

The Menace Due to Fake Antimalarial Drugs

Sankalp Yadav^{1,*}, Gautam Rawal²

¹General Duty Medical Officer-II, Department of Medicine & TB,
Chest Clinic Moti Nagar, North Delhi Municipal Corporation, New Delhi, India

²Attending Consultant, Department of Respiratory Intensive Care,
Max Super Specialty Hospital, Saket, New Delhi, India

***Corresponding Author**

Email: drsankalpyadav@gmail.com

Abstract

The present situation in the sub-Saharan Africa and South East Asia due to malaria is gruesome. The mortality due to malaria is very high. The higher rate of casualties is not because of poor treatment or lack of facilities rather it is due to substandard antimalarial drugs. The huge market of counterfeit drugs supplying the fake antimalarial drugs, particularly artesunate is flourishing. The wide availability of such fake drugs has resulted in panic and fear. Several studies reported the problem of fake antimalarial drugs in the past. A number of radical steps to curb this problem have been taken yet the results are far from acceptable. In this paper authors discuss the issue of fake antimalarial drug Artesunate and suggest methods to control the same.

Keywords: Antimalarial drugs, Artesunate, Fake drugs, Malaria.

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-2797.2016.00007.1

Introduction

The availability of essential medicines to the masses is very important. Around the globe around one third of the population lacks access to these lifesaving medicines[1]. The situation is even alarming in low income countries where most of the public is not having access to better health facilities[1]. One of the reason could well be the large scale and ever growing market of fake or spurious drugs[1]. The prevalence of spurious drugs in the market has not only led to higher number of morbidity and mortality, but it has also instilled a feeling of fear, confusion and distrust on the health facilities[1].

Malaria has been a leading cause of death in the developing countries and is a very big public health problem[2]. As per the World Health Organization (WHO) in the year 2015, approximately 3.2 billion people constituting almost half of the world's population were at risk of malaria with approximately 214 million cases of malaria and 438000 deaths[3]. The maximum number of these cases occur in sub-Saharan Africa[3]. Along with this around the globe the ongoing transmission of malaria is found in 97 countries and territories[3].

The problem of Plasmodium falciparum malaria has been known for ages[2]. The situation in resource constrained countries is even graver where the timely access to antimalarial drugs is not easy[2]. Artemisinin-based combination therapies (ACTs) are recommended by the WHO as first-line treatment for Pf malaria[4]. The

Artemisinin derivatives like Artesunate are an essential part of the malaria control and treatment due to its fast antimalarial effects and good tolerance[5]. However, since 1998 there has been continuing problem of fake or counterfeit Artesunate tablets containing no or suboptimal content of the drug[5]. The situation is so pathetic in some countries that most of the available antimalarial drugs like Artesunate is counterfeit and is not as per the International Pharmacopoeia content requirements[5-10]. The reason could well be due to the price, tolerability and its fast action as an antimalarial thus having a wider use, thereby a preferable drug for those involved in the fake drug racket[5].

The hope to control the large scale deaths due to falciparum malaria is by the development of ACT and financial support from various international agencies in order to allow a low cost or free dissemination of the drug to the needy[2]. However, a major drawback in these initiatives is wide spread fake Artemisinin derivatives like Artesunate[2]. The fake antimalarial drugs have been reported from various parts of the globe and is one of the most counterfeited drugs[1,2,12].

The extent of fake antimalarial Artesunate: The fake or spurious antimalarial drugs are widespread in countries like South East Asia and Africa[1,9,13]. The detailed reports of the quality of antimalarial drugs are lacking from the majority of malaria endemic countries[4,14]. A number of ad-hoc surveys and large scale studies from most malarious countries like Cambodia, the Lao People's Democratic Republic (Lao PDR, Laos), Burma, the Thai/Myanmar border, and Vietnam, reported that 33%–53% of bought Artesunate was fake, containing either no or subtherapeutic amounts of Artesunate[2,5-9,15,16]. The reports of spurious Artesunate are also available from the southern China and other parts of Africa[4,5]. Few studies have reported

the extent of this problem in four sub-Saharan African countries[5].

Besides, the latest results from a meta-analysis reported that 35% of over the counter antimalarial drugs from 21 Sub-Saharan African countries, were fake[4]. In a study by Kaur et al. 2015, from Nigeria the generic Dihydroartemisinin formulations were found to be counterfeit as compared to Artemether or Artesunate formulations[4]. However, recent findings in Angola where an antimalarial from a big and famous brand, were found to be counterfeit[4,17-19].

The source of the problem: The Artemisinin derivative like Artesunate had been developed in the People's Republic of China (China)[2,20]. It is extensively used in South East Asia and increasingly in Africa[11]. In the South East and East Asia there are a minimum 16 manufacturers of Artemisinin and its derivatives and thus, huge quantities of medicine are produced for consumption in Asia and export to Africa[21]. Although Artesunate is a vital part of ACTs and an integral part of national malaria control programs, yet is often misused as a monotherapy[2].

A study conducted by Newton et al. 2008, found the roots of these fake antimalarial artesunate to China[2]. Subsequently steps were taken to control wide scale manufacturing of the counterfeit antimalarial[2]. Since then no sincere efforts to control this problem has been reported in the medical literature. The market of fake drugs is flourishing in many countries where the drug companies are producing large amounts of drugs to be exported to the resource poor endemic countries[1].

The solution to control the problem of fake antimalarial drugs: Best quality antimalarial drugs are an essential and very important part of the efficacious malaria control and treatment[22]. The counterfeit drugs are dangerous to the malaria patients and may even lead to the development of drug resistance[23,24]. Besides, it will also affect the aim of meeting the Millennium Development Goals and achieving health for all[25]. The study by Kaur et al. 2015, reported that the generic Artesunate was highly counterfeited, but the reports from the various parts of the world in studies conducted on various other drugs suggest that the higher chances of counterfeit drugs are in the over the counter medicines as compared to the medicines under the control of government agencies[1,4]. The WHO has provided the guidelines for the development of measures to fight the counterfeit drugs[1,26].

The problem of counterfeit antimalarial drugs is not new and requires the action at the level of the lawmaking bodies and the consumers. There is a need to build strict laws and the implication of these laws at the grassroots level[1]. The role of surveillance is also important and may help in controlling this problem of spurious drugs[1]. The companies involved in making fake drugs should be blacklisted. The easy access to the market of

the blacklisted companies should be checked[1]. The law breakers should be punished. Frequent surprise checks on the pharmacies are essential[1]. Also, there should be cancellation of the license of the regular defaulters along with imposing hard punishments[1].

Besides, the latest techniques like Raman spectroscopy, tensiography, near-infrared spectroscopy, isotopic characterization, chromatographic and mass spectrometric radio-frequency identification (RFID), electronic pedigree (E-Pedigree) system, or handheld refractometer can be used to identify the spurious drugs[1,27,28]. The reports of paper test to detect fake Chloroquine are available and thus similar tests could be developed for other antimalarial drugs as well[29]. The efforts should be put in to develop complex labels, which are difficult to copy and the use of SMS text message to check the authenticity of a particular pharmaceutical product are examples of the important steps that could help in controlling the problem of counterfeit antimalarial drugs like Artesunate[1]. However, all these is difficult in resource constrained countries with low per capita income and poor contribution from the annual health budget[1,30,31]. The role of diffusion of healthcare information to all is essential to control this problem and thus the role of public and private agencies including the NGO's like HIFA2015 is very important[1,25,32,33].

Conclusions

The malaria has been a public health problem. The role of ACTs involving drugs like artesunate are an integral part of the national malaria control programs in many countries. The fake drugs have not only led to serious implications on the patients' health, but it has also resulted in development of distrust on the health facilities. It is a high time that the strict actions should be taken against those involved in the fake drug market. It is very important to control this evil as the fake drugs could even result in the development of resistant strains of malaria. However, in the present context involving poor law enforcement, rampant corruption, the lackluster attitude of the supervising agencies, and paucity of healthcare information to the masses the same may look like a distant dream.

Conflicts of Interest: None declared

Source of Support: Nil

Acknowledgements: None

References

1. Yadav S, Rawal G. Counterfeit drugs: Problem of developing and developed countries. *Int J Pharmaceut Chem Anal.* 2015;2(1):46-50.
2. Newton PN, Fernández FM, Plançon A, Mildenhall DC, Green MD, Ziyong L, et al. A Collaborative Epidemiological Investigation into the Criminal Fake Artesunate Trade in South East Asia. *PLoS Med.* 2008;5(2):e32.

3. WHO. Malaria. Available from URL: <http://www.who.int/mediacentre/factsheets/fs094/en/>. Last accessed 2016 on March 15.
4. Kaur H, Allan EL, Mamadu I, Hall Z, Ibe O, El Sherbiny M, et al. Quality of Artemisinin-Based Combination Formulations for Malaria Treatment: Prevalence and Risk Factors for Poor Quality Medicines in Public Facilities and Private Sector Drug Outlets in Enugu, Nigeria. *PLoS ONE*. 2015;10(5):e0125577.
5. Newton PN, McGready R, Fernandez F, Green MD, Sunjio M, Bruneton C, et al. Manslaughter by Fake Artesunate in Asia—Will Africa Be Next? *PLoS Med*. 2006;3(6):e197.
6. Rozendaal J. Fake antimalarials circulating in Cambodia. *Bull Mekong Malaria For*. 2000;7:62–68.
7. Newton P, Proux S, Green M, Smithuis F, Rozendaal J, Prakongpan S, et al. Fake artesunate in southeast Asia. *Lancet*. 2001;357:1948–1950.
8. Newton PN, Dondorp AM, Green M, Mayxay M, White NJ, Bruneton C, et al. Counterfeit artesunate antimalarials. *Lancet*. 2003;362:169.
9. Dondorp, AM, Newton PN, Mayxay M, van Damme W, Smithuis FM, Yeung S, et al. Fake antimalarials in Southeast Asia are a major impediment to malaria control: Multinational cross-sectional survey on the prevalence of fake antimalarials. *Trop. Med. Int. Health*. 2004;9:1241–1246.
10. Phanouvong S, Reiss S, Smine A. Why be concerned about the quality of antimalarial and ARV drugs? Poster presented at 7th International Congress on AIDS in Asia and the Pacific, Kobe, Japan, 1–5 July 2005. Available from URL: <http://www.uspdqi.org/pubs/other/whyDrugQuality.pdf>. Last accessed 2016 on March 15.
11. Arrow KJ, Panosian CB, Gelband H. Saving lives, buying time: economics of malaria drugs in an age of resistance. Washington (DC): Institute of Medicine of the National Academies; 2004. Available from URL: <http://www.nap.edu/books/0309092183/html/>. Last accessed 2016 on March 15.
12. Newton PN, Green MD, Fernández FM, Day NJP, White NJ. Counterfeit anti-infective medicines. *Lancet Infect Dis*. 2006;6:602–613.
13. Atemnkeng MA, De Cock K, Plaizier-Vercammen J. Quality control of active ingredients in artemisinin -derivative antimalarials within Kenya and DR Congo. *Trop. Med. Int. Health*. 2007;12:68–74.
14. Taberner P, Fernandez FM, Green M, Guerin PJ, Newton PN. Mind the gaps—the epidemiology of poor-quality antimalarials in the malarious world—analysis of the World Wide Antimalarial Resistance Network database. *Malar J*. 2014;13:139.
15. Lon CT, Tsuyuoka R, Phanouvong S, Nivanna N, Socheat C, Sokhan C, et al. Counterfeit and substandard antimalarial drugs in Cambodia. *Trans R Soc Trop Med Hyg*. 2006;100:1019–1024.
16. Hall KA, Newton PN, Green MD, De Veij M, Vandenaabele P, Pizzanelli D, et al. Characterization of counterfeit artesunate antimalarial tablets from southeast Asia. *Am J Trop Med Hyg*. 2006;75:804–811.
17. Faucon B, Murphy C, Whalen J. Africa's Malaria Battle: Fake drug pipeline undercuts progress. *Wall Street Journal* May 29th 2013. Available from URL: <http://online.wsj.com/article/SB10001424127887324474004578444942841728204.html>. Last accessed 2016 on March 15.
18. Newton PN, Taberner P, Dwivedi P, Culzoni MJ, Monge ME, Swamidoss I, et al. Falsified medicines in Africa: all talk, no action. *Lancet Glob Health*. 2014;2(9):e509–10.
19. How to identify counterfeit Novartis Coartem Malaria Drugs. Available from URL: <https://thecounterfeitreport.com/product/395/Novartis-Coartem-Malaria-Drugs.html>. Last accessed 2016 on March 15.
20. World Health Organization. WHO guidelines for the treatment of malaria. Geneva: WHO; 2006. Available from URL: www.who.int/malaria/docs/TreatmentGuidelines2006.pdf. Last accessed 2016 on March 15.
21. Anon. Table recording ACT producers – Artepall Project. Available from URL: http://www.artepall.org/index.php?option=com_docman&task=doc_download&gid=13&Itemid=60. Last accessed 2016 on March 15.
22. WHO malaria report 2013. Available from URL: http://www.who.int/malaria/publications/world_malaria_report_2013/en/. Last accessed 2016 on March 15.
23. Chaccour CJ, Kaur H, Mabey D, Del Pozo JL. Travel and fake artesunate: a risky business. *Lancet*. 2012;22;380(9847):1120.
24. Newton PN, Amin AA, Bird C, Pass more P, Dukes G, Tomson G, et al. The primacy of public health considerations in defining poor quality medicines. *PLoS —One*. 2011;8:e1001139.
25. Yadav S, Rawal G. Self-medication practice in low income countries. *Int J Pharmaceut Chem Anal*. 2015;2:139–42.
26. World Health Organization. Counterfeit drugs—guidelines for the development of measures to combat counterfeit drugs. Geneva: WHO; 1999. Available from URL: <http://apps.who.int/medicinedocs/en/d/Jh1456e/>. Last accessed 2016 on March 15.
27. Swaminath. Faking it-II: Countering and preventing counterfeiting of drugs. *Indian J Psychiatry*. 2009;51(1):9–11.
28. Sukhlecha A. Counterfeit and substandard drugs: The need for an effective and stringent regulatory control in India and other developing countries. *Indian J Pharmacol*. 2007;39:255.
29. Weaver AA, Lieberman M. Paper test cards for presumptive testing of very low quality antimalarial medications. *Am J Trop Med Hyg*. 2015;92(Suppl 6):17–23.
30. Yadav S, Rawal G. Swine flu—Have we learnt any lesson from the past? *Pan Afr Med J*. 2015;22:118.
31. Yadav S, Rawal G, Baxi M. Plagiarism—a serious scientific misconduct. *Int J Health Sci Res*. 2016;6(2):364–366.
32. Yadav S, Rawal G. Healthcare information for all—Is it achievable? *Int J Sci Res Rev*. 2015;4:101–5.
33. Yadav S, Rawal G. The HIFA and the Health Phone: Laying the foundation for combating malnutrition in India. *Int J Health Sci Res*. 2015;5:368–71.