Vol. 10 (2007) 59-62

Quality of Antimalarial Drugs Analysed in the National Quality Control Laboratory during the Period 2002–2005

H. K. CHEPKWONY*[1], N. MWAURA[1], E. GUANTAI[1], E. GATHONI[1], F. N. KAMAU[2], E. MBAE[1], G. WANG'ANG'A[1], S. MUTERU[1], N. BIRGEN[1] AND M. WANDETO[1]

[1]*National Quality Control Laboratory (NQCL) For Drugs and Medical Devices, P.O. Box 29726–00202 Nairobi, Kenya.*
[2]*Department of Pharmaceutical Chemistry, School of Pharmacy, University of Nairobi, P.O. Box 19676–00202 Nairobi, Kenya.*

During the period 2002–2005, the National Quality Control Laboratory analysed 229 samples of antimalarial drugs. In 2002, 42% of these products failed to comply with compendial specifications, with the sulfadoxine/ sulfamethoxypyrazine and pyrimethamine combination products forming 39% of the total failures. The respective percentages were 46% and 84% for 2003 and 36% and 72% for 2004. By May 2005, the only failures reported were of sulfadoxine/sulfamethoxypyrazine and pyrimethamine combination products. Until recently, sulfadoxine/sulfamethoxypyrazine and pyrimethamine combination products were the first-line malaria treatment regimen in Kenya. These analytical results raise concerns that the reported therapeutic failures associated with the use of these products could possibly be due to the administration of sub-standard sulfadoxine/sulfamethoxypyrazine and pyrimethamine combination products to patients. The same could be true of artemisinin based combinations which are the current first-line treatment regimen if the observed trend continues.

Key words: Antimalarials, dissolution, assay, quality control tests

INTRODUCTION

Malaria accounts for 30% of all outpatient attendance and 19% of all admissions to health facilities in Kenya. It affects 20 million Kenyans annually and is a debilitating disease that kills 26,000 children per year. The toll the disease exerts must be viewed not only in terms of the physical, financial and emotional pain inflicted on individual families but also by its macroeconomic impact [1].

Efforts by the government, private and non-governmental healthcare providers to solve this problem have focused on streamlining healthcare services and drug delivery as outlined in both the National Malaria Strategy (NMS) 2001-2010 [2] and the National Health Sector Strategic Plan II (2005-2010) [3]. However, the pertinent issue of drug quality has not been adequately addressed.

The National Quality Control Laboratory (NQCL) is routinely involved in the assessment of the quality of the antimalarial drugs for registration and re-registration purposes, as well as during post-marketing and post-distribution surveillance exercises. This paper reports on the quality of antimalarial drug samples analysed at the laboratory from January 2002 to May 2005, which should provide some insight into the quality situation of antimalarials in Kenya.

MATERIALS AND METHODS

The samples were submitted to the NQCL for analysis by the Pharmacy and Poisons Board and were evaluated in accordance with tests outlined in official product monographs prescribed in the United States Pharmacopoeia (U.S.P.), the British Pharmacopoeia (B.P.), the European Pharmacopoeia (Ph. Eur.) or in accordance with the manufacturer's in-house methods of analysis. The chemical reference substances used were obtained from the U.S.P., Ph. Eur and International Pharmacopoiea (I.P.) among others. All reagents used were of analytical grade.

*Author to whom correspondence may be addressed.

ANALYTICAL TESTS

The products sampled were subjected to the tests for identity, uniformity of weight, friability, dissolution test, assay, microbial contamination and sterility as appropriate.

RESULTS

Table 1 is a breakdown of the different antimalarial drugs analyzed from January 2002 to May 2005 while Table 2 is the summary of the results from the analysis of antimalarial products during the same period. Table 3 is a breakdown of the failed products during the relevant period.

Table 1: Antimalarial drugs analysed at the NQCL during the period 2002-2005

Year	Number of samples							Total
	S/P	AMQ	PRO	QUI	ART	ACT	OTHERS	
2002	34	45	5	-	-	-	1	**85**
2003	29	11	-	11	3	-	-	**54**
2004	23	8	11	5	16	4	3	**70**
2005 (Jan-May)	8	1	-	2	6	3	-	**20**

S/P: sulfadoxine/sulfamethoxypyrazine and pyrimethamine combination, AMQ: amodiaquine, PRO: proguanil, QUI: quinine, ART: artemisinin-based derivatives (artesunate, β-artemether, dihydroartemisinin), ACT: artemisinin-based combination therapy, OTHERS: chlorproguanil-dapsone combination and chloroquine.

Table 2: Results of drugs analysis at the NQCL during the period 2002-2005

Year	Total	Total Passed	Total Fail
2002	85	49 (58)	36 (42)
2003	54	29 (54)	25 (46)
2004	70	45 (64)	25 (36)
2005 (Jan-May)	20	16 (80)	4 (20)

Figures in parentheses represent the percentage pass or fail.

Table 3: Breakdown of failed products analysed at the NQCL during the period 2002–2005

Class	Number of failures			
	2002	2003	2004	2005
S/P	14 (41)	21 (72)	18 (78)	4 (50)
AMQ	21 (47)	2 (18)	-	-
PRO	-	-	1 (9)	-
QUI	-	1 (9)	2 (40)	-
ART	-	1 (33)	4 (25)	-
ACT	-	-	-	-
OTHERS	1 (100)	-	-	-
TOTAL	**36**	**25**	**25**	**4**

Figures in parentheses represent the percentage failure rate in each class of antimalarial products, S/P: sulfadoxine/sulfamethoxypyrazine and pyrimethamine combination, AMQ: amodiaquine, PRO: proguanil, QUI: quinine, ART: artemisinin-based derivatives (artesunate, β-artemether, dihydroartemisinin), ACT: artemisinin-based combination therapy, OTHERS: chlorproguanil-dapsone combination and chloroquine.

DISCUSSION

The antimalarial products analyzed at the NQCL showed considerable variation in quality relative to official or in-house specifications. Failure rates were 42%, 46% and 36% for the years 2002, 2003 and 2004 respectively, with those analyzed from January to May 2005 having a failure rate of 20%. When specific classes are examined, the SP products showed consistently high failure rates throughout the period considered being 41%, 72%, 78% and 50% for 2002, 2003, 2004 and 2005 respectively. Amodiaquine formulations had a high failure rate of 47% in 2002, falling to 18% in 2003 while no failures were reported in 2004. Single component artemisinin-based dosage forms had a failure rate of 33% in 2003 and 25% in 2004. No failures were reported between January and May 2005 for this category. Formulations containing quinine had a high failure rate of 9% in 2003 rising to 40% in 2004. Only a small number of ACT preparations were analysed, all of which complied with the relevant specifications. The same was observed for chloroquine as well as chlorproguanil-dapsone dosage forms.

The majority of reported failures among the SP group were tablet preparations that did not comply with the USP specifications for dissolution [4]. In 2002, 79% of the non-compliant SP products were tablets that failed to comply with the USP specifications for dissolution of at least one of the active ingredients. This percentage rose to 90% in 2003 and 94% in 2004. Pyrimethamine was the component that failed in the specifications for dissolution in a majority of such cases. Quality concerns on SP products in the East African Market have been raised previously [7, 8]. In a similar study covering 1996–2000, the failure rate for antimalarial drugs examined was 27.7% where SP products had a failure rate of 40.5%, the major problem being dissolution [9].

The SP products were the first-line antimalarial treatment regimens in Kenya in the period 1997–2002 after which they were replaced with artemisinin-based combination products principally β-artemether-lumefantrine combination due to widespread therapeutic failure arising from resistance [10]. The results obtained show that the therapeutic failure could possibly be due to administration of sub-standard SP products. The administration of sub-standard SP products could bring about therapeutic failure by delivery of sub-therapeutic doses of the active ingredients. Subtherapeutic doses could arise from low content of the active principle ingredient or failure of the formulations to release sufficient amounts of the actives when administered.

The bulk of the products analyzed by the NQCL are products submitted to the Pharmacy and Poisons Board for purposes of registration or re-registration. The results may therefore not be a true reflection of the quality situation in the market. Data on the actual quality of drugs in circulation can only be obtained by regular sustained market surveillance. It is therefore imperative that efficient and comprehensive mechanisms for post-market surveillance of drugs in Kenya be instituted, with priority given to the most commonly used drugs such as anti-infective drugs including antimalarials.

CONCLUSION

The present study raises quality concerns with respect to antimalarial drugs submitted for registration in the Kenyan market. Substandard drugs can lead to therapeutic failure and development of resistance. Quality monitoring before and after registration of such drugs represents one way of ensuring that only products of proven quality enter the market.

ACKNOWLEDGEMENTS

Support for the work by the NQCL is gratefully acknowledged**.**

REFERENCES

[1] K. Njagi and E. Were, Malaria, Kenya Demographic and Health Survey, Ministry of Health, 2003.
[2] National Malaria Strategy 2001–2010, Division of Malaria Control, Ministry of Health, Kenya.
[3] National Health Sector Strategic Plan II, Ministry of Health, Kenya, 2005–2010.

[4] United States Pharmacopoeia, U.S. Pharmacopeial Convention Inc., Rockville, MD, 2002.
[5] British Pharmacopoeia Vol. II, Her Majesty's Stationery Office, London, 2001.
[6] European Pharmacopoeia, Council of Europe, Strasbourg, 1997.
[7] I.O. Kibwage and J.K. Ngugi, East and Cent. Afr. J. Pharm. Sci. 3 (2000) 14–19.
[8] M. B. Jande, O. Ngassapa and I.O. Kibwage, East Cent. Afr. J. Pharm. Sci. 3 (2000) 20–24.
[9] G.N. Thoithi, K.O. Abuga, J.M. Nguyo, G. Mukindia, O. Kingondu, J.K. Ngugi and I.O. Kibwage, East Cent. Afr. J. Pharm. Sci. 5 (2002) 28–32.
[10] National Guidelines for Diagnosis, Treatment and Prevention of Malaria in Kenya, Ministry of Health, 2006.