

Original Article

Quality of Antimalarial Drugs in Sudan: Results of Post-Marketing Surveillance

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Abstract

Background: Every government allocates a substantial proportion of its total health budget to drugs. This proportion tends to be greatest in developing countries, where it may exceed 40%. This indicates the importance of assuring the quality of medicines. This study was conducted to assess the quality of antimalarial drugs in Sudan. It was a part of a comprehensive study to test the quality of medicines in Sudanese market (post-marketing surveillance).

Methods: Six states in Northern, Eastern, Western and Central Sudan were chosen for samples collection to represent all Sudanese market. The sampling procedure was designed in a way to determine whether these products were adversely affected by the transport and storage conditions at the periphery. Official inspectors (pharmacists) at state level were responsible for sample collection, coding and transportation to the National Drug Quality Control Laboratory at Khartoum for analysis.

Results: The results identified several significant problems of substandard products in all states. They included percentage failures ranging from 0% to 100% for different antimalarial drug products.

Conclusion: This data indicates significant problems of substandard antimalarial products circulating in the Sudanese market. This appears to be due to non-suitable distribution mechanisms as well as non-suitable storage conditions. Non-compliance with Good Manufacturing Practice (GMP) guidelines by manufacturers in production also seemed to have contributed to this.

Keywords: Antimalarial Drugs, Post-Marketing Surveillance, malaria.

Background

Malaria accounts for about 17-44% of the disease burden in Sudan, causing over 35,000 deaths a year⁽¹⁾. With this high percentage of deaths, malaria presents a serious health and socio-economic challenge. Effective drug treatment continues to be a critical element of any strategy to control malaria. There have been widespread reports of antimalarial drug resistance in the African region at a time when globally the development of resistance is said to exceed the pace at which new antimalarial drugs are being developed⁽²⁾. Reference is made to a study in Nigeria that concluded that 30% of 500 randomly selected samples were counterfeit⁽³⁾.

In many settings, antimicrobial therapy is usually complicated because of not only microbial drug resistance but also patient-related factors, such as poor adherence to therapy, drug side effects, such as vomiting, which may lead to under-dosage, drug interaction and individual variations. Therapeutic

failure also occurs due to medicine problems resulting from poor quality of products, instability of products before they reach the patient, or the use of counterfeit products. Several WHO-sponsored studies have demonstrated significant instability of products during transport by sea, and also during road transport to final destination⁽⁴⁾.

It should also be noted that pharmaceutical products of poor quality might contribute to the emergence of resistance. This is because when patients are treated with poor-quality drugs, resulting in low bioavailability, it leads to drug under-dosage, this in turn promotes the development of resistance. It is therefore important to consider product quality when dealing with the problem of anti-malarial drug resistance. Treatment failure, ascribed to resistance, may also be due to low quality drugs. There was a need to clarify the nature and magnitude of the problem of quality and consequently how it could be specifically

addressed. This study on the quality of antimalarial drugs - as a part of a comprehensive survey of the quality of all drugs circulating in Sudanese market - aims to provide an indication of the nature and magnitude of the problem. The study results would then guide the design of intervention strategies.

Study design and sampling

The most widely used antimalarial drugs, chloroquine, quinine, artemether and mefloquine were evaluated. Four dosage forms: tablets, syrup, suspension and injections were sampled for chloroquine. Two dosage forms: tablets and injections were sampled for quinine. Injectable dosage forms were sampled for artemether and tablets dosage form for mefloquine. Several batches of drugs tested were collected from Northern, Eastern, Western and Central of Sudan to represent all parts of the country. The study was designed to collect samples at various levels of the drug distribution chain, such as hospitals, community pharmacies, public pharmacies, drug stores, health centres and all pharmacy and non-pharmacy outlets. Quality indications were physical and chemical test results in comparison to standard specifications for these products in the relevant pharmacopoeia or in-house specifications for non-pharmacopoeial products.

The sample identification system was based upon an agreed coding method for all states chosen for this post-marketing survey. Samples were collected at the various levels of distribution chain. Each chosen state collected a minimum of 50 samples of each of the eight drug products. The sample collectors made labelling and coding for samples using the following steps:

- They identified the level and institution from which samples were collected.
- They visited the authorities at the institution and household and acquainted them with purpose and importance of the study.

- Agreed on basis for paying the price of drugs that were obtained for samples.
- Collected and carefully labeled samples at the point of collection.
- Sent the collected samples, including coding, to the National Drug Quality Control Laboratory.

Information obtained for each sample included the name of the drug (brand and generic), strength, dosage form, date of manufacture, date of expiry, remarks on storage, location of sample collection and date of sample collection.

Pharmacopoeial drugs samples were analysed according to pharmacopoeial specifications while non-pharmacopoeial were analysed according to the special methods and specification of their manufactures to assess the quality of the products.

Limitations of the study

Samples availability: The most important limiting factor was that samples required for testing were not available in all states. Although the results might give an indication of the quality situation evaluated, statistical variance would be high, due to the limited number of drug products tested. In such cases the results had to be interpreted with caution when trying to conclude something.

Sample quantities: Some samples did not have the required number of units for performing all the required tests.

Results

Figure 1 presents findings by states with the results expressed as a percentage of the samples failing pharmacopoeial standards out of the total number of samples analyzed. The results according to supplier also (public or private), was expressed as percentage failure (Figure 2). Figure 3 showed the causes of failures. Almost 84% of failures were due to change in the physical characteristics (highest was observed in quinine injection due to change in colour, followed by chloroquine syrup and suspension), 8% due to low content of active

ingredient (chloroquine tablets), and 8% due to low dissolution rate (chloroquine tablets). No failure was observed in chloroquine injection, quinine tablets, artemether injection and mefloquine tablets.

Figure (1): Percentage failure of antimalarial drugs

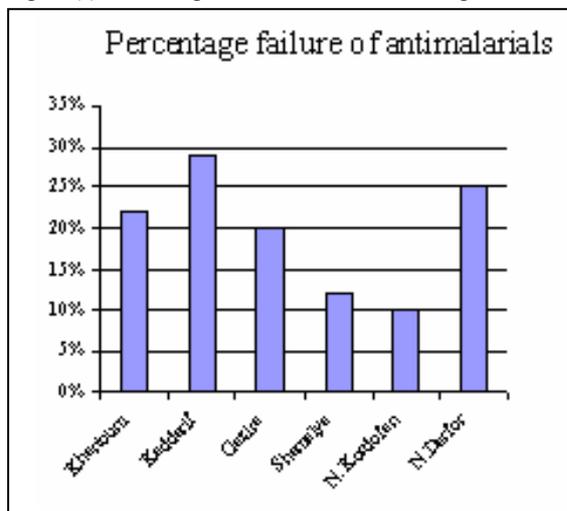


Figure (2) Percentage failure (supplier)

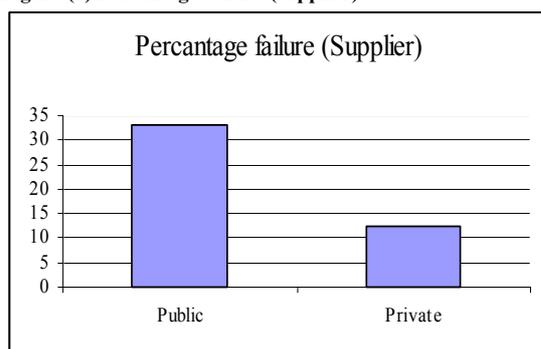
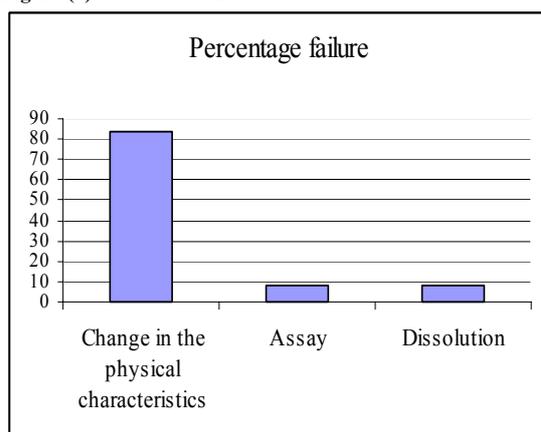


Figure (3): Causes of failure



Discussion

Every government allocates a substantial proportion of its total health budget to drugs. This proportion tends to be greatest in developing countries, where it may exceed 40%. This indicates the importance

of assuring the quality of medicines⁽⁵⁾. Significant quality problems were detected in this study. Figure 2 shows higher failure level in public than private supply system. However, failure levels in both were significant.

As change in the physical characteristics of the tested samples stand for more than 80% of failures, this indicates that, most probably, transport and storage conditions throughout Sudan affect quality of the tested products. As problem of substandard products found in Khartoum at a level almost similar to other states, it is very difficult to suggest whether transport conditions have significant contribution to the problem of substandard or not. Nevertheless, this high rate of failure due to physical characteristics indicates a very serious problem especially for quinine injection which needs further investigation and quick intervention.

This data indicates that there is a significant problem of substandard antimalarial drug products circulating in the Sudanese market. However, as this study faced a number of problems, i.e. from 16 items requested for testing only a range of about 60% (highest in Khartoum state with 68.8%) received in the laboratory, therefore these results can only be taken as indicative, but not conclusive.

In conclusion significant problems of substandard products exist in the Sudanese Market. Percentage failure of samples based on physical appearance ranging from 27% for chloroquine syrup to 100% for quinine injection cannot be ignored. In view of the potential danger that substandard antimalarials could already be posing in the fight against malaria, an intervention plan should be developed immediately. There is a need for more carefully planned and executed studies in order to define quality problems further. The lessons learnt from this first round survey could be valuable in the next phase of investigation, as well as when carrying out interventions to improve the quality of antimalarials

and other medicines circulating in the Sudanese market.

This study was conducted as a first round of a comprehensive study on the quality of drugs circulating in the Sudanese market. The critical methodological and analytical considerations highlighted in this report should be taken into account when planning further studies.

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