Comparative Cost and Availabilty of Artemisinin-Based Combination Drugs in Benin City, Nigeria-a multicentre sampling

*AGHAHOWA SE[1], OBIANWU HO[1], ISAH AO[2]

1. Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Benin, Benin City, PMB 1154, Benin City, Nigeria
2. Department of Medicine, School of Medicine, University of Benin, Benin City, Nigeria,

ABSTRACT

Due to the change in the policy governing the treatment of malaria in Nigeria, it became necessary to assess the cost and availability of Artemisinin-Based Combination Therapies (ACTs) in Benin City, Nigeria. This study was carried out using structured data forms that were systematically randomized in twenty-three pharmaceutical outlets on the streets and the University of Benin Teaching Hospital, Benin City, Nigeria. Seven types of Artemisinin-Based Combination Drugs were available in Benin City, Nigeria. These accounted for the forty-seven brands from different companies. There was a significant difference in cost per unit pack of treatment in the pharmaceutical shops and the tertiary institution ($p<0.05$). Artemether-Lumefantrine was the most expensive 1237.50±3.62 (Naira) and Artesunate-sulphadoxine-pyrimethamine 545.21±1.62 (Naira) as least expensive. Reports showed that there were reduced stocks of Chloroquine available. Others drugs such as Artemether, Artesunate, Artheether and Quinine were available as monotherapies for oral and parenteral use. Sulphadoxine-pyrimethamine and Pyrimethamine were available as prophylactic antimalarials. Other combinations such as Piperaquine-Dihydroartemisinin-Trimethoprim, Piperaquine-Dihydroartemisinin-Trimethoprim-primaquine, Pyronaridine-Artesunate, Naphthoquine-Dihydroartemisinin, Artesunate-Chloroquine, Chlorproguanil-Dapsone plus artesunate were unavailable. The report showed that some ACTs were expensive and available in Benin City. It is therefore suggested that concerted efforts should be made to reduce cost and enhance availability of the drugs.

KEY WORDS: Cost, Availability, ACTs, Malaria, Policy.

INTRODUCTION

Malaria afflicts an estimated 90% individuals in the sub-Saharan Africa (WHO 1990). Antimalarial drugs should be readily available and the cost per unit treatment affordable at all times due to the burden posed by the disease on large populations. In recent years new drug therapies have been introduced in the treatment of major tropical diseases because of resistance(WHO, 2001). The questions are: whether these new drugs are available and if they are available what are the cost?

The policy guiding the use of antimalarial drugs has been defined as a set of recommendations and regulations concerning the availability and rational use of antimalarial drugs (WHO, 2001). Selection of antimalarial drugs should enable the populations at risk of malaria have access to safe, effective, good quality and affordable antimalarial drugs so that malaria disease can be promptly treated (WHO, 2001). Following the recommendations by the World Health Organization, Nigeriachanged the policy for malaria treatment in the year 2005. This adoption was as a result of reported resistance to many monotherapies that were sampled in the six geo-political zones. Thus, Artemether-Lumefantrine was recommended as the first line therapy and Artesunate-Amodiaquine as the alternative (FMOH, 2003). Before this time, ACTs were relatively expensive, costs were approximately US$1.20−3.50 per adult treatment (Yeung *et al*, 2004) and ten times more expensive than previously used monotherapies (Salako, 2006). Antimalarial combination therapies may be efficacious as claimed by some authorities (Falade *et al*, 2008), the cost and availability are factors that can influence patients' satisfaction (Personal communication). To address these issues, many models have been proposed in the assessment of the cost of antimalarials (Yeung *et al*, 2004). This work seeks to assess the cost and availability of different brands of ACTs in Community pharmacies and the University of Benin Teaching Hospital, Benin City, Nigeria. The purpose of this sampling is to provide a reference data for individuals and corporate bodies in the selection of ACTs.

***Correspondence: Pharma_sea@yahoo.com**

METHOD

Out of the sixty-four registered pharmacy shops in Benin City as at the time of the study, twenty-three were systematically randomized. The cost per unit pack and brands of ACTs available were assessed in both thecommunity pharmacy outlets and the University of Benin Teaching Hospital, Benin City, using a structured data form. Prior to this, ethical consent was sought and obtained from the institution. Data regarding the ACT brands and prices were collected. These shops were visited within working hours of the pharmacists on duty for adequate information. Unregistered pharmaceutical shops with the Ministry of Health and registered shops whose attendants were not receptive at the time of study were excluded from the sampling.

STATISTICAL ANALYSIS

Data collected were grouped according to brands, generics and cost in naira. They were entered intoMicrosoft excel, SPSS version 11.0 (SPSS, Inc. Chicago, IL) and further computed as mean ±SD. Comparisons were made using Analysis of Variance. *P*-values less than 0.05 were regarded as significant.

RESULTS

Seven different types of Artemisinin-based Combination Therapies were available. These accounted for the forty-six brands of antimalarials available in Benin City, Nigeria. Their cost varied within pharmaceutical shops and in the University of Benin Teaching Hospital, Benin City pharmacy unit. Table 1 showed Artemether-Lumefantrine as most expensive 1237.50±3.62 (Naira) and Artesunate-sulphadoxine-pyrimethamine545.21±1.62(Naira) as least expensive.

Table 1: Comparative cost of acts in naira in community pharmacies and a tertiary institution

BRANDS OF ACTs	COMMUNITY PHARMACIES COST IN NAIRA	TERTIARY PHARMACY COST IN NAIRA	*p*-Value
ARTEMETHER-LUMEFANTRINE CELO[R] ARTRIN[R] COATAL[R] ARTEMETHER-PLUS[R] ASKAMETHER[R]AMATEM[R] ARENAX-PLUS[R] TAMETHER[R] LONART[R] FANTERM[R]ACTPRO[R] CO-ARTESIANCE[R] LUMETHER[R] FALCET[R]	862.56±129.85	1237.50±3.62	<0.05
ARTESUNATE-AMODIAQUINE ARTESUNATE-PLUS[R], CAMOSUNATE[R] , QUINSUNATE[R] DART[R] ACTA[R]ARTESMODIA[R] DIASUNATE[R] OXACIN[R] AROFEN[R] MALMED[R] MALMAX[R]JOARTIN[R] GSUNATE KIT[R] ATC[R] TRIMA[R] ARTEPLUS[R] ZEROMAL[R]	642.06±251.37	900.86±0.06	<0.05
ARTESUNATE-MEFLOQUINE ARFLOQUINE[R] ARTEMEF[R] ARTEQUINE[R] BIOFAST[R]	789.52±134.40	816.25±9.01	<0.05
DIHYDROARTEMISININ-PIPERAQUINEDUOCOTEXCIN[R] P-ALAXIN[R] ARTERAKINE[R] FALCIDIN[R] WAIPA[R] AXCIN[R]	539.29±59.42	620.57±1.25	<0.05
ARTESUNATE-SUPHAMETHOXYPYRAZINE-PYRIMETHAMINE CO-ARINATE[R]	709.00±105.29	730.62±0.25	<0.05
ARTESUNATE-SULPHADOXINE-PYRIMETHETAMINE AMALAR PLUS[R], FARENAX[R]MALOSUNATE[R]	625.00±178.40	545.21±1.62	<0.05
ARTESUNATE-NAPTHOQUINE ARCO[R]	560		

Note that as at the time of this study 1United.States Dollar was equivalent to 160 Nigeria Naira

There was a significant difference in cost per unit pack $p<0.05$. As at the time of this study, 1United States Dollar was equivalent to 160 Nigeria Naira.They all claimed to have procured their antimalarials either directly from manufacturing companies or their representatives. Combinations in the pipeline as classified by WHO, 2001 were out of stock. Representatives of the various outlets claimed to have very reduced stock of chloroquine available on shelf despite the withdrawal by the Federal Ministry of Health Nigeria. Artemether, Artesunate, Artheether were available as monotherapies for oral and parenteral use. Sulphadoxine-pyrimethamine and Pyrimethamine were available as prophylactic antimalarials.

DISCUSSION

The availability as seen in this study showed a clear adherence to the new anti-malarial policy. Nigeria as one of the 106 countries that adopted the use of ACTs has made concerted effort through advocacy and financial support in ensuring that these antimalarials are made available to the populace (WHO, 2001; FMOH, 2003). The availability of ACTs observed is a reflection of awareness among stakeholders of different outlets whether public or private sector; this can however contribute to the reduction of malaria mortality through procurement and stocking of essential antimalarials. Meanwhile, this practice is in line with the principles of essential medicines which emphasized that drugs are made available to satisfy the health-care need of the majority of the populace in any geographical locality. Essential drugs should be safe, efficacious and are available in adequate amount and in different dosage forms (WHO, 1997)

Many brands of ACTs that were available in different outlets are true reflections of availability. The only drawback may be high cost as observed with Artemether-Lumenfantrine. Since this study was done within Benin City, it is therefore suggested that sampling should be extended to rural areas where individuals may also be infected. To verify if these brands are available in the suburban and rural areas. It is worthy to note that many rural dwellers are also prone to having malaria more frequently due to the thriving nature of vectors in the remote areas. The study therefore suggests that ACTs should be well subsidized by the government and corporate organisations so that the affected groups have access to adequate drugs. The advocacy of home-based treatment by some authorities (D'Alessandro *et al*, 2005) suggested training of persons to enable adequate skills in the handling of malaria cases. This approach will be laudable since many cases of uncomplicated malaria are managed outside formal health sectors and has been shown to bring about reduction in mortality associated with malaria in some countries (Kidane and Morrow, 2000).

The cost of ACTs was found to be significantly different in outlets. This may be due to different pattern and sources of procurement. It was generally observed that drugs were sourced from manufacturers and distributed to wholesale and retail outlets. The cost of Artemether-Lumefantrine was found to be the most expensive; this may be related to the cost of production by *Norvatis* as the sole innovator of the product. Most innovator manufacturers spend much in terms of capital and human resources in ensuring safety and efficacy are built-in during preclinical and clinical phases. This may have contributed to the high cost of the drug. The disadvantage of this is that; other manufactures explore the opportunity without going through the rigorous processes of the original drug development. To cut down the cost, it is therefore recommended that the government and agencies should subsidize cost of importation and encourage more indigenous companies to produce and market ACTs in an affordable rate as noticed (Olurishe *et al*, 2007).

Different brands were found to be available in virtually all the pharmaceutical outlets; this reflects suitable availability pattern of drugs for malaria control. The national drug policy principles, emphasized adequate availability in order to allow population at risk have access to safe and efficacious drugs. This availability pattern also supports the principles of rational prescribing. If drugs are prescribed in brands or generics, they can be substituted for one another since many brands were available. Having these brands as alternatives can improve patients' satisfaction since they can have direct access to them when needed. For adequate availability, this will strengthen the home-base management most especially in the vulnerable group. Some of the ACTs were observed to be co-formulated which reflects compatibility of the agents in combination.It is expected that drug in combination should be compatible to ensure *in-vivo* safety and avoid physicochemical degradation on shelf. Availability of different brands of a particular combination can influence prescription pattern negatively. Prescribers may not be aware of the specific brand on shelf, most especially when new agents are introduced into therapies.

It is worthy to note that the cost of a drug does not necessarily relate to efficacy. In this study, some ACTs were found to be expensive compared to others. Drugs can be predicted to have cost advantage due to less frequency in repeating treatment in relation to efficacy as reported by some authors (Hien *et al*, 2003). However, cost alone may not be the overriding determinant of specific antimalarial consumption as observed (Mokuolu *et al*, 2007); other factors such as availability, efficacy and safety can thus have an influence the utilization. The availability seems to be influenced by the existing safety of the monotherapeutic component where safety has been assured in an existing component such as amodiaquine, mefloquine, and pyrimethamine. Although there may be reports of resistance; their use in combination may have been well enhanced in terms of efficacy. Comparative pharmacokinetic profile is recommended for ACTs that have different brands as observed with the combination therapies in order to ascertain their bioequivalence. It is worthy to note that generic substitution can adversely lead to therapeutic failures most especially in centers where quality control assessments are not routinely carried out. There is need for quality control assessment in order to make choices of brands that have outstanding bioequivalence. Facilities may be lacking most especially in developing centers. It is therefore suggested that authorities should establish quality control unit for primary assessment pharmaceutical profile before the drugs are used on patients. This will ultimately aid in effective health care delivery.

Prior to 2005, the cost of some monotherapies and fixed dose combination have been reported (Barnish *et al*, 2004). This high cost may not be peculiar to Benin City and its environs; ACTs could have been expensive in other states of the country since the same policy regulates the procurement and stocking of medicines. Cost-effectiveness assessment was one of the limitations of this study. It is therefore recommended that cost-effectiveness of ACTs should be assessedas a wider pharmaco-economic phenomenon; this shall include a measure of unit costs, distribution costs, media costs of labour costs and other cost profiles in malaria control programmes.

The inherent efficacy and safety may have influenced the stocking and utilization as formerly stated by some authorities (White and Olliaro, 1996). Due to lack of pre-clinical data, especially toxicology data of other combinations, this may have influenced the stocking pattern. A malaria-free environment can be achieved as in Morocco and Turkmenistan (WHO, 2010), if proper adherence to the policy is ensured at all levels of health care delivery.

Limitation of the study: Cost effectiveness was observed as one of the limitations of this study. This was not carried out due to lack of funding.

CONCLUSION

The study showed a wide distribution of ACTs in Benin City; which is reasonably acceptable considering the large populace affected by malaria. It is therefore recommended that agencies should subsidize the cost in order to ameliorate burden to an appreciable level.

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