Original Research Article

Self-medication as a factor in treatment failure in patients treated for malaria with ACTs in a rural community of Enugu State, Southeast Nigeria

Emmanuel I. Umegbolu*, Nwachukwu C. Ugwunna, David C. Ikwuka

ABSTRACT

Background: Self-medication (SM) is the taking of drugs, herbs or home remedies on one’s own initiative, or following the advice of another person, without consulting the doctor. Drugs that are prone to SM include analgesics, antibiotics, cough syrups, and antimalarials. Treatment failure (TF) in malaria is defined as the inability to clear malarial parasitaemia or resolve clinical symptoms despite administration of an antimalarial medicine. Among other factors, SM has been implicated as a cause of TF. The study aimed to determine the role of SM in TF observed in patients treated with artemisinin-based combination therapies (ACTs) and the strategies employed to tackle this problem.

Methods: 172 patients diagnosed with malaria within the period of the study, were interviewed and 102 of them who engaged in SM with ACTs prior to presentation to the hospital were purposively selected. Data were collected over a period of one month (January 2021) and analysed as descriptive statistics of proportion.

Results: Prevalence of SM among the patients diagnosed with malaria was 59%, and TF in those who engaged in SM 99%. 100% cure rate was recorded using modified triple ACT (TACT) and drug cycling with chloroquine tablets.

Conclusions: The prevalence of SM was 59%, TF 99% and cure rate with modified TACT and drug cycling 100%. The drug regulatory body needs to ensure quality assurance of the ACTs used in the country, and in addition, promote patient education on the adverse effects of irrational SM.

Keywords: Self-medication, Treatment failure, Triple ACT, Drug cycling, Antimalarial

INTRODUCTION

Self-medication (SM) is the taking of drugs, herbs or home remedies on one’s own initiative, or following the advice of another person, without consulting the doctor.1 This practice has been recognised by WHO as part of self-care,, and therefore when done appropriately, can help the individual’s health. On the other hand, if done inappropriately, SM could constitute a problem to the individual and the society at large. By convention, SM has been classified into rational (responsible SM) and irrational types. Responsible SM involves the use of non-prescription, safe, quality medicinal product for the conditions that are easily self-diagnosed or for recurrent conditions that have been previously diagnosed by a physician.2 Benefits of responsible SM include increased access to medication and relief of symptoms for the patient, the active role of the patient in their own healthcare, better use of physician’s and pharmacist’s skills and reduced burden on the government due to health expenditure linked to the treatment of minor conditions, among others. However, the major problems associated
with SM are wastage of resources, increased health risks such as misdiagnosis, drug resistance and interactions, delays in seeking medical advice, adverse drug reactions and polypharmacy.  

Often, patients are compelled by various reasons to resort to SM. Some of their reasons for doing so include urge of self-care, feeling of sympathy towards family members in sickness, lack of time, lack of health services, financial constraints, ignorance, misbeliefs, extensive advertisements, and availability of drugs in outlets other than drug shops. The common sources of information for SM include families, friends, neighbours, the pharmacist, previously prescribed drugs and suggestions from an advertisement in newspapers or popular magazines. In practice, SM can take various forms, including taking one or more medications without physician’s prescription, using the previous drugs in similar situations, using drugs available at home, and not adhering to physician’s prescription. Not all drugs can be used for SM. The ones that are prone to SM include analgesics, antibiotics, cough syrups, and antimalarials. Over the years, SM has gradually grown to become a global practice, occurring both in the developed and developing countries. Some past studies had reported a prevalence of 68% in Britain, 72% in the USA, 75% in Chile, 65% in Brazil and 53% in Mexico.  

Apparently, there is a relationship between SM and treatment failure (TF) through the links of microbial resistance either from inadequate dosing or inadequate duration of treatment, and substandard or fake drugs. With respect to malaria, TF is defined as the inability to clear malarial parasitaemia or resolve clinical symptoms despite administration of an antimalarial medicine. Identifiable factors that give rise to TF include incorrect dose, poor patient compliance in respect of either dose or duration of treatment, poor drug quality and drug interactions, individual pharmacokinetics (poor absorption, distribution, biotransformation and rapid elimination) and SM. Similarly, concurrent treatment with other drugs (example- folate administration in pregnancy) can increase the likelihood of TF. Drug quality has also been implicated in ineffective treatment and possible drug resistance. When quality has been compromised, either through poor manufacturing practices, intentional counterfeiting, or deterioration due to inadequate handling and storage, drugs may not contain sufficient quantities of the active ingredients. While resistance can cause TF, not all TF is due to resistance. Recognising TF in malaria can prove difficult sometimes. In individual patients this is made difficult in many settings by operational issues such as availability and quality of microscopy. Often in Africa, where presumptive diagnosis and treatment for malaria is the rule, detection of TF also tends to be presumptive (persistence or reappearance of clinical symptoms in a patient recently receiving malaria treatment). But in cases where microscopy is used, presence of parasitaemia in a supposedly fully treated patient may indicate TF. And reappearance of parasites within 14 days of treatment is more likely due to recrudescence than reinfection.  

Currently, artemisinin-based combination therapies (ACTs) are recommended by WHO as the first- and second-line treatment of uncomplicated P. falciparum malaria as well as for chloroquine-resistant P. vivax malaria. ACTs combine an artemisinin derivative with a partner drug. While the role of the artemisinin compound is to reduce the number of parasites during the first three days of treatment (reduction of parasite biomass), the role of the partner drug is to eliminate the remaining parasites (cure). The commonly used ACTs include artemether-lumefantrine (A-L), amodiaquine (ASAQ), and dihydroartemisinin-piperaquine (DP). Others include artesunate-mefloquine (ASMQ) and artesunate-pyronaridine (ASPY) (not yet recommended by WHO).  

The WHO recommended three days use of an artemisinin-based combination treatment (ACT) for uncomplicated malaria in endemic areas is obviously failing in some places already. This is due to the gradual emergence of resistance to artemisinin-based treatment over the years. However, findings from various studies have revealed that artemisinin resistance is limited to the Great Mekong sub-Region (GMR) (Cambodia, Thailand, Lao DPR, Myanmar, Vietnam, Myanmar-China-Indian border) at the present. Among other suspected factors, low quality and counterfeit antimalarial drugs have been blamed in this emerging resistance. Recent estimates from Southeast Asia suggest that 50% of the artesunate sold is fake. Also ACTs sold without quality control are ubiquitous in sub-Saharan Africa, both in the private and public sectors. In seven African countries audited under the ACT watch project (Benin, Democratic Republic of Congo, Kenya, Tanzania, Uganda and Zambia), non-quality-assured ACTs accounted for 32% to 89% of the total ACTs used, and, surprisingly, non-quality-assured ACTs were more expensive than the quality-assured drugs.  

Although artemisinin resistance is said to be limited to the GMR presently, the threat of artemisinin and partner drug resistance emerging or spreading to Africa is imminent and efforts need to be made to develop effective anti-malarial treatment.  

Among all the ACTs, arteether-lumefantrine (A-L) is the most widely used antimalarial in endemic countries. In 2017, it was established that A-L alone, accounted for almost 75% of all quality assured ACTs. Unfortunately, some recent reports have revealed a decreased efficacy of A-L in countries like Angola, the Gambia and Malawi. In Nigeria, in 2013, three cases of possible artemisinin-based combination therapy-resistant malaria were reported. Years later, in 2019, another three cases of possible parasite resistance to A-L were also reported in the country. These reports are quite worrisome because, there is no alternative to ACTs presently. This makes it imperative to develop strategies which are needed to prolong the useful therapeutic lifespan of the current
medicines in order to tackle this emerging problem. The possible strategies being considered include extending the duration of the current 3-day regimen of ACT, increasing the dose of the partner drugs, using triple combination therapies (TACT-triple ACT), and utilising multiple first-line treatments.\textsuperscript{30,36} Drug cycling, the process of reintroducing a drug that has formerly lost its efficacy due to resistance of microorganism with the hope that susceptibility to it has been restored, may also be used to combat TF with ACTs. This strategy has been tried in Zambia and Malawi where chloroquine was re-introduced following restoration of susceptibility of P. falciparum to the drug.\textsuperscript{31} The results are yet to be observed. Available records have shown that most of the patients who presented to our hospital within the period of the study had had SM for malaria with various brands of ACTs (mostly A-L) but were still manifesting symptoms of the disease (TF). Therefore, the present study is designed to determine the role SM played in the TF observed in the study participants and the strategies presently being employed to tackle this problem.

METHODS

This was an observational study carried out in Cottage Hospital Inyi in January 2021. The area of the study, Inyi, is one of the five towns that make up Oji River Local Government Area (LGA) in Enugu West Senatorial District of Enugu State. Oji River LGA is located on latitude 6°15’13”N and longitude 7°16’24” E. It is bounded in the north by Udum LGA, in the south by Anambra State, in the east by Awgu LGA, and in the west by Ezeagu LGA. It has an area of 403 km\(^2\) and a population of 126,587 according to the 2006 national census.

The study site, Cottage Hospital Inyi, situated in Inyi, was founded in 1985. The hospital serves the inhabitants of Inyi and other adjoining towns of Akpugoce, Alaw, Achi, Oji River urban community and communities from the neighbouring state of Anambra. The hospital has an average patients’ attendance of 5000 annually.

The study population was made up of all the patients diagnosed with malaria within the period of the study using microscopy. In all, 172 malaria patients were selected. The sample size of 102 patients who engaged in self-medication for malaria treatment with different brands of ACTs was selected purposively through oral interview.

Data were collected over a period of one month, from the beginning to the end of January 2021. The collected data were analysed as descriptive statistics of proportion.

RESULTS

Table 1 shows the participants demographics. From the table it is seen that 24 (24\%) out of 102 patients were less than 18 years of age, while 78 (76\%) were adults older than 18 years. Children to adults were in the ratio of 1:3. The table also shows that 35 (34\%) males and 67 (66\%) took part in the study, constituting a ratio of 1:2.

Table 1: Participants’ demographics (N=172).

| Age (in years) | Number of patients | Proportion (%) |
|---------------|--------------------|---------------|
| <18           | 24                 | 24            |
| >18           | 78                 | 76            |
| Total         | 102                |               |

| Sex      | Number of patients | Proportion (%) |
|----------|--------------------|---------------|
| Male     | 35                 | 34            |
| Female   | 67                 | 66            |
| Total    | 102                |               |

Table 2: Prevalence of SM with ACTs.

| Number of patients | +SM | -SM |
|--------------------|-----|-----|
| 172                | 102 (59\%) | 70 (41\%) |

Table 3: Prevalence of treatment failure (TF) with ACTs.

| Number of patients | +TF | -TF |
|--------------------|-----|-----|
| 102                | 101 (99\%) | 1 (1\%) |

The prevalence of self-medication (SM) is displayed in Table 2. As shown in the table, 102 (59\%) out of 172 patients engaged in self-medication, while 70 (41\%) did not.

Table 3 shows the prevalence of treatment failure among the patients who engaged in self-medication with ACTs. From the table, it is evident that 101 (99\%) of the 102 patients who engaged in SM had treatment failure, while only 1\% had complete cure.

DISCUSSION

Self-medication (SM), defined as the selection and use of drugs by individuals to treat self-recognised or self-diagnosed conditions or symptoms, without consulting the doctor, is a common practice all around the world today. The prevalence of SM ranges from 53\% in Mexico to 75\% in Chile.\textsuperscript{13,15} These data show that the prevalence of SM is on the rise around the world, when compared with previous statistics from past studies which showed that it was 13\% in the USA in 2006.\textsuperscript{7} Antimalarials, in this case ACTs, are among the drugs prone to SM.\textsuperscript{10} The study found a prevalence of SM of 59\% among the patients diagnosed with malaria who had previously taken an ACT as at the time of presentation at the hospital. This finding compares to what had been reported in India by.\textsuperscript{37} However, it contrasts with other studies which found a prevalence of 72\% in the USA, 75\% in Chile, and 75.5\% in Addis Ababa.\textsuperscript{12,13,38} An Egyptian study reported a prevalence of 96\% among the Egyptians.\textsuperscript{39}
In Iran positive correlations between locality (more in urban locations) and high socio-economic status (more in well-to-do people) had been demonstrated by. The finding of a relatively lower prevalence of SM among the study participants could be as a result of the area of the study which is a rural locality. Furthermore, most of the participants were rural farmers, belonging to the lower socio-economic class who had been found to have lower prevalence of SM according to the Iranian study. The fact that the prevalence of SM was only determined among malaria patients could also be a factor in the determination of the prevalence figure. There is a possibility that a higher figure could be obtained if prevalence of SM not limited to ACTs, is measured in the general patient population.

Although resistance can cause TF, not all TF is due to resistance. Low quality and counterfeit antimalarial drugs, among other factors, have been implicated in TF for malaria. The prevalence of TF due to SM among the study participants was 99%. Treatment failure for this study was defined as persistence or non-clearance of patient’s symptoms within two weeks of taking an ACT supported by microscopic evidence of persisting infection determined by the presence of malarial parasite in the patient’s blood sample. This finding could represent a novel one since very few studies have found treatment failure among malaria patients treated with ACTs in Nigeria, although two Nigerian studies have hinted on the possibility of ACT resistance and therapeutic failure after artemether-lumefantrine (A-L) therapy. While one study reported three cases of possible ACT-resistant malaria, the other reported three cases of therapeutic failure after regimen with AL. Treatment failure found in this study could be attributed to low quality and counterfeit ACTs prevalent in sub-Saharan Africa, including Nigeria. Self-medications with such drugs will definitely lead to TF.

Almost all the failed treatment cases in our hospital were treated with a version of triple ACT (TACT) we called modified TACT, by combining injectable artesunate (three doses every 12 hours) to be followed by A-L. Very few of them were treated with drug cycling using chloroquine tablets. 100% cure rate for these cases was recorded. Although TACT and drug cycling, suggested strategies by some researchers for preventing ACT resistance (and subsequently treatment failure), are still subjects of discussion, their applications in this setting were met with successes. On the other hand, those patients that were treated with repeat courses of ACT still experienced treatment failure, until they were switched over to our modified TACT. If the demonstrated TF represents the true situation of things with ACT in the country, then it is time to review the quality and sources of ACT in the country. Also, a review of the national malaria treatment policy may need to be done, taking into consideration the apparently emerging trend of TF with ACTs.

CONCLUSION

The prevalence of SM among the patients diagnosed with malaria was 59%. Treatment failure among those who had taken ACTs as SM before presenting at the hospital was 99%. A cure rate of 100% was achieved using modified TACT and drug cycling. There is need, therefore, for the drug regulatory body to ensure quality assurance of the ACTs used in the country to reduce the prevalence of TF with these drugs. In addition, patient education is necessary to highlight the adverse effects of irrational SM.

ACKNOWLEDGEMENTS

The authors are grateful to the management of Cottage Hospital Inyi for providing an enabling environment for data collection for this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Hernandez JM, Job QJR. Dentistry and self-medication: a current challenge. Med Oral. 2002;7:344-7.
2. World Health Organisation. The role of the pharmacist in self-care and self-medication. Hangue: WHO;1998.
3. World Self-medication Industry. WSMI declaration on self-care and self-medication, 2006a. Available at: https://www.wsmi.org/pdf/boarddeclarationselfcard. pdf . Accessed on 9 January 2021.
4. Almasdy D, Sharrif A. Self-medication practice with nonprescription medication among university students: a review of literature. Arch Pharm Pract. 2011;2:95-100.
5. Patil AD. Self-medication: a potentially avoidable cause of antibiotic nuisance and resistance. Int J Bas Clin Pharmacol. 2013;2:498-99.
6. Bennadi D. Self-medication: a current challenge. J Bas Clin Pharmacol. 2014;5(1):19-23.
7. Phalke VD, Phalke DB, Durgawale PM. Self-medication practices in rural Maharashtra. Ind J Com Med. 2006;31:34-5.
8. Sarahroodi S, Maleki-Jamshid A, Sawalha AF, Mikaili P, Safacian L. Pattern of self-medication with analgesics among Iranian University students in Central Iran. J Fam Com Med. 2012;19(20):125.
9. Jalilian F, Hazavehei SMM, Vahidinia AA, Jalilian M, Moghimbeigi A. Prevalence and related factors for choosing self-medication among pharmacies visitors based on health belief model in Hamadan Province, West of Iran. J Res Health Sci. 2013;1391:81-5.
10. Osemene KP, Lamikanra A. A study of the prevalence of self-medication practice among
11. James D, French H. The development of the self-medicating scale (SMS): a scale to measure people’s belief about self-medicating. Pharm World Sci. 2008;30:794-800.

12. Ren J, Kan H, Duan G. Present situation, problems, countermeasures and suggestions of self-medication. China Pharm. 2016;27:4888-90.

13. Fuentes AK, Villa ZI. Analysis and quantification of self-medication patterns of customers in community pharmacies in southern Chile. Pharm World Sci. 2008;30:863-8.

14. Bertoldi AD, Carmago AL, Silveira MP, Merezes AM, Assunção MC, Gonçalves H et al. Self-medication among adults aged 18 years: the 1993 Pelotas birth cohort study. J Adolesc Health. 2014;55:175-81.

15. Balbuena F, Aranda A, Figueras A. Self-medication in older urban Mexicans: an observational, descriptive, cross-sectional study. Drugs Aging. 2009;26:51-60.

16. World Health Organisation. Global report on antimalarial drug efficacy and drug resistance: 2000-2010. Geneva: WHO. 2010.

17. van Hensbroek MB, Morris-Jones S, Meisner S, Jaffar S, Bayo L, Dackour R et al. Iron but not folic acid, combined with effective antimalarial therapy provides haematologic recovery in African children after falciparum malaria. Trans R Soc Trop Med Hyg. 1995;89:672-6.

18. Bioland PB. Drug resistance in malaria. Switzerland: WHO. 2001.

19. Schapira A, Almeida FLT, Averkiev L, Omawale SJF, Suleimanov G. The Plasmodium falciparum chloroquine in vivo test: extended follow-up is more important than parasite counting. Trans R Soc Trop Med Hyg. 1998;82:39-43.

20. World Health Organisation. World malaria report. Geneva: WHO. 2018.

21. Ouija M, Augerean JM, Paloque L, Benoit F. Artemether-lumefantrine combination therapy: a report of three cases in Benin City, Nigeria. J Braz Soc Trop Med. 2019;52:20190163.

22. Tun KM, Jeeyapant A, Miyint AH, Kyaw ZT, Dhorda M, Mukaka M et al. Effectiveness and safety of 3 and 5 day courses of artemether-lumefantrine for the treatment of uncomplicated falciparum malaria in an area of emerging artemisinin resistance in Myanmar. Mal J. 2018;17:258.

23. Klokrogge F, Workman L, Borrmann S, Teltele M, Lefevre G, Hamed K et al. Artemether-lumefantrine dosing for malaria treatment in young children and pregnant women: a pharmacokinetic-pharmacodynamic meta-analysis. PLoS Med. 2018;15:e1002579.

24. Ursing J, Romro L, Bergqvist Y, Rodrigues A, Kofoed P-E. High-dose chloroquine for treatment of chloroquine-resistant Plasmodium falciparum malaria. J Infect Dis. 2016;213:1315-21.

25. Dipanjan B, Shivaprakash G, Balaji O. Triple combination therapy and drug cycling-tangential strategies for countering artemisinin resistance. Curr Infect Dis Rep. 2017;19-25.

26. Dini S, Zaloums S, Cao P, Price RN, Fowkes FJL, van der Pluijm RW et al. Investigating the efficacy of triple artemisinin-based combination therapies for treating Plasmodium falciparum malaria patients using mathematical modelling. Antimicrob Agents Chemother. 2018;62:e01068-18.

27. Okell LC, Reiter LM, Ebbe LS, Baraka V, Bisanzio O, Watson OJ. Emerging implications of policies on malaria treatment: genetic changes in Pfmdr1 gene affecting susceptibility to artemether-lumefantrine and artesunate-amodiaquine in Africa. BMJ Glob Health. 2018;3:e00099.
37. Kuriachan KE, George GS, Cherian J, Cherian SM, Paul L. A cross-sectional study on the prevalence of self-medication practices and its associated factors among housewives in rural areas of Emakulan district. J Evol Med Dent Sci. 2016;5(46):3009-13.

38. Shalfie M, Eyasu M, Muzeyin K, Worku Y, Martin-Aragon S. Prevalence and determinants of self-medication practice among selected households in Addis Ababa community. PLoS One. 2018;13(3):e0194122.

39. Zeid W, Hamed M, Mansour N, Diab R. Prevalence and associated risk factors of self-medication among patients attending El-Mahsama family practice centre, Ismaila, Egypt. Bull Nat Res Centre. 2020;44:92.

40. Ahmed NM, Sulaiman KH. Self-medication practice among patients attending a sample of primary healthcare centres in Erbil City. J Edu Pract. 2016;7(24):73-9.

Cite this article as: Umegbolu EI, Ugwunna NC, Ikwuka DC. Self-medication as a factor in treatment failure in patients treated for malaria with ACTs in a rural community of Enugu State, Southeast Nigeria. Int J Community Med Public Health 2021;8:5765-70.