Physician and patient preferences for sustained release antihypertensive preparations in the Kumasi metropolis, Ghana

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ABSTRACT

Background: Non-adherence to therapy is a major reason for the low control rate of hypertension in Ghana today. Sustained release (SR) antihypertensive preparations are useful in promoting adherence to therapy because of the reduced daily dosing frequency, stable drug levels and reduced toxicity which enhances compliance. One major concern about SR antihypertensives is whether they can be substituted with one another to produce the same effect.

Objectives: This study sought to determine the preferences of physicians and patients for various SR antihypertensive medications in the Kumasi metropolis of Ghana. The views of the respondents on whether the brands of the most used SR antihypertensive were therapeutically equivalent and interchangeable were ascertained.

Methods: Seventy-three (73) community pharmacies, 66 doctors and 150 patients in 50 public, private and mission hospitals and clinics within the Kumasi metropolis were purposively sampled. Respondents were interviewed via interviewer administered structured questionnaires and the information gathered was coded, entered into SPSS software version (16) and analysed. The results were presented as frequencies and proportions, and in tables as well as in figures.

Results: SR nifedipine was the most stocked and used SR antihypertensive drug while Nifecard XL (30 mg) was the preferred brand of patients and doctors. Clinicians considered effectiveness and compliance as two major reasons for their preference for SR nifedipine while patients considered affordability and availability. Sixty percent of prescribers and 41% of patients were of the opinion that all brands of SR nifedipine were interchangeable**.**

Conclusion: There is a gap between prescribers and patients about SR nifedipine brands interchangeability which needs to be bridged to optimize their use to attain better treatment outcomes in Ghana. There is need for continuous education on concepts of therapeutic equivalence and generics substitution for all stakeholders to address the problem of non-adherence to hypertension therapy in Ghana.

Key words: Sustained release, antihypertensive medications, nifedipine, generic drugs, drug interchangeability

Les préférences du médecin et du patient pour la libération prolongée des préparations anti-hypertensives dans la métropole de Kumasi, Ghana

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RESUME

Contexte: La non-observation d'une thérapie est une raison majeure pour le faible taux de contrôle de l'hypertension au Ghana aujourd'hui. La libération prolongée des préparations anti-hypertensives sont utiles dans la promotion de l'observation d'une thérapie à cause de la fréquence réduite du dosage quotidien, des niveaux de médicament stable et de la toxicité réduite, qui améliorent l'observation. Une préoccupation majeure de la libération prolongée des anti-hypertensifs est s'ils peuvent être substitués l'un contre l'autre pour produire le même effet.

Objectifs: Cette étude a cherché à déterminer les préférences des médecins et des patients pour plusieurs médications de libération prolongée anti-hypertensive dans la métropole de Kumasi au Ghana. On a pu établir les avis des personnes interrogées pour savoir si les marques des libérations prolongées (SR) anti-hypertensives étaient équivalentes et interchangeables sur le plan thérapeutique.

Méthodes: Soixante-treize (73) pharmacies communautaires, 66 docteurs et 150 patients dans 50 hôpitaux publics, privés et missions ainsi que les cliniques au sein de la métropole de Kumasi ont servi d'échantillons empiriques. Les répondants ont été interviewés par l'intermédiaire de questionnaires structurés administrés par l'intervieweur et les *informations recueillies étaient* **codées, portées dans la version logiciel** SPSS (16) et analysées. The résultats étaient présentés en fréquences et proportions, et en tableaux ainsi qu'en figures.

Résultats: La nifédipine SR était le médicament anti-hypertensif SR le plus stocké et utilisé tandis que le Nifecard XL (30 mg) était la marque la plus préférée des patients et des docteurs. Les cliniciens ont considéré l'efficacité et la conformité comme deux raisons majeures pour leur préférence de la nifédipine (en libération prolongée) alors que les patients ont considéré le prix et la disponibilité. Soixante pourcent des prescripteurs et 41% des patients étaient d'avis que toutes les marques de nifédipine SR étaient interchangeables.

Conclusion: Il existe une lacune entre les prescripteurs et les patients à propos de l'interchangeabilité des marques de nifédipine SR qui doit être comblée pour optimiser leur usage afin d'arriver à un meilleur traitement au Ghana. Il faut une éducation continue sur les concepts d'équivalence thérapeutique et de substitution générique pour toutes les parties prenantes pour aborder les problèmes de la non-observation de la thérapie de l'hypertension au Ghana.

Mots clés: Libération prolongée, médicaments anti-hypertensifs, nifédipine, médicaments génériques, interchangeabilité de médicaments

INTRODUCTION

Hypertension is the most common cardiovascular condition in the world and the problem of defining a suitable strategy for drug therapy confronts all. In Ghana, reports confirmed the high prevalence of hypertension but worrisome low rates of detection, treatment, and control. [1, 2] One major contributory factor to the low treatment and control rates in Ghana is the high cost of antihypertensive medications which contributes to non-adherence. For example, 93% of patients in Ghana were noncompliant with their antihypertensive regimens, and 96% of these patients cited unaffordable drug prices as the main reason for non-compliance. [3] Even with the introduction of the National Health Insurance Scheme (NHIS), due to inefficiencies in the drug supply management system, patients do not consistently receive their preferred brands and may have to obtain them by cash elsewhere or be served with substituted brands. Hakonsen and Toverud in a study also revealed that among hypertensives, generics substitution has been an important reason for intentional non-adherence since a fraction of the respondents (33%) reported that it was more demanding to keep track of their medication after substitution. [4] Therefore, the choice and use of a convenient dosage form that addresses the patient challenges like cost and frequency of drug administration is very necessary to improve upon control rates of the disease.

The concept of sustained release was developed to eliminate the need for multiple dosage regimens for management of chronic conditions like hypertension which particularly requires constant drug-blood levels over a long period of time. Other potential benefits of sustained-release anti-hypertensive drugs include reduced dosing frequency, enhanced compliance and convenience, reduced toxicity, stable drug levels, uniform drug effect, and decreased total dose. [5] However, with the influx of a variety of imported brands of SR antihypertensive drugs (generics) on the Ghanaian market, the prescriber and pharmacist have been faced with the challenge of selecting from among them one of acceptable quality that will ensure good bioavailability within its shelf-life and thereby yield high treatment outcomes. There are also issues about sub-standard medications which have a possibility of therapeutic failure when used.

Generic drug use, with a few exceptions, has been promoted in western countries by allowing pharmacists to substitute drugs defined as therapeutically equivalent generics. In Canada for example, drug product interchangeability decisions can be based on Health Canada's Declaration of Equivalence, as indicated by the identification of a Canadian Reference Product on a Notice of Compliance for a generic drug. Furthermore, according to Canada's Health Professions Act, an "Interchangeable drug" means a drug that contains the same amount of the same active ingredients, possesses comparable pharmacokinetic properties, has the same clinically significant formulation characteristics and has to be administered in the same way as the drug prescribed. [6] In Ghana today, there is no such detailed drug product interchangeability policy as practiced in Canada and other advanced countries. However, the existence of the Ghana National Drug Policy allows for the selection and prescribing of drugs by their generic or international non-proprietary (INN) names. [7] Prescribers therefore have no control over brands of SR antihypertensive given to hypertension patients at the pharmacies. Scarcity of one product, due to challenges of the drug supply management in health institutions, may cause a patient to be switched over from one brand to another of the same drug (generic). Consequently, due to differences in manufacturing variables of these products and variation in their storage conditions, differences in bioavailability may be observed among brands of a particular SR drug product. The question of interchangeability or substitution among brands has therefore become an issue. [8]

METHODS

Ethical approval considerations

Ethical clearance was sought from the Committee on Human Research and Publication Ethics (CHRPE) at the School of Medical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi and the Komfo Anokye Teaching Hospital, KATH. Official permission was also sought from the medical administrators of the selected hospitals and clinics within the Kumasi metropolis. Before the survey questionnaires were administered, the objectives of the study were explained to the patients. Interviews took place in a private area within the health facilities. Questionnaires were anonymous, with no personal identifying information recorded on them. Study participants were assured of strict confidentiality of the information they provided.

The study area

The survey was conducted in the Kumasi Metropolis which is one of Ghana's 30 political and administrative districts and the capital city of the Ashanti Region,

located in the south-central part of the country. Kumasi is located in the transitional forest zone and is about 270 kilometers north of the national capital, Accra. The metropolis has an area of about 254 square kilometers. With a 5.4% annual growth rate, Kumasi Metropolis is the most populous district in the Ashanti, representing 42.6% of the total population of the region.[9, 10] Health services within the metropolis are organized around 5 Sub-Metro health teams namely, Bantama, Asokwa, Manhyia North, Manhyia South and Subin. Health facilities in the city exist in both the public and private sectors. Notable among them are the Komfo Anokye Teaching Hospital (KATH), which is one of the two (2) national autonomous hospitals, four (4) quasi health institutions, five (5) health Care Centres owned by the Church of Christ and the Seventh-Day Adventist Church. There also exist 13 industrial Clinics in the metropolis and over two hundred (200) known private health institutions. There is an even distribution of all these facilities which is expected to improve the accessibility to health care delivery in the Kumasi Metropolis. [10]

Sampling procedure
Seventy-three (73) community pharmacies, 50 health institutions (comprising 13 public, 32 private and 5 mission hospitals/clinics) and 66 doctors within these facilities were selected. Selection was based on hypertension management. 150 patients were selected purposively based on the use of SR antihypertensive brand for the disease control. The selection of community pharmacies was done by referring to an updated list of all registered pharmacies within the metropolis obtained from the Pharmacy Council office in Kumasi during the survey period (2nd December, 2011 – 5th March, 2012). The selection of facilities ensured that each of the 10 Kumasi sub-metropolis areas was represented as shown in Figure 1.
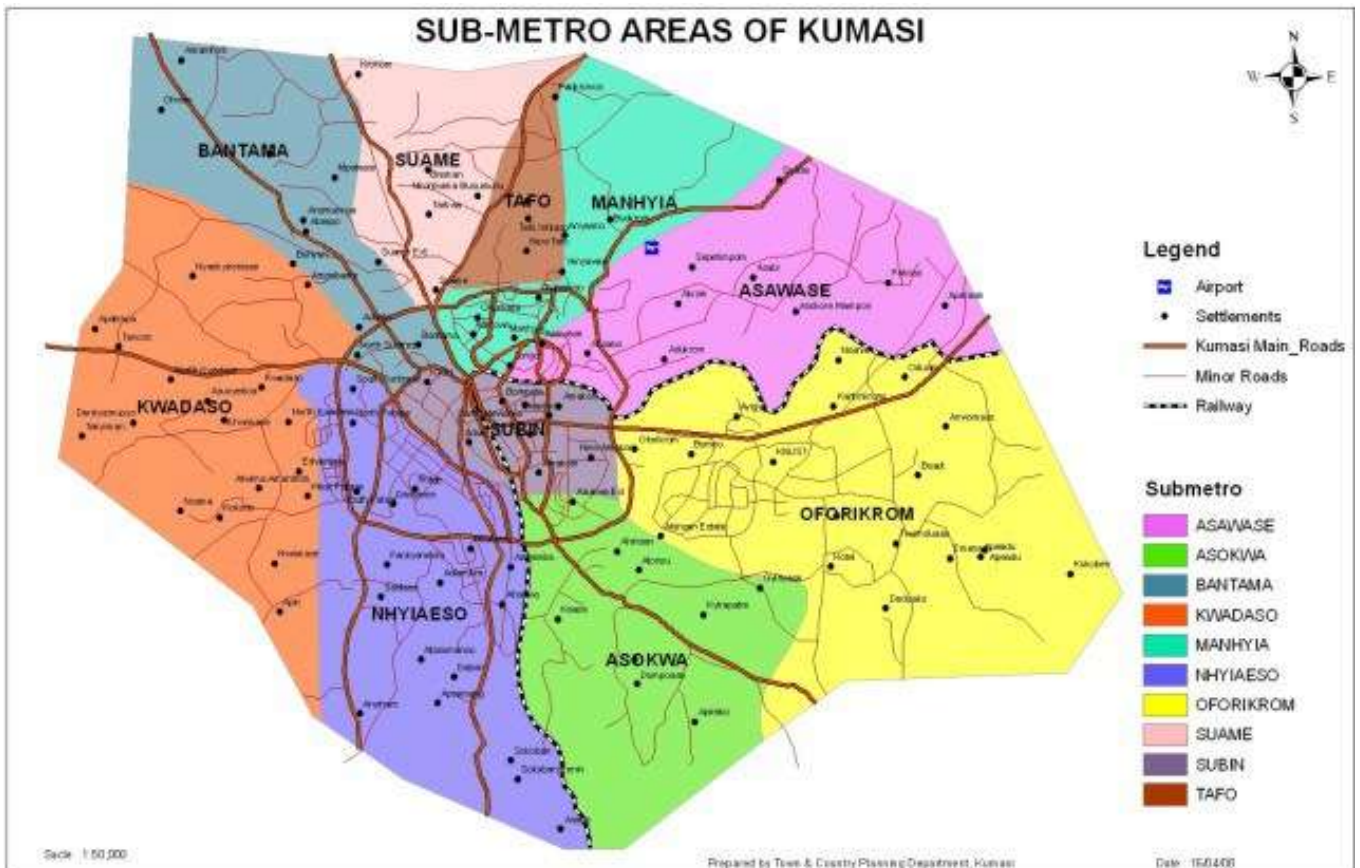

Figure 1: **Sub-metro areas of Kumasi**
Source: Google images

Data collection method
An initial pilot study was done with the aid of an interview guide to collect data on the various types of SR antihypertensive drugs stocked in 73 community pharmacies and 50 hospitals and clinics (which were public, private or mission) within the metropolis. SR nifedipine was the commonest among the SR antihypertensives stocked in the study facilities. A list of the names of the various brands of nifedipine (20 mg and 30 mg) stocked in the facilities visited were captured in the questionnaire to make it easier for prescribers and patients to recollect brand names easily. Information was obtained from two groups of respondents: doctors who handled hypertensive cases and hypertensive patients (from *outpatient Departments*). They were *interviewed via interviewer administered structured questionnaires. The average interview time was about twenty minutes per respondent.*

Data processing and analysis
Information gathered from the survey was edited, coded and entered into the version 16 of Statistical Package for Social Science (SPSS) software. The same software was used for data analysis. The descriptive data was presented as frequencies and proportions (percentages). Subsequently, the analysed data was presented in tables and figures as shown in the results.

RESULTS
Table 1 presents the SR antihypertensive medications found in the study sites. SR nifedipine ranked first in each of the pharmacies/health centres visited followed by indapamide, atenolol and diltiazem hydrochloride, respectively.

Table 1: Study sites and SR products found in pharmacy outlets

Health centre	SR drug	Frequency*
Community pharmacy (N=73)	Nifedipine	50
	Indapamide	13
	Atenolol	7
	Diltiazem HCl	3
Public hospitals (N=13)	Nifedipine	10
	Indapamide	2
	Atenolol	1
	Diltiazem HCl	0
Private hospitals and clinics (N=37)	Nifedipine	30
	Indapamide	5
	Atenolol	2
	Diltiazem HCl	0

NB: *for the multiple response questions, frequency instead of percentage is used

Results showing patients initial assessment on their ability to identify/distinguish between the various brands they had ever used before their views were solicited on brand preference and interchangeability are shown in Table 2. Seventy four percent (74%) of patients could identify the SR brands they use while 26% could not. Also, while 40% of patients could attest to receiving the same SR brand on each visit to the health outlets, 60 % said they were given different SR brands on their visits. Ninety six percent of patients were concerned about receiving different SR brands on their visits to the health outlets.

Table 2: Patients knowledge on SR brands

Statement	Yes (%)	No (%)
I can identify the SR brand I use	111 (74)	39 (26)
I receive the same SR brand every time	44 (40)	67 (60)
I worry about not receiving same brand	64 (96)	3 (4)

Figures 2 and 3 present the rank of SR nifedipine brands preferred by patients and doctors, respectively. The top 2 brands preferred by doctors and patients were Nifecard XL (30 mg) and Caredin 30, while Adalat was the least preferred brand of both group of respondents. However, there was a slight contrast in preference of SR brands between the two categories of respondents from the 3rd to 5th brands.
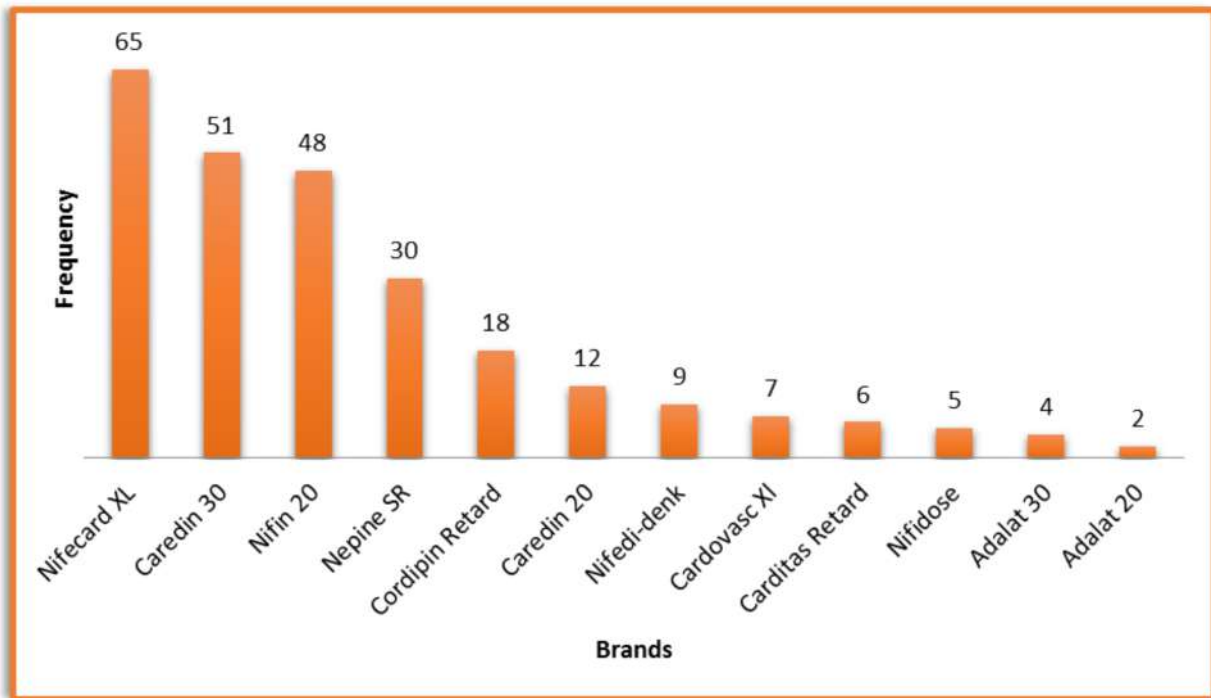

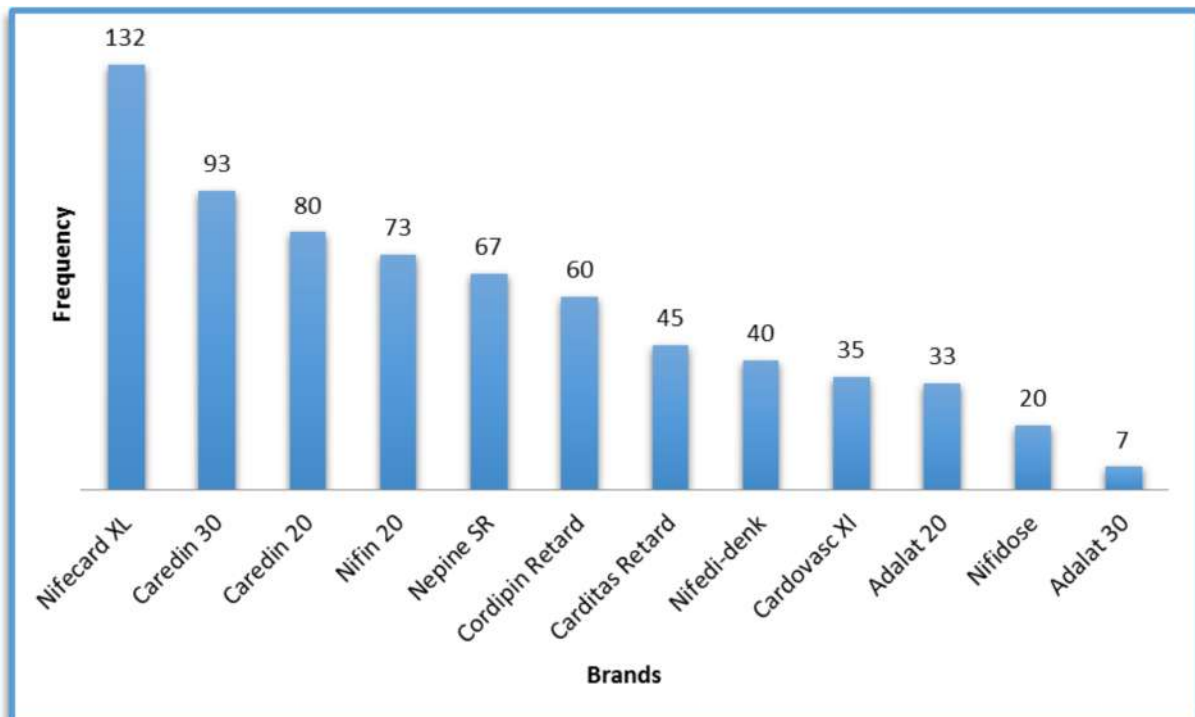**Figure 2: Rank of SR nifedipine brands used by patients in the Kumasi metropolis**

Figure 3: Rank of SR Nifedipine brands prescribed by doctors in the Kumasi metropolis

The reasons given by patients and clinicians for their preference of SR nifedipine brands were different. From Table 3, the major reasons which influenced a clinician's preference of SR nifedipine brands were efficacy and compliance. For patients, the choice of SR nifedipine brands centred mostly on affordability and availability of the prescribed medication.

Table 3: Reasons for preference of SR nifedipine brands by doctors and patients

Respondents	Reasons for preference	Frequency*	Rank
Doctors (N=66)	Perceived efficacy	49	1
	Compliance	47	2
	Tolerability	39	3
	Availability	26	4
	Insurance coverage	15	5
Patients (N=150)	Affordability	105	1
	Availability	87	2
	Insurance coverage	72	3
	Tolerability	69	4
	Efficacy	63	5
	Compliance	50	6

NB: *for multiple response questions, frequency instead of percentage is used

Patients expressed concern about not receiving the same brands of SR nifedipine medications because of possible side effects and perceived lack or variable efficacy of the new brands they receive (Table 4). Results on patients and doctors attitude towards SR nifedipine brands interchangeability are presented in Table 5. Both patients and doctors gave different reasons why different SR nifedipine brands would be interchangeable or not. Forty one percent of patients felt the different brands were interchangeable while 59% said they were not. In the case of clinicians, 60% believed different SR nifedipine brands were interchangeable while 40% said they were not interchangeable.

Table 4: Patients main concerns for not receiving same brands of SR nifedipine

Concern	Frequency
Side effects	25
Efficacy	18
Availability	13
Affordability	8

Table 5: Respondents attitude towards brand interchangeability of SR nifedipine

Respondents	Attitude	Percent
Patients	SR nifedipine brands are interchangeable because they have the same active ingredients and strengths	30
	Different physical characteristics and costs of brands make them not interchangeable	28
	Different manufacturers of various brands have different specifications rendering drugs non-interchangeable	31
	All brands are interchangeable since they are supplied by NHIS as substitutable brands	11
Doctors	SR brands are interchangeable since our training allows for generic prescription	24
	SR brands can be interchanged when their names, strengths and administration modes are similar	36
	Psychological factors, different tolerability and efficacy makes them non-interchangeable	40

DISCUSSION

The major reasons influencing a clinician's preference of SR nifedipine were how effective they presumed the medication to be (efficacy) and ease of adherence to medication regimen (compliance). According to majority of the doctors, their most preferred brand was a product which patients exhibited better clinical outcomes (obtained improved BP readings) on and showed greater compliance due to relatively better tolerability compared to other brands in the group. Some prescribers, however, admitted that their constant choice for some particular brands was simply out of habit, probably due to culture developed right from their training as they understudied specialists in their field. Their reason is a confirmation of Hellerstein's assertion on the effect of habit influencing prescriber's consistent choice of the same version of a given drug.[11] Other reasons clinicians considered for their preference were minimum side-effects in patients, availability and coverage of the drugs in the National Health Insurance Scheme (NHIS) list. Alday *et al*. have also opined in their study that medical histories, drug insurance and personal preferences may also influence a clinician's decision for a particular brand of product.[12]

On the part of the patients, the most important factor (rank 1) influencing their choice of a particular brand was affordability. This finding supports Buabeng *et al*. and Harries *et al.* who found cost as a major contributing factor to patients' non-compliance and subsequently low control rate of the hypertension disease.[3, 13] According to the majority of these patients, although they usually accepted substitution by the

pharmacy as the NHIS list allowed, they considered the inexpensive generics supplied to be of poorer quality than the brand-name products but they had to accept the offer because of economic reasons. This view of inferiority in the quality of substituted generics was similar to that by Himmel *et al.*, who in a study to assess the opinions of primary care patients in Germany on generic drug use revealed that one-third of the participants considered inexpensive generics to be inferior to, or different from, more expensive brand-name drugs because of their lower price.[14] Other considerations informing patients' preferences were by importance, availability, inclusion in NHIS medicines list, side effects (tolerability), efficacy and adherence to medication regimen (compliance).

On the basis of availability and NHIS coverage, most patients' preferred particular brands since as NHIS holders these brands were always available at their respective hypertension clinics. They expressed dissatisfaction when their usual brands were not available. Across various disease states, the feeling of dissatisfaction (such as confusion, anxiety, and misconceptions) reported among patients whenever there were differences in name, appearance and packaging between brands of drugs has also been reported in a study.[15] This consequently leads to non-adherence since patients do not have faith in the effectiveness of other brands and decide not to take them at all. Findings from an earlier study in the Ashanti region in Ghana revealed that only 6.2% of hypertension patients on treatment had their BP adequately controlled.[16] Definitely, such intentional attitude of

non-adherence to therapy could account for low control rates noted in the metropolis and high rates of hypertension in Ghana as indicated in earlier studies. [1,2]

One major contributor to the low control rate of hypertension is the issue of non-adherence as a result of side effects (poor tolerance) associated with certain antihypertensive drugs. [17] In the current study, patients considered issues of side-effects (tolerability) and effectiveness of medications as other major reasons for preferring particular brands with respect to others in the group. Issues about side-effects or tolerability have also been mentioned in a Norwegian survey, in which one-third of the participants reported one or more negative experience with generics substitution, e.g. more side effects or a poorer effect, and 21% reported an overall negative experience with the change. [18]

In the current study, 60% of prescribers were of the view that Nifedipine SR brands were interchangeable, whereas 40% were of the opposing view. Generally, 41% of patients were of the opinion that Nifedipine SR brands are interchangeable whereas 59% thought they were not interchangeable. Moreover, patients (41%) who believed that brands were interchangeable claimed that because all brands had the same active ingredients and were all covered by the NHIS as substitutable brands of the drug, they were interchangeable. For the 59% of patients who believed that brands were not interchangeable, their reasons were that different physical attributes and different costs of the various brands, such as the packaging and different specifications or manufacturing variables among producers of the brands made them not interchangeable.

The opinions of the 40% of doctors who believed that brands were not interchangeable were based on the fact that different tolerability/side effects and efficacy among the various brands did not make them therapeutically equivalent, thus they were not interchangeable. Additionally psychological factors could at times determine a patient's level of adherence and affected the outcome of the treatment, and contributed to it being a decisive factor on possible brand interchangeability or otherwise. This view has been also raised in a study which reported that psychological factors could have effect on how patients saw general tolerability and anticipated effect of substituted brands given them. [8]

However, for the 60% of doctors who believed in possible interchangeability, they were of the opinion that brands of SR drugs like other groups of drugs could be interchanged, as their training allowed for generic prescribing, which works in most cases. In addition, the existence of many generic medicines list in western countries like Canada which allowed for drugs in the medicine list to be prescribed by their generic name attested to the fact that interchangeability was possible. Furthermore, they based their stance on interchangeability with reference to the definition of interchangeable drug as defined in the drug interchangeability update of Canada as "a drug that contains the same amount of the same active ingredients, possesses comparable pharmacokinetic properties, has the same clinically significant formulation characteristics and is to be administered in the same way as the drug prescribed". [6] Therefore since the various SR brands bear these properties, they were interchangeable.

The two contrasting opinions of doctors on brand interchangeability confirm the quote that "Concerns over the therapeutic equivalence of branded products and generics are common amongst physicians too". [8] The views of the respondent doctors in this study confirm that variability of effect of generic substitution, although accepted by clinicians as possible, is little discussed or even understood by them as postulated in a study on generic substitution. [8]

The study encountered a few challenges/limitations. Firstly, participants in the study were not randomly selected. Secondly, the survey did not take into consideration possible changes in respondents preferences over time as the data only reflected the views obtained over a definite time period. Thirdly, respondents were not representative of all hypertensive patients on SR nifedipine brands who attended the hypertension clinics before and after the survey. Finally, the study excluded hypertensive patients who were unable to recollect the names of SR nifedipine brands they were using and also could not identify them from displayed samples.

CONCLUSION

SR nifedipine was the most stocked and used SR antihypertensive drug within the Kumasi metropolis. Between clinicians and patients, there was a slight contrast in preference regarding their 3rd to 5th choice of SR nifedipine medications. Whereas clinicians considered effectiveness of medications and their ease of adherence to medication regimen (compliance) a priority in prescribing, patients preferences were influenced by affordability and availability. On the subject of interchangeability of SR brands of nifedipine,

60% of prescribers and 41% of patients were of the opinion that brands of SR nifedipine brands are interchangeable. There appears to be a gap between prescribers and patients about SR antihypertensive interchangeability which needs to be bridged in order to optimise their use and enhance treatment outcomes in Ghana. Continuous education on concepts of therapeutic equivalence and brand substitution for all stakeholders is a major step in addressing the issue of non-adherence with chronic diseases such as hypertension in Ghana.

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