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Adherence and generic substitution among hypertensive patients in a specialist hospital, Nigeria

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Abstract

Hypertension is the commonest non-communicable disease in Nigeria with a prevalence of about 20-25 per cent in adult Nigerians. This research work examined generic drug substitution and its impact on drug adherence among hypertensive patients attending the Consultant Out-Patient Department of Sobi Specialist Hospital, Ilorin, Nigeria. Self-report adherence, personal interview, structured questionnaires and patients? prescriptions were used to determine drug adherence and treatment outcomes of 167 hypertensive patients on antihypertensive drugs. Adults between the ages of 40 and 80 years were mostly affected, and women were more vulnerable to the disease. The clinical signs and symptoms mostly reported by the patients include severe headache, chest pain, numbness of extremities and general body weakness. The widely utilized generic antihypertensive agents in the studied hospital include Amlodipine, Methyldopa, Nifedipine, Lisinopril, and constituted 91.6

Index terms— Hypertension, drug adherence, generic, prescriptions, substitution, Nigeria.

igh blood pressure (hypertension) is one of the major cardiovascular diseases which ranked third as a cause of disability-adjusted life-years worldwide. It has affected millions of people in both the developed and developing world, and the problem is likely to increase dramatically over the next 15 years (Kearney et al., 2005). Hypertension is the commonest non-communicable disease in Nigeria with a prevalence of about 20-25 per cent in adult Nigerians (Alebiosu, 2010).

The silent nature of hypertension often encouraged the tendency of patients to be nonadherent. The reasons for non-adherence are complex which include; ambivalence about taking drugs, concerns over side effects and complexity of treatment regimen (Ekwunife et al., 2010). Numerous studies have demonstrated that patients' adherence with antihypertensive medications is poor (Inkster et al., 2006). One retrospective study reported just 36% of patients hypertension were adherent with their antihypertensive therapy 12 months after initiating the medications (Cardinal et al., 2004;Chapman et al., 2005; **??**garwal et al., 2009). In Ibadan, Nigeria, Yusuff and Alabi (2007) reported adherence level of 49%, while Ekwunife et al. (2010) observed 70.7% adherence level in Nsukka. However, tackling the widespread failure to take medication correctly could lead to a major reduction in stroke and heart disease. Non-adherence to drug treatment is an established major obstacle in health improvement especially chronic and symptomfree conditions like hypertension (Burnier, 2003). A long term reduction of blood pressure would lead to a reduction in stroke of 56% and a reduction in chronic heart disease of 37% suggesting that adherence therapy would likely be a cost-effective intervention (Fadwa, 2011).

The ultimate economic goal of hypertension management is to balance costs and benefits, but defining these entities may be difficult. The overall cost of treating high blood pressure includes direct costs, such as drug acquisition, physician fees, laboratory and diagnostic tests as well as management of side effects. Indirect costs are inadequate blood pressure control, non-adherence with therapy, and loss to follow up. Generics are a class of lower cost medications prescribed by the physician, and the patient expected same therapeutic effects as the brand-name. The United States Food and Drug Administration (FDA) considered generic and branded drugs to be therapeutically equivalent if they were pharmaceutically equivalent and bioequivalent **??**Duh et al.,

2009). In an era of continuously rising health care costs, the increased use of generic prescription drugs as alternatives to more expensive brand-name products is encouraged by health authorities worldwide. Promotion of cheaper generics, either by generic prescribing or generic substitution, has led to substantial savings in the health care sector in many countries (Duh et al., 2007). When generic substitution takes place, concerns about drug adherence tend to occur. In this respect, drug adherence is defined as the extent to which a person's medication-taking behaviour corresponds with agreed recommendations from a health care provider. The use of brand names may lead to increased cost of drugs for these patients. This means that prescribers were not complying fully with World Health Organization (WHO) recommendation that drugs should be prescribed using their international non -proprietary names. Factors that may be responsible for this trend include the influence of drug promotional activities, pressures of pharmaceutical representatives (detail men), lack of continuing education on the principles of rational prescribing and non-familiarity with generic names among the prescribers. Since generic drugs have the same therapeutic effect as the original formulation but at generally lower costs, their use should be more heavily promoted (Berg, 2007). However, a considerable number of barriers to their wider use have been observed in many countries. Generic substitution has been associated with notable monetary savings for society in several settings and represents one of several strategies aimed at curb pharmaceutical expenditure (Kramer et al., 2007). Generic drugs which contain the same therapeutic substance as the original formulation, become available once the patent protection granted to the brand name drug has expired, leading to greater market competition and lower prices (Jobst and Holmes, 2004). There are, however, different barriers to the wider use of generic drugs. The first is the concern of patients. Secondly, generic substitution is generally met with skepticism by health professionals despite a lack of proven differences in the clinical outcomes of generics and original formulations (Crawford et al., 2006). Physicians who play a central role in the prescription decision have their individual prescribing habits (Danish agency) and tend to prescribe by brand name, generally ignoring drug prices (Nielsen et al., 2008).Thirdly, Pharmacies may also influence the choice of medication by informing patients of the costs or by adopting procedures that increase generic use. Finally, economic and regulatory conditions play a major role on the drugs market, with financial incentives for all parties (prescribers, pharmacists, and patients) being an important factor (Kramer et al., 2007). One major barrier to drug adherence in hypertensive patients is cost of their medications. Blood pressure in un-medicated patients adversely affects cognitive function and social activity with a deterioration of the sense of well being, as the duration of illness increases. To prevent patients' from being trapped in this vicious circle, it is important to consider generic drug substitution (affordable option) along with drug adherence of 90% in achieving blood pressure control. However, little effort has been put into studying generic substitution specifically. The aim of this study was therefore to investigate whether, and in what way, generic substitution might have on drug adherence in hypertensive patients, using personal interviews, drug prescriptions and self report adherence. One hundred and sixty-seven patients made up of 47 males and 120 females diagnosed to have High Blood Pressure (using Sphygmomanometer and Stethoscope) and on antihypertensive agents therapy between February, 2011 and October, 2011 were selected for the study. Inclusion criteria were outpatients diagnosed and confirmed to be hypertensive, between ages of 30 -80 years, attending the Consultant Outpatient Department and refilling their prescriptions in the hospital Pharmacy Department within the study period. The patients who keep to appointments at the hospital and using their drugs for upwards of 2 months prior to the study were included. The benefits, confidentiality and voluntary participation features of the study were explained and written informed consent were obtained from the patients. Three classes of antihypertensive agents considered in the study include the use of Centrally acting drugs (Methyldopa), Angiotensin Converting Enzyme Inhibitors (Lisinopril, Enalapril, Ramipril) Inhibitors and Calcium Channel Blockers (e.g Nifedipine, Amlodipine). Patients excluded were adults below age of 30 years, Psychiatric patients, Prisoners and patients with history of HIV/AIDS.

1 c) Study design

Ethical approval was sought from the management of the hospital and informed consent from all the patients participating in this study at the time of enrollment. All data collected were obtained from the structured questionnaires, drug prescriptions and personal interview with the patients. The patients were asked to show their prescriptions and drugs dispensed to them during interview with the Pharmacist. Within the study period of eight months, 6,122 prescriptions were dispensed of which 91.6% were generic drugs. Also, the different classes of antihypertensive drugs utilized by the patients were recorded. The interview was carried out in local language (Yoruba) which was the main spoken language in the area of study.The importance of the study was duly highlighted to the patients by the researcher. Learned patients themselves completed a paper format questionnaire, which was explained in details prior to completion. Patients who had no formal education or had primary education were interviewed by the pharmacist using the survey forms. Generic drug counseling for each patient was usually carried out at the counseling room of the hospital Pharmacy using standard procedures whenever visit is made to refill their prescriptions.

2 d) Adherence assessment

Self-reporting method was used to determine hypertension treatment medication adherence at the end of each month during drug refilled for eight months.

In the self-reporting patients' adherence method, the patients were interviewed on adherence by asking them to recall how they administered drugs at home during refill of prescription. The Special Projects of National Significance (SPNS) Adherence Initiative self-report questions were used to determine adherence rate among these patients. The number that corresponded with the answer to the questions were added together to get their scores. Scoring greater than 10 equals to good adherence while less than 10 symbolizes poor adherence.

3 e) Statistical analysis

Data generated from the structured questionnaires, drug prescriptions and personal interview were keyed into Genstat statistical package (Genstat, 1995) and analysed for frequencies and percentages. a) Demographic and socio economic characteristics of hypertensive patients at Sobi Specialist, Ilorin.

In the present study one hundred and sixtyseven patients met the inclusion criteria. Female patients dominates with 120 (71.9%) while 47 (28.1%) were males. Twenty-one (12.3%) of them were of the age range of 30-39 years, one hundred and five patients (63.1%) were between 40-60 years old while forty-one (24.6%) of the patients ranged between 61-80 years. On the marital status, most of the patients interviewed were married with one hundred and thirty one (78.4%), while single, widowed and divorced were 2(1.2%), 28(16.8%) and 6(3.6%) respectively. Based on educational career, one hundred and thirty seven (82.4%) had no formal education, nineteen (11.1%) received primary schooling, eleven (6.5%) patients possessed secondary certificates while none had tertiary training. As many as eighty five

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(50.9%) were traders, the rest were civil servants 25 (15.0%), professionals 18 (10.6%), farmers 27(16.2%) and retired workers 12 (7.2%) (Table 1).

5 b) Therapy initiation period

Most of the patients eighty four (50.2%) were in the early stage of therapy of 2-4 months, followed by thirty two (19.1%) for 5-6months, seventeen (10.2%) for 7-9 months, while 10 months and above with thirty four (20.5%) also constituted some parts (Table **??**).

6 c) Clinical symptoms of patients

The clinical conditions experienced by the patients were indicated in Table 3. Patients with severe headaches; seventy three (43.8%) rank first among other symptoms. Chest tightness; thirty-four (20.2%), numbness of extremities; nineteen (11.33%), fatigue; eighteen (11.1%), breathing difficulty; seventeen (10.3%) and six (3.3%) pounding in the head, neck and ears were other conditions that brought the patients to the hospital.

7 d) Antihypertensive drugs prescribed for patients at Sobi Specialist Hospital

The most commonly prescribed antihypertensive drugs in the hospital being studied were as follows, sixty-one (36.5%) were on Amlodipine, thirty-eight (22.7%) patients were on methyldopa, thirtyfive(21.0%) were placed on Nifedipine. Only thirty (18.0%) remained on lisinopril. Rarely use antihypertensive drugs were Ramipril 1(0.7%) and Enalapril 2(1.2%) (Table 4). e) Outcomes of hypertensive patients at Sobi Specialist Hospital, Ilorin of these patients, one hundred and thirty three (79.9%) had no knowledge about their disease state while only 34(20.1%) had an idea about the disease condition being treated for. Most patients, one hundred and fifty-four (92.2%) received comprehensive drug counselling from the pharmacist during prescription refills and very few, thirteen (7.8%) could not benefit from the counselling. A total of six thousand one hundred and twenty-two prescriptions were seen during the study period, of which (91.6%) constituted generic drugs and only (8.4%) were branded drugs. Many patients, one hundred and fifty-one (90.4%) showed no concern or fear for the generic drugs offered to them at the Pharmacy, while minority, sixteen (9.6) patients were uneasy with the generic drugs. On the classification of hypertension, fifty-nine (35.3%) were in stage 1 while majority; eighty-three fell into stage 2, and only twenty-five (15.0%) had Isolated systolic hypertension. In comparison with cost of drugs for a patient per month, generic drug cost four hundred and eighty Naira ($3) while for branded counterpart was two thousand two hundred and twenty Naira ($14) (Table 5)

8 f) Adherence

In the present study, based on patients' selfreport adherence rating (Table 6), one hundred and twenty-three (67.7%) of the patients adhered strictly to their medications while only forty-four (32.3%) were poor adherents.

If a generic drug is deemed to be bioequivalent and has the same active ingredient as the branded drug with the same dose availability and routes of administration, the drug is approved as therapeutically equivalent and substitution is allowed without risk of toxicity or diminished efficacy (Jobst, and Holmes, 2004; Feely et al., 2005;Crawford et al., 2006;Liow et al., 2007). Therefore it is advised that physicians stress the importance of patient compliance and drug adherence to patients and caregivers as it is paramount to treatment success whether

they are taking brand, generics, old or new hypertensive agents (Hakonsen, 2009). In this study, about two-third of the patients were Minnesota and Degl' Innocent (2004) in UK. Contrary to this was the studies of Helle et al. (2009) in Norway whereby 56.9% were males and study of Alebiosu, (2010) in Nigeria that risk factor for essential hypertension include male. The rational for large proportion of women in this study was that women visit hospital more often during their reproductive years (antenatal) whereby they were exposed to different medical tests and received comprehensive counselling on various health diseases including high blood pressure. As soon as they perceived medical ailment, they tend to seek advice from healthcare providers. This contributed to better life expectancy of 48 years for women compared with 46 years for men (CIA World Factbook, 2010).

More than three quarter of the patients receiving treatment for hypertension were within the age range of 40 years and above. This finding is synonymous to study of Alebiosu, (2010), in Nigeria that age greater than 40 years is a risk factor for essential hypertension. This is attributed to the aetiology of hypertension whereby blood pressure generally tends to rise with age. This same patients were victims of rheumatoid arthritis consuming a substantial amount of Nonsteroidal antiinflammatory drugs (NSAIDs) that produce increases in blood pressure averaging 5 mm of mercury (Chobanian et al., 2003). In this study, less than one fifth of the patients were literate while the rest of the patients could not read nor write. This is the consequence of low literacy level of Nigeria citizens compared with developed countries whereby the minimum years of education received by the patients was12 years in Norway (Helle et al, 2009). The high level of ignorance among the population in this country has deprived them March of information on how to prevent and manage hypertension as publicised on radio, television and papers. In support of this research work is The World Health Organization. The World Hypertension League (WHL) recognized that more than 50% of the hypertensive populations worldwide are unaware of their condition. To address this problem, the WHL initiated a global awareness campaign on hypertension in 2005 and dedicated May 17 of each year as World Hypertension Day (WHD). In 2007, there was record participation from 47 member countries of the WHL. During the week of WHD, all these countries -in partnership with their local governments, professional societies, nongovernmental organizations and private industries, -promoted hypertension awareness among the public through several media and public rallies. Using mass media such as Internet and television, the message reached more than 250 million people. As the momentum picks up year after year, the WHL is confident that almost all the estimated 1.5 billion people affected by elevated blood pressure can be reached , 2008) Cenedese, s) females ame as reported by **??**2006 in In the present study, most of the patients were traders. This is in line with study of Enwere et al., (2006) in Ibadan, Nigeria. In the origin of hypertension, stress is a contributory factor to the development of hypertension. Stress which involves physical exertion, psychological disturbance and mental arithmetic stimulate sympathetic nervous system resulting in acceleration of heart rate. These effects of sympathetic stimulation serve elevate blood pressure **??**Aguwa, 2004). This reflected in the present study as more than half of the patients were traders. These patients when interviewed were able to give information on their daily schedule has been rigorous accompany by sleepless nights (recalling the day's sales).This has proned them to severe high blood pressure. Almost half of the patients were new on treatment and showed up within a short period of 4 months to reduce cases of complications. Dispensing of generic drugs to these patients raise little concern as they are new in the therapy and can be easily convinced through drug counselling by the Pharmacist. This improves medication adherence among this category of patients in this setting. Hypertension, being a silent killer, as it is asymptomatic in nature; most patients could not discover the disease at early stage. Almost half of the patients showed up at stage two of the disease. There are generally no symptoms of high blood pressure, people do not feel it. When the blood pressure is extremely high, signs and symptoms now emerged.

In the present research work, severe headache, numbness of the extremities and breathing difficulty were the common symptoms that prompt people to visit primary healthcare providers for treatment. The asymptomatic nature of hypertension tends to subject patients to sudden death as a consequence of nonadherence to their medications. However, patients with such symptoms usually recognize the severity of hypertension and have higher tendency to adhere to their medications. The choice of antihypertensive drug will depend on the relevant indications or contraindications for the individual patients. In this institution, Amlodipine, a dihydropyridine calcium channel blocker is mostly prescribed compared to other antihypertensive agents. Reason being that acceptability of Amlodipine among hypertensive patients is high because of its milder side effects, availability, affordability and simple dosing of once daily regimen. Also, it is the drug of choice in isolated systolic hypertension in the elderly (BNF, 2007).

Systolic hypertension is common among the elderly who constituted the greater percentage of patients receiving treatment for hypertension. Lisinopril, an Angiotensin Converting Enzyme Inhibitor is widely prescribed for patients because of its renoprotective effect. This is an advantage for hypertensive patients with diabetes mellitus. The side effects of dry cough which irritate and inconveniencing patients is a setback to its use. The dry cough could be alleviated by the use of Cromoglycate Sodium. Methyldopa is a centrally acting antihypertensive drug preferred by some physicians because of its cheapness, availability and safety in pregnancy. The side effects of decreased libido and severe depression restricted its acceptability by some patients. However, these side effects could be minimised if the daily dose is kept below 1g **??**BNF, 2007). In this study, Nifedipine is valuable in the management of hypertension because of its cost effectiveness and accessibility but the disadvantages of palpitations and chest pain experienced by few patients limited its use. Generic Enalapril and Ramipril were scantily available in the market except the branded types which seems to be out of pocket for most patients. In

support of this work is the generic prescribing pattern of antihypertensive agents by the study of Jan and Eoin (2007) in Belgium and Enwere et al. (2006) in Ibadan, Nigeria. Furthermore, in agreement with present study is the trials involving beta-blockers, diuretics, calcium channel blockers, anti-platelet agents, statins, angiotensin-converting enzyme inhibitors, and alpha-blockers, no evidence of superiority of brandname drugs against generics was found (Pawel and Przemyslaw, 2010). Patients taking generic drugs appear to be more willing to continue therapy than those taking brand-name medications. Lower co-pays are a key factor. In one recent study of patients with hypercholesterolemia or diabetes, those taking generics had greater adherence compared with patients receiving brand-name drugs (Pawel and Przemyslaw, 2010). The high cost of medications and the large number of prescribed drugs were the common reasons given by patients for non-adherence to prescribed drugs. This further emphasizes the need to reduce the March cost of medications to patients through increased prescription of drugs in their generic names and rational drug prescription without a fall in treatment standards (Enwere et al., 2006).

In this setting, generic drugs were encouraged with almost all the prescriptions from the physicians carrying generic anti hypertensive drugs as recommended by World Health Organisation that drugs should be prescribed using their international nonproprietary names. This contributed to the better drug adherence of 67.7% recorded in this study, since the patients were able to afford the cost of the drugs compared to brand drugs which were almost five times the price of generic drugs. It is a better adherence because the average, adherence to antihypertensive drug therapy is 50% (Berg, 2007), and this is an important factor in why only half of the patients on these drugs achieve adequate blood pressure control **??**Chobanian et al., 2003, Hajjar andKotchen, 2003) (Johnston and Stergiou, 2010). This is reflected in the present study whereby the small number of patients (fifty-four nonadherent patients) could not meet the expenses of branded drugs, hence influencing adherence negatively. The use of brand names may lead to increased cost of drugs for these clients. Factors that may be responsible for this trend include the influence of drug promotional activities, demands of pharmaceutical detail medical representatives, lack of continuing education on the principles of rational prescribing and non-familiarity with generic names among the prescribers. Since generic drugs have the same therapeutic effect as the original formulation but at generally lower costs, their use should be more heavily promoted (Duh et al., 2007). A patient experiencing financial hardship may find it difficult to spend money on a drug particularly if it does not result in an immediate change in health status or the benefit of the drug, is not properly understood (Crawford et al., 2006). Quality healthcare outcomes depend upon patient adherence to recommended treatment regimen. Patients' non-adherence cannot only be a pervasive threat to health, but also carry an appreciable burden as well as human well being (Martin et al., 2005).

Adults between the ages of 40 and 80 years were mostly affected by the hypertension, and women were more vulnerable to the disease. The clinical signs and symptoms mostly reported by the patients include severe headache, chest pain, numbness of extremities and general body weakness. The widely utilized generic antihypertensive agents in the studied hospital include Amlodipine, Methyldopa, Nifedipine, Lisinopril, which constituted 91.6% of all the prescriptions. The high rate of generic drug prescriptions in this hospital coupled with the consistent drug counselling offered to the patients by the pharmacist had greatly improved adherence rate to 67.7%.

9 Generic

drug substitution should be encouraged in all tiers of healthcare system to improve drug adherence and stem the tide of hypertension in the society. Also, public enlightenment and education should be created on media to keep the populace abreast of symptoms, risk factors, lifestyle modifications and complications of this silent killer disease.

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1

Variable	Description	Number of patients	Percentages

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Figure 1: Table 1 :

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Symptoms	Number of patients	Percentage (%)
Severe headache	73	43.8
Chest tightness	34	20.2
Numbness of hands and legs	19	11.3
Fatigue	18	11.1
Breathing difficulty	17	10.3
Pounding in the head, neck or ears	6	3.3

Figure 2: Table 3 :

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Prescribed Drugs	Number of patients	Percentage (%)
Amlodipine	61	36.5
Methyldopa	38	22.7
Nifedipine	35	21.0
Lisinopril	30	18.0
Ramipril	1	0.6
Enalapril	2	1.2

Figure 3: Table 4 :

5

Parameters Studied	Classification	Number of patients	Percentage (%)
Patients knowledge about disease condition	Patients with knowledge	34	20.1
	Patients without knowledge	133	79.9
Fear about medication use	no fear	151	90.4
	Showing fear	16	9.6
Drug counselling received from	Well counselled	154	92.2
Pharmacist	Not well counselled	13	7.8
Prescription studied	Generic drugs	5, 608 (prescriptions)	91.6
	Brand drugs	514 (prescriptions)	8.4
Classification of hypertension	Stage 1	59	35.3
	Stage 2	83	49.7
	Isolated systolic	25	15.0
Cost of antihypertensive drugs per month	Generic drugs	?480 ($3)	
	Brand drugs	?2, 220 ($14)	

Figure 4: Table 5 :

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Self-report patient assessment of adherence	Number of patients	Percentage (%)
Good Adherent	113	67.7%
Poor Adherent	54	32.3%

Figure 5: Table 6 :

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