenticity by mobile authentication service. For the purpose of this study, an antimalarial drug brand or brand name was defined as any patented antimalarial medicine produced and marketed by a legally licensed pharmaceutical company. Herbal preparations and supplements were not captured by this definition and in this survey.

MATERIALS AND METHODS

Study Area and Population

Sokoto metropolis is the capital of Sokoto State, Nigeria, and the seat of the Caliphate. It is located in the Northwestern part of the country, and lies between latitude 13° 3' 490N and longitude 5° 14' 890E. It is at an altitude of 272 m above the sea level, and is in the dry Sahel belt, surrounded by the sandy savannah, and is dotted with isolated hills. It has an annual average temperature of 28.3°C (82.9 °F), and has a warm and dry weather with day-time temperatures generally around 40 °C (104.0 °F) during the months of February to October. The rainy season usually extends from June to October, while the dry season is usually dominated by the cold harmathan wind, particularly between late October and February (Tsoho, 2007). According to the 2006 National population census, Sokoto metropolis has a population of 427, 760 consisting predominantly of Muslims with a minority Christian population. The major indigenous tribes are Hausa and Fulani, but there are also other tribes such as the Zabarmawa, Nupes, Yorubas, Ibos, Edos, and Ebiras. The indigenous residents are majorly subsistence farmers, while those from other tribes are involved in trading/commerce and civil service. Pharmaceutical retail outlets are found in almost all parts of the city with at least a patent medicine store within a 5 minutes' walk from most households.

Data Collection and Analysis

Several randomly selected commercial medicine outlets in Sokoto metropolis were paid covert visits by the research team (in order not to reveal the purpose of the survey) in the months of July and August 2014. Unit samples of antimalarial drug brands were randomly selected and inspected for relevant data such as the manufacturing company, brand names, presence or lack of NAFDAC product registration numbers. Other data obtained were batch numbers, year of manufacture and expiry, formulation forms, whether single or combination therapy, and presence or lack of NAFDAC 12-digit mobile authentication PIN numbers. The drug packs were scratched and the PIN numbers were texted to any of NAFDAC codes 38353 and 1393 via cell phones. Instantaneous electronic responses from these codes indicating whether the drug samples were fake or authentic/original, were recorded. Where and when there was need for further clarification in the course of the study, the alternative NAFDAC GSM number 08039012929 was used. Between August 2015 and May 2018 physical visits were made by our research team to the Sokoto, Ibadan and Abuja NAFDAC offices to seek clarifications/further information on some of our findings regarding some samples of the antimalarial agents that were encountered during the survey, and the number of portals/codes approved by NAFDAC for this mobile authentication service. Data were analyzed as descriptive statistics and summarized as frequencies and percentages.

RESULTS

Electronic drug authentication profile of antimalarial drugs

Pharmaceutical retail outlets were fairly evenly distributed in all the residential areas of the metropolis with a commercial medicine store within 5 minutes' walk of most households. Forty-six retail outlets were visited for this study. In all, a total of 2002 units of anti-malarial drugs were examined in the survey. All the anti-malarial medicines had valid expiry dates as well as NAFDAC product registration numbers but only 202 (10.09%) of the 2002 units carried the 12-digit (NAFDAC) PIN numbers for mobile authentication. The 2002 antimalarial drug samples belonged to 78 different brand names. While only 202 anti-malarial samples belonging to 17 brand names had PIN numbers for mobile authentication service, the remaining 1800 samples belonging to 61 different brands did not possess PIN numbers. Further details of the brands surveyed are as shown in Tables 1-4.

The fourteen brand names with PIN numbers in tablet formulations were: Co-arinate (Artesunate-Pyramethamine-Sulfametoxypyrazine) FDC Adult dose, Amalar (Sulphadoxine-Pyramethamine) tablets, Codisin Plus (Dihydroartemisinin-Piperaquine Phosphate) tablets, Famter ds (Artemether 80mg/Lumefanthrine 480mg) tablets, Tamether Fort (Artemether 80mg-Lumefanthrine 480mg) tablet, Laridox (Suphadoxine-Pyramethamine) tablets, Gvither-Plus (Artemether-Lumefanthrine) Dispersible Tablet, Coatal Forte Artemether 80-Lumefanthrine 480) ACT tablet, ACT Pro AL Forte (Artemether 80mg-Lumefanthrine 480mg)

tablets, Camosunate (Amodiaquine-Artesunate) tablet adult dose, Lonart DS (Artemether 80mg/Lumefantrine 480mg) tablets, Camosunate (Amodiaquine 150mg-Artesunate 50mg) tablets, Camosunate (Amodiaquine 75mg-Artesunate 25mg) tablets, Artequin (Artesunate 600mg-Mefloquine 750mg) tablets and Amatem Forte (Artemether 160mg-Lumefanthrine 960mg) tablets. Of these tablet formulations, Camosunate (Amodiaquine 150mg-Artesunate 50mg) tablets, Camoquine (Amodiaquine 75mg-Artesunate 25mg) tablet and Gvither-Plus (Artemether 20mg-Lumefanthrine 120mg) dispersible powder were in pediatric dosage forms. All of these 17 antimalarial formulations having mobile authentication PIN numbers were electronically confirmed to be original or of authentic sources. Twelve of the fourteen brands of antimalarial tablet formulations were combination therapies while only two (Laridox and Amalar; both of which are Sulphadoxine-Pyramethamine synergies) were monotherapies. Two of the antimalarial brands with PIN numbers for mobile authentication were injections: α-β arteether (E- MAL) and Beether α-β-Arteether. All the units of α-β arteether (E- MAL) and Beether α-β-Arteether injections inspected were electronically confirmed to be original or of authentic quality. None of the antimalarial syrup or suspension samples had PIN numbers for mobile authentication

Table 1: Brand distribution of antimalarial drugs in Sokoto metropolis, Nigeria

Brand formulation	With PIN numbers			Without PIN numbers		
	Combina1tion therapies	Monotherapies	Total	Combination therapies	Monotherapies	Total
Tablets	12	2	14	22	12	34
Syrups	0	0	0	9	8	17
Powders	1	0	1	2	0	2
Injections	0	2	2	0	8	8
Total	13	4	17	33	28	61

Table 2: Percentages of antimalarial brand formulation with or without PIN numbers

Brand formulation	Brand formulations with PIN numbers		Brand formulations without PIN numbers	
	Frequency	Percentage	Frequency	Percentage
Tablets (n = 48)	14	29.17	34	70.83
Syrups (n = 17)	0	0	17	100
Powders (n = 3)	1	33.33	2	66.67
Injections (n = 10)	2	20.00	8	80.00
Total (n = 78)	17	21.79	61	78.21

Table 3: Percentages of combination antimalarial brands with or without PIN numbers

Brand formulation	Combination brands with PIN numbers		Combination brands without PIN numbers	
	Frequency	Percentage	Frequency	Percentage
Tablets (n = 34)	12	35.29	22	64.71
Syrups (n = 9)	0	0	9	100
Powders (n = 3)	1	33.33	2	66.67
Injections (n = 0)	0	0	0	0
Total (n = 46)	13	41.30	33	71.74

Table 4: Percentages of monotherapy antimalarial brands with or without PIN numbers

Brand formulation	Monotherapy brands with PIN numbers		Monotherapy brands without PIN numbers	
	Frequency	Percentage	Frequency	Percentage
Tablets (n = 14)	2	14.29	12	85.71
Syrups (n = 8)	0	0	8	100
Powders (n = 0)	0	0	0	0
Injections (n = 10)	2	20.00	8	80.00
Total (n = 32)	4	12.50	28	87.50

DISCUSSION

The seventy-eight different commercial brands of antimalarials encountered in the survey provided a variety of malaria chemotherapeutic agents (which comprised tablet, suspension, powdery and injectable formulations) that are available to the consumers in Sokoto metropolis. However, these consumers would not be able to determine the genuineness of a greater proportion of these drugs by electronic authentication as only 17 (21.79%) of the 78 commercial antimalarial brands inspected had the 12-digit PIN numbers for electronic drug quality authentication. This could put the Sokoto populace at risk of exposure to counterfeit/substandard antimalarial treatments with the attendant dire consequences. Not the least of these consequences are economic burden on patients, their families, the health system, and manufacturers of good quality drugs, as well as loss of confidence in the health care system (Johnbull and Ume, 2013). Other undesirable consequences of intake of poor-quality antimalarial drugs that could result from this situation whereby medicines of uncertain quality are left to circulate freely include increased morbidity and mortality, development of drug resistance and treatment failures (Akinyandemu, 2013). This risk becomes highly probable judging from the reported high prevalence of drug counterfeiting in Nigeria (Chika *et al.*, 2011; Buowari, 2012), especially in fringe states and remote communities (including Sokoto, Nigeria) where surveillance and other drug regulatory activities may not be as effective as in areas near the central seat of government (Newton et al., 2006). Also, previous similar drug surveys had reported high levels of counterfeit anti-infective medicines in Nigerian pharmaceutical outlets (Shakoor *et al.*, 1997; Taylor *et al.*, 2001).

It is important to note that all the 17 anti-malarial brands that had the PIN numbers for mobile quality authentication were confirmed to be original. It is also instructive to note that only 4 (23.53%) of the 17 antimalarial brands with mobile PIN numbers were monotherapies as compared to 28 (45.90%) of the 61 brands without the NAFDAC PIN numbers. While the monotherapeutic brands with the NAFDAC PIN numbers consisted of only Sulphadoxine-Pyramethamine prophylactic drug, the list of monotherapeutic brands without the PIN number was awash with different anti-malarial mono-therapeutic drugs including banned antimalarial mono-therapeutic drugs such as chloroquine and halofantrine. The finding of higher proportions of unapproved antimalarial brands being on the list of antimalarial brands without the NAFDAC PIN numbers in this study is a pointer to the fact that the mobile authentication scheme can, and should be, a veritable tool in the fight against drug counterfeiting by government and regulatory agencies by ensuring that antimalarial drug manufacturers are mandatorily enrolled into the scheme (WHO, 2011; Akinyuli, 2007). This position is supported by the discovery that all the 17 brands that had the PIN numbers in this study were returned as original on testing; it is therefore arguable that if all the 78 brands were made to possess the PIN numbers, the chances that all of them would be of original and of authentic sources are high.

It presupposes that if malaria drug manufacturers are made to key into the mobile drug quality authentication scheme by NAFDAC, Chloroquine and other unsafe antimalarial mono-therapeutic agents that are not desirable to be in circulation would be effectively screened out at the point of enlisting into the program. It is obvious from this survey that the continued sale/use of Chloroquine (Ughuro *et al.*, 2009) and other single-agent antimalarial chemotherapeutic drugs in the study area several years after their ban for malaria treatment highlights not only the risk to which consumers are exposed, but perhaps also the paucity of

drug regulatory activities and policy enforcement in the metropolis. Continued use of mono-therapeutic agents for the treatment of malaria clinical cases has severally been implicated in the development of malaria parasite's resistance to malaria chemotherapeutic agents (Mutabingwa, 2005; Dodoo *et al.*, 2009). Antimalarial mono-therapeutic drugs are still rampant in the market today due to factors bothering on their supply and demand. Factors on the supply end of the chain have been outlined to include reduced unit cost of producing these mono-therapeutic agents and hence increased profits for desperate drug manufacturers, and also weak drug supply regulation, in addition to poor drug supply monitoring and supervision. On the demand end of the antimalarial drug distribution chain is the continued attraction of these mono-therapeutic agents to consumers because they are far cheaper than the Artemisinin-based combination malaria therapeutic agents (Arrow *et al.*, 2004). One of the findings of this survey was the observation that on the average, most antimalarial monotherapies cost about 200 naira while most antimalarial Artemisinin-based combination therapies cost from 450 – 1,200 naira. More so most consumers can not differentiate between the packages of Artemisinin-based monotherapies and combination therapies, and so they ignorantly go for the more affordable drugs with the belief that both classes of drugs are equally effective.

This study also found that none of the several units of the 17 antimalarial brands in syrups or suspension forms inspected had mobile identification (PIN) numbers. This finding implies that none of the syrup antimalarial medications as at the time of the survey could have their quality electronically authenticated. This scenario could expose the pediatric end users to risk of adulteration because it has been known that pediatric formulations are by their physical nature prone to adulteration, and the pediatric tissues/organs are more sensitive to the adulterants/toxic substances contained in these poor-quality drugs. This is the reason behind the strict global requirements for extra pre-cautionary measures in the formulation of pediatric dosage forms; but in Nigeria, widespread counterfeiting of syrups such as Chloroquine and Sulphadoxine-Pyramethamine has been previously reported (Taylor *et al.*, 2001; Aina *et al.*, 2007; Bonati, 2009). The finding of only two of ten brands of antimalarial injections encountered in this study possessing the PIN numbers may indicate not only poor compliance of manufacturers to this anti-drug counterfeit policy but also weak enforcement by relevant regulatory agencies. Antimalarial injections are employed to treat severe and acute malaria attacks for prompt reduction in the anticipated high malaria parasitemia in such scenarios. Now, if the authenticity/genuineness of the greater number of these drugs could not be confirmed before use, it is obvious that the therapeutic efficacy of treatment with such drugs cannot be guaranteed. These foregoing postulations could have played out in previous reported incidence of circulation/use of counterfeit antimalarial injections (Taylor *et al.*, 2001; Cockburn *et al.*, 2007).

CONCLUSION

Although optimal utilization of the NAFDAC-linked electronic drug authentication scheme has been reported to be beneficial in the fight against drug counterfeiting, this study has shown that several antimalarial commercial brands across all formulations available to consumers in Sokoto metropolis, Nigeria, as at the time of this survey were yet to enroll into the scheme. All stakeholders should gear efforts towards the enrollment of antimalarial, and indeed, all drugs in all parts of the country into the scheme.

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Nil.

Conflict of interest

None declared.

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