

Antihypertensive Medicines Prescriptions before and after the Nigeria Hypertension Society Guidelines and Prescriber's Awareness of the Guideline

Abimbola Olowofela, Ambrose O. Isah

Department of Medicine, University of Benin Teaching Hospital, Clinical Pharmacology and Therapeutics Unit, Benin City, Edo State, Nigeria

Abstract

Objectives: The Nigerian hypertension guideline (2005) was based on 1999 ISH/WHO and the 2003 Sub-Saharan Africa hypertension guidelines. The changes in the prescribing pattern of physicians before and following the introduction of these guidelines as well as physicians' awareness of the guidelines in Southern Nigeria are unknown. **Subjects and Methods:** A retrospective study of antihypertensive prescriptions and a cross-sectional descriptive study of the physicians' awareness of the guidelines. The study was carried out at a tertiary health facility in Southern Nigeria and reviewed the case records (1999–2008) of 3379 hypertensive patients who had attended the medical outpatient clinic; it also assessed the awareness of 48 postregistration doctors working in the same hospital using a self-administered questionnaire. **Results:** Calcium channel blockers were the most prescribed class over the entire period (44.7%–69.2%) while angiotensin-converting enzyme inhibitors prescriptions increased by 325% (11.8%–51.5%). Annual prescriptions of diuretics increased steadily from 38% in 1999 to a peak of 58% in 2005. A total of 37/48 doctors responded, and a high proportion (32/37; 86.5%) were aware of the national guidelines, but only 13/37 (35.1%) were satisfied with the recommendations. Diuretics were stated as the most preferred class of antihypertensive medicines by 26/37 (70.3%) of respondents. **Conclusions:** The findings suggest disconnect in the prescribers' knowledge of recommendations in the guidelines, their stated preferences for medicines, and the observed findings in the case records. This may be due in part to the observed dissatisfaction of doctors with the guidelines.

Keywords: Antihypertensive agents, guidelines, Nigeria, physicians

INTRODUCTION

The use of medicines and other forms of nonpharmacological therapy in treating hypertension has been shown to reduce the morbidity and mortality that is associated with hypertension.¹ The armamentarium of antihypertensive medicines has increased over the years with newer ones being introduced.

Over the years, different authorities in hypertension have drawn up practice guidelines based on available evidence to tailor the management of hypertension.^{2–6} Nigeria is no exception to this development with the release of a Nigerian hypertension guideline in 2005.⁷ This guideline was based on the WHO/ISH 1999 guideline² with inferences drawn from the Sub-Saharan guideline.⁴

Various factors have been shown to contribute to the prescribing habits of physicians and inevitably to blood pressure control, these include physician-related factors such as clinical inertia, overt advertising, insufficient knowledge of available

medicines,^{8,9} and patients'-related factors which may include the development of adverse reactions, cost, and adherence issues.¹⁰

This study set out to review the trend in the use of antihypertensive medicines over a 10 year period and to assess changes in prescribing of antihypertensives before and after the 2005 guideline as well as physicians' awareness of the guidelines in a tertiary hospital in south-south Nigeria.

SUBJECTS AND METHODS

Study site: The study was carried out at the consultant medical outpatient department of a tertiary hospital in southern Nigeria.

Address for correspondence: Dr. Abimbola Olowofela,
Department of Medicine, Clinical Pharmacology and Therapeutics Unit,
University of Benin Teaching Hospital, Benin City, Edo State, Nigeria.
E-mail: felabimbola@yahoo.com

Access this article online

Quick Response Code:



Website:
www.nigeriamedj.com

DOI:
10.4103/nmj.NMJ_131_16

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Olowofela A, Isah AO. Antihypertensive medicines prescriptions before and after the Nigeria hypertension society guidelines and prescriber's awareness of the guideline. *Niger Med J* 2017;58:107-13.

The consultant medical outpatient department houses the hypertension clinic as well as other medical subspecialties. This study is in two parts: a retrospective analysis of the trends in antihypertensive medicines use from 1999 to 2008 as well as a cross-sectional study reviewing the knowledge attitude and practice of doctors toward the 2005 Nigerian hypertension society guidelines.

Ethical approval was obtained for the study from the ethics and research committee of the University of Benin Teaching Hospital.

Retrospective analysis of trends in drug use from 1999 to 2008

Study design

The retrospective study addressed the trends in the use of antihypertensive medicines over 10 years from 1999 to 2008.

Study population

The clinical case records of adult patients from the age of 18 years and above with a diagnosis of hypertension, notably those who have had antihypertensive medicines prescribed at the specialty clinics at the consultant medical outpatient department were included in this study.

Sample size

The number of patients who attended the consultant medical outpatient clinic annually over the study years ranged from 11,000 to 47,000. Total population over the 10 years was approximately 240,000. The minimum sample size was 384 with a proportion (50%), a 95% confidence interval and a margin of error of 5% using the Raosoft sample size calculator.¹¹ To compensate for potential missing data, an attrition ratio of 10% was used, achieving a total number of 422 cases to be sampled yearly. The case records were selected using a proportional probability sampling.

Methodology

The case records of the hypertensive patients, (hypertension as defined according to the Nigerian Hypertension Society guidelines that were based on the 1999 WHO/ISH recommendations, as blood pressure $\geq 140/90$ mmHg) who had attended clinic from 1999 to 2008 were accessed. A hypertension diagnosis was confirmed when at least one of the following terms was found in the case record: hypertension, high blood pressure.

Case selection was by stratified sampling method with each year representing a stratum. Total population sampling was carried out on all case records of hypertensive patients available in each stratum were then selected for all the years.

From each case record sampled, the information was entered into a data collection form. The presence of comorbidities as well as complications of hypertension was also documented. The medicines prescribed at the end of each year, reasons documented for changes, and documented adverse drug reactions were also noted. This was done for each year under review.

Data analysis

Each year under review was analyzed based on the different classes of antihypertensive medicines, fixed dose combinations (FDC) were classified based on the number of antihypertensive medicines in each combination. The components of the FDC were handled independently. Antihypertensive medicines were classified into different classes (angiotensin-converting enzyme inhibitor, beta blocker, calcium channel blocker, diuretics, centrally acting agonists, angiotensin-receptor blockers (ARBs), others which included reserpine-dihydroergocristine-clopamide combinations).

The data were analyzed using Statistical package for the Social Sciences (SPSS) (SPSS Inc., Chicago, IL, USA) software version 16 for Windows. Data were presented descriptively as mean \pm standard deviation (SD), frequencies, percentages for the demographic variables, and prescribing pattern. Nonparametric statistics such as the Mann-Whitney test, Wilcoxon rank sum test was used for categorical data and parametric test (Student *t*-test) for continuous variables.

Doctors' knowledge, attitude, and practice regarding hypertension guidelines

Study population

This included post full registration medical doctors practising in the Department of Internal Medicine, and involved in running the hypertension clinic.

Eligibility criteria

All post full registration doctors in the Department of Internal Medicine who consented to the study.

Methodology

The doctors who consented to the study were assessed using a self-administered questionnaire to determine their knowledge and use of existing guidelines.²⁻⁷

Information sought included duration of practice, subspecialty, awareness of the provisions in the available guidelines; antihypertensive medicines prescribed as first-line therapy, reasons for change in medicine and commonly observed adverse reactions to antihypertensive medicines.

Data analysis

Descriptive analyses (mean \pm SD, frequencies and percentages) of demographics, gender, duration of practice, and prescription habits was carried out.

The data were analyzed using SPSS (SPSS Inc., Chicago, IL, USA) software version 16 for Windows.

RESULTS

Retrospective study of trends

A total of three thousand three hundred and seventy-nine (3379) case records of hypertensive patients were reviewed over the ten years in the retrospective study. Two thousand three hundred and ninety-six (71%) were women. The comorbid conditions commonly documented in the case records were

diabetes mellitus, osteoarthritis, obesity, bronchial asthma, and peptic ulcer disease as shown in Table 1. Some patients had multiple comorbid conditions.

Trends of antihypertensive medicine prescriptions

During this period reviewed, the mean number of antihypertensive medicines prescribed increased from 2.5 ± 1.0 (median 3) in 1999– 2.9 ± 1.3 (median 3) in 2008. This was statistically significant ($Z = -3.630$, $P \leq 0.001$).

The use of 2 or more medicines was high in 1999; 146 (78.9%), and it increased to 547 (85.9%) in 2008. In addition in the group who used 2 or more medicines, more patients were placed on combination pills (FDC) rather than individual pills. The prescriptions of FDC were higher in 1999 compared with 2008 (69.1% against 54.0%). Majority of these FDC were thiazide diuretic-based (amiloride-hydrochlorothiazide), and the use of this combination ranged from 52% in 1999–89% in 2008. Other FDC medicines prescribed over the years ranged from prazosin/polythiazide with 34% in 1999–12% in 2004 but were no longer present from 2005 onward. However, from 2006, there was another combination of prazosin/hydrochlorothiazide accounting for 0.8% of prescriptions in 2006 – 3% in 2008.

The FDC of reserpine/dihydroergocristine/clopamide was seen in 10% in 1999 and 8.7% in 2008. Other FDCs seen in the study were atenolol/chlorthalidone, (0.02% in 1999–0.8% in 2008) lisinopril/chlorthalidone, triamterene/hydrochlorothiazide, ramipril/hydrochlorothiazide, and telmisartan/hydrochlorothiazide. The use of these combinations ranged from 0.8% to 0.2% over the years.

The use of two or more antihypertensive medicines increased gradually over the years [Figure 1] and the use of 3 medicines was initially the most common form of polytherapy, and it ranged from 36.2% in 1999–28.2% in 2008 of all the case records reviewed. From the different possible combinations of antihypertensive medicines, a combination that had a calcium channel blocker and a diuretic were the medicines mostly prescribed.

In patients who used only one antihypertensive medicine, calcium channel blockers (CCBs) especially nifedipine was

the initially the most prescribed (50% in 1999–37% in 2005 and 20% in 2008). However, lisinopril became the most prescribed antihypertensive medicine for monotherapy in the years 2006 till 2008 (44%–53%). The other medicines used in monotherapeutic treatment of hypertension over the 10 years include propranolol, amlodipine, captopril, atenolol, lacidipine, felodipine, alpha-methyldopa, enalapril, losartan, valsartan, bisoprolol, and telmisartan were infrequently prescribed as monotherapy. Notable in this study was the relative absence of diuretics being prescribed as a single medicine. There was only a mention of bendrofluazide (1% in 2008).

Trends of antihypertensive medicines prescribed by medicine classes

There was a variation in prescribing between 1999 and 2008 across the various medicine classes. In 1999, the most frequently prescribed medicine classes were the CCB 83 (45%), diuretics 70 (37%) followed by Beta Blockers 54 (29%) while in 2008, CCB's 441 (69%), diuretics 349 (55%) followed by Angiotensin Converting Enzyme Inhibitors (ACEI) 327 (54%) [Figure 1].

Prescriptions of CCB and diuretics remained relatively stable throughout the years studied. ACEI's had a noticeable increase from 1999 where the usage was 11.8% but increased to 51.5% in 2008. A decline in the prescriptions was observed for Beta and alpha blockers during this period. Centrally acting alpha 2 agonists had a slight decline but negligible change in prescriptions over the ten years. An increase was seen in the prescriptions for angiotensin receptor blockers (ARBs), from <0.5% prescriptions in 2000–6% of all prescriptions in 2008 [Figure 2].

Doctors' awareness of provisions in guidelines

The total number of doctors approached was 48 but a total number of 37 responded giving a response rate of 77.1%. Fourteen (14) of them were women (37.8%). Senior registrars were the largest number of respondents at 15 (40.7%), registrars 13 (35.1%), and then consultants 9 (24.3%). The mean duration of practice was 12.0 ± 8.5 years (range of 3.0–36 years).

Table 1: Comorbid conditions of hypertensive patients as documented in the case records over the study period, 1999-2008

	Diabetes mellitus, n (%)	Osteoarthritis, n (%)	Peptic ulcer disease, n (%)	Obesity, n (%)	Asthma, n (%)	Others, n (%)	Nil documented, n (%)
1999 (185)	29 (15.7)	25 (13.5)	5 (2.7)	5 (2.7)	9 (4.9)	5 (2.7)	108 (58.4)
2000 (205)	34 (18.4)	24 (11.7)	8 (3.9)	13 (6.3)	10 (4.9)	15 (7.3)	102 (49.8)
2001 (219)	38 (17.4)	27 (12.3)	10 (4.6)	13 (5.9)	10 (4.6)	18 (8.2)	107 (48.9)
2002 (241)	50 (20.7)	31 (12.9)	9 (3.7)	13 (5.3)	10 (4.1)	25 (10.4)	117 (48.5)
2003 (271)	55 (20.3)	35 (12.9)	14 (5.2)	14 (5.2)	13 (4.8)	29 (10.7)	130 (48.0)
2004 (302)	63 (20.8)	40 (13.2)	17 (5.6)	17 (5.6)	12 (4.0)	45 (14.9)	138 (45.7)
2005 (348)	75 (21.6)	58 (16.7)	18 (5.1)	20 (5.7)	10 (2.9)	42 (12.1)	145 (41.7)
2006 (445)	115 (25.8)	74 (16.7)	19 (4.3)	26 (5.8)	14 (3.1)	57 (12.8)	177 (39.8)
2007 (528)	139 (26.3)	65 (12.3)	24 (4.5)	25 (4.7)	17 (3.2)	71 (13.4)	205 (38.8)
2008 (635)	165 (26.0)	92 (14.5)	25 (3.9)	28 (4.4)	21 (3.3)	110 (17.3)	247 (38.9)

Some patients had multiple comorbidities

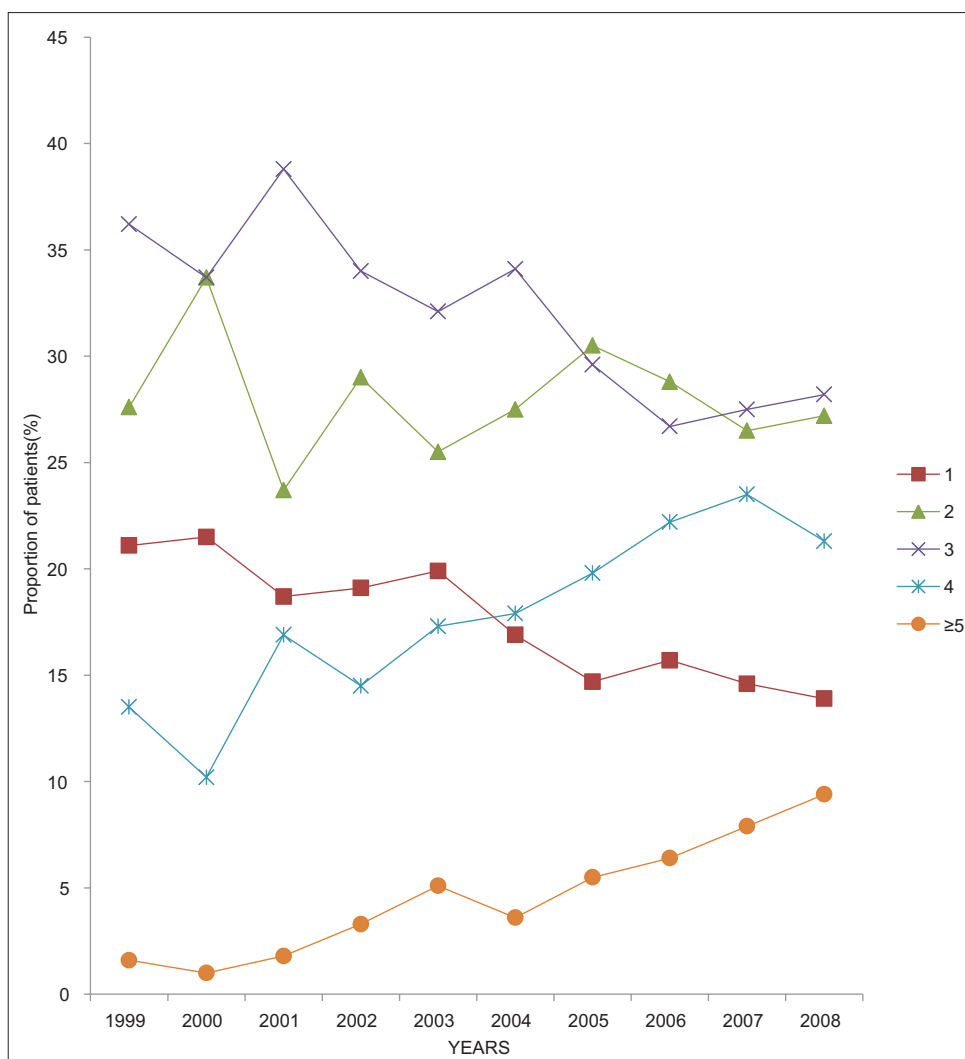


Figure 1: Proportion of the patients on varying numbers of antihypertensive medicines from 1999 to 2008 at the consultant outpatient department

In response to the knowledge of the existence of a national guideline in managing hypertension 32/37 (86.5%) were aware of its existence, 19/37 (51.4%) had read the guidelines and were influenced by the recommendations, but only 13/37 (35.1%) were satisfied with the recommendations. The doctors were also aware of the provisions in other guidelines, notably, JNC VII (40.5%) and the WHO/ISH (29.7%), British Hypertension Society guideline (BHS) 10.8%.

All the doctors also indicated that comorbidity (100%) played an important role in their prescriptions, this was closely followed by adverse reactions (94.6%), age of the patient (91.6%), cost of the medicines (91.6%), occupation (64.9%), and sex of the patient (51.4%).

Diuretics were stated by the doctors as the most preferred class of antihypertensive they would prescribe for uncomplicated hypertension 26 (70.3%) followed by CCB by 9 (20.4%) while ACEI was the third medicine that was preferred by 2 (5.4%) of the doctors.

In their preference for combination therapy, a combination of CCBs and diuretics were the most preferred 21 (56.8%), the second preference was a combination of ACEI and Diuretics by 13 (35.1%) and a combination of ACEI/CCB by six 6 (16.2%) of the doctors. Other combinations which were less common chosen were ARB/diuretic, CCB/beta blocker, methyl dopa/diuretic, ARB/CCB.

Poor control was cited as the commonest reason for changing a patient's therapy 31 (83.8%) of the respondents. This was closely followed by adverse reactions 26 (70.3%). Other reasons were cost (56.8%), unavailability of medicine (54.1%), and patient's request (18.9%).

More females doctors 12 (85.7%) adhered to the use of diuretics as first choice antihypertensive medicine than males 14 (60.9%) although this was not statistically significant (Fisher's exact test = 0.15). Those who had been practicing for ≤ 10 years had better adherence to diuretics as the first choice, 20/22 (90.9%) than doctors who had been practicing for longer than 10 years 5/13 (38.5%). This was statistically significant ($\chi^2 = 11.014$, $P = 0.002$).

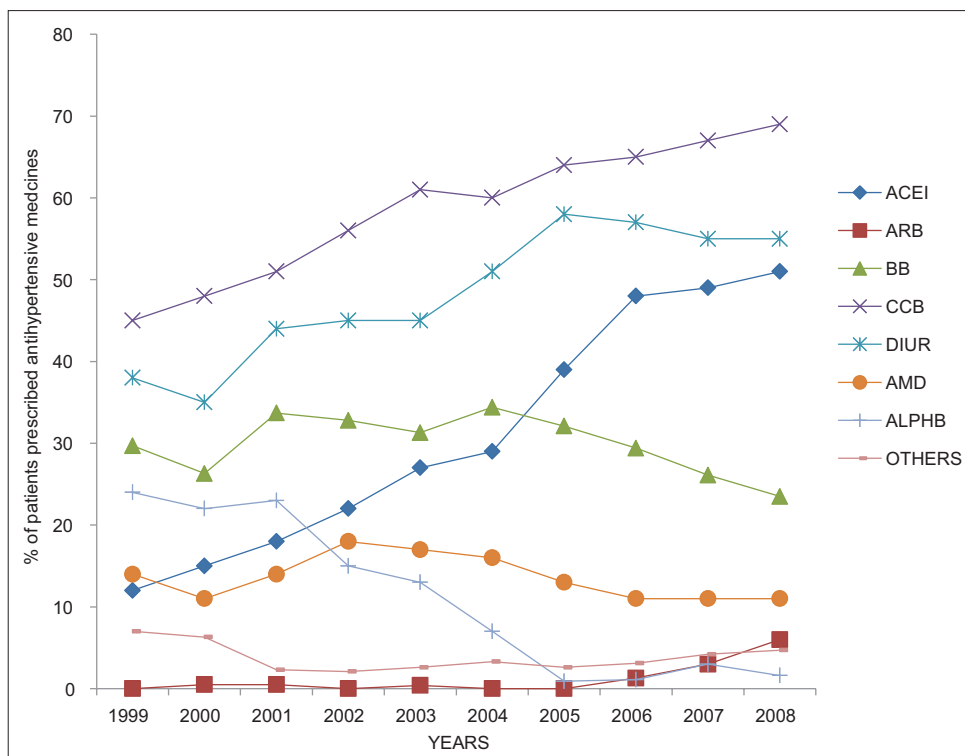


Figure 2: Trends of classes of antihypertensives prescribed during the period 1999–2008 at the hypertension clinics in the consultant outpatient department. ACEI – Angiotensin-converting enzyme inhibitor; ARB – Angiotensin receptor blocker; BB – Beta blocker; CCB – Calcium channel blockers; DIUR – Diuretics; AMD – Alpha methyl dopa; ALPHB – Alpha blockers

DISCUSSION

Trends of antihypertensive prescribing

The use of 2 medicines from different classes has been advocated in different hypertension guidelines to reduce the burden of adverse reactions and improve blood pressure control.²⁻⁷ This study showed agreement with this recommendation with the proportionate increase in prescriptions of 2 or more medicines over the period studied.

The use of combination medicines was equally recommended to reduce pill burden and improve adherence, although there was a high rate of use of FDC that may have reflected this paradigm shift, there was a downward trend in the proportion of patients on FDC's over the period studied. The essential medicine list concept may have contributed to this with the prescribed use of individual generic medicines rather than FDCs to reduce cost. This differed from what was seen in the study undertaken in Canada over an 11 year period that showed an increase in the rate of prescription of FDC over the period.¹²

CCBs were the most prescribed class of medicines during the period studied as observed in similar studies.^{13,14} However, in other studies, diuretics were found to be the most commonly prescribed antihypertensive medicine.^{15,16} The ALLHAT study¹⁷ which was released in 2002 showed that newer agents were not superior to diuretics in managing hypertension, this did not change the prescribing pattern. This may have been due to physician's inertia as most physicians are wary of changing a patient's medicine despite evidence that may suggest a need

to do so.⁹ In addition, the efficacy of CCBs in controlling blood pressure in blacks^{16,18} may have been the reason for this result.

Another reason that could be adduced for diuretics being the second most prescribed medicine class could be the presentation of the combination thiazide diuretic (amiloride/hydrochlorothiazide), at a higher dose that is associated with more adverse reactions or the reluctance of the doctors to prescribe diuretics to avert these adverse reactions, especially the perceived diabetogenic effect of thiazide diuretics.

The study also revealed an increase in the rate of ACEI prescribing by 325% over the study period so making fewer physicians prescribe diuretics as either first line or as combination therapy. This was also reflected in the fact that a higher proportion of patients who had a single antihypertensive medicine prescribed from 2006 to 2008 were placed on an ACEI. This could be explained by the preference of the doctors for this class as the next preferred medicine and the effect of comorbidity which played the most important role in choosing an antihypertensive medicine. This finding is similar to that of Ernst.¹⁹

The rate of rise of this class may be attributed to intense marketing strategies of the pharmaceutical sales representatives. It also could be due to the trial that claimed ACEI had benefits beyond BP lowering thus debunking the myth that ACEI were not effective in blacks.²⁰ Majority of the ACEI in the market are long-acting requiring single daily dosing, thus reducing the pill burden and this could have influenced the pattern seen.

Beta-blockers had a noticeable decrease in the rate of prescription from 2005; this may be due to the suggestion that the adverse effects of this class in hypertensive patients may be more than the benefits and they were downgraded in the management of uncomplicated hypertension in the NICE/BHS pharmacological update from the first line.²¹ A poor response to beta blockers has also been documented in blacks who have volume-dependent hypertension and this may have contributed to the Nigerian guidelines making it a second-line medicine.⁷

Centrally, acting alpha 2 agonists (alpha-methyldopa) is one of the oldest medicines being used in the management of hypertension; it has been associated with erectile dysfunction and other adverse reactions. This may have accounted for the decline in the prescription rates from 2002, but the study still showed that up to ten percent were still using this medicine, as seen in another study in south western Nigeria.¹³ These medicines have been found to be cheap and cost-effective,¹³ also the Nigerian guidelines⁷ and the WHO/ISH recommended their use in resource-poor settings. The medicine is also still useful in pregnancy.

Alpha blockers were the fourth most prescribed medication in 1999, however, a sharp decline to near negligible levels in 2005 may be due to the nonavailability of the medicines in the Nigerian market. It could also be further attributed to the ALLHAT study¹⁷ that stopped the doxazosin arm early due to increased cardiovascular morbidity. An increase in the levels of alpha-blockers prescribing rate seen in the later part of the trends may reflect the reintroduction of a combination of prazosin and hydrochlorothiazide into the market, as a fixed dose combination and the usefulness of this class of medicine in patients with prostatic hyperplasia may play a role in the increased rate seen.

Following the introduction of angiotensin-receptor blocker into clinical practice, the low prescribing rate may be attributed to cost, and the unwillingness of patients or clinicians to change to newer medicines, also available guidelines did not recommend their use as first-choice antihypertensive medication although the ISHIB consensus statement pointed out the reduced frequency of new-onset diabetes in those with ARBs.²²

The subsequent rise may also be attributed to the mechanism through which ACEI-mediated cough is dampened and is being used as substitutes in the patients who develop ACEI cough. This rise was also seen in a study conducted in the US between 1993 and 2004.²³

Doctors' awareness of provisions in guidelines

This study showed that a high proportion of the physicians reported a high awareness of the existence of the National Guideline. Other guidelines that also influenced the physicians' choices were the JNC VII and the 1999 WHO/ISH guidelines.^{2,3}

The WHO/ISH recommendation for resource-poor settings such as Nigeria, that diuretics should be the medicine of the first choice was observed in the choices made by the doctors, this was different from what was found in a similar study in

which CCBs were chosen as first-line therapy⁸ and another study that saw diuretics being underutilized by the doctors.¹⁹ The trends in this study have shown that this knowledge did not translate into clinical practice as it would have been expected that diuretics would be the most prescribed medication and this might explain why less than half were satisfied with recommendations.

Factors that had been described in the literature as affecting the choice of antihypertensive by physicians include among others duration of practice and gender.^{8,24} This may explain why female doctors and doctors who had been practicing for <10 years were more willing to prescribe diuretics as first choice antihypertensives as shown in a similar study²⁵ where the female sex was also found to have a better awareness of the guidelines than men, also in the same study they found that a longer duration of practice and older age to be poor indices of adherence to guideline.

This may suggest that clinical experience and familiarity with particular medicines rather than clinical guidelines may dictate prescriptions of antihypertensive medicines.

CONCLUSIONS

The findings suggest a less than optimal compliance with the guidelines with growing preference for newer medicines. There was disconnect in the prescribers' knowledge of recommendations in the guidelines, their stated preferences for medicines, and the observed findings in the case records. This may be due in part to the observed dissatisfaction of doctors with the guidelines.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Neal B, MacMahon S, Chapman N; Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: Results of prospectively designed overviews of randomised trials. *Blood Pressure Lowering Treatment Trialists' Collaboration. Lancet* 2000;356:1955-64.
2. 1999 World Health Organization – International Society of Hypertension guidelines for the management of hypertension. Guidelines Subcommittee. *J Hypertens* 1999;17:151-83.
3. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LE, Izzo JL, *et al.* Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension* 2003;42:1206-52.
4. Lemogoum D, Seedat YK, Mabadeje AF, Mendis S, Bovet P, Onwubere B, *et al.* Recommendations for prevention, diagnosis and management of hypertension and cardiovascular risk factors in sub-Saharan Africa. *J Hypertens* 2003;21:1993-2000.
5. Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, *et al.* British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): Summary. *BMJ* 2004;328:634-40.

6. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, *et al.* 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2007;25:1105-87.
7. Kadiri S, Onwubere B, editors. Nigeria Hypertension Society Guidelines Committee. Enugu, Nigeria: Ezu Books; 2005.
8. Wang L. Physician-related barriers to hypertension management. *Med Princ Pract* 2004;13:282-5.
9. Oliveria SA, Lapuerta P, McCarthy BD, L'Italien GJ, Berlowitz DR, Asch SM. Physician-related barriers to the effective management of uncontrolled hypertension. *Arch Intern Med* 2002;162:413-20.
10. Isah A, Isah E, Shah D, Obasohan A. An assessment of patient's knowledge and experience in a Nigerian Teaching Hospital Hypertension Clinic. *Niger PMJ* 1998;5:173-5.
11. Raosoft Sample Size Calculator. Available from: http://www.raosoft.com/sample_size.html/sample_size/calculator. [Last accessed on 2008 Jul 09].
12. Hemmelgarn BR, Chen G, Walker R, McAlister FA, Quan H, Tu K, *et al.* Trends in antihypertensive drug prescriptions and physician visits in Canada between 1996 and 2006. *Can J Cardiol* 2008;24:507-12.
13. Amira CO, Okubadejo NU. Antihypertensive pharmacotherapy in a developing economy: Pattern, acquisition costs and conformity to international guidelines in a tertiary-care setting. *J Hum Hypertens* 2006;20:894-7.
14. Katibi IA, Olarinoye JK. Antihypertensive therapy among hypertensive patients as seen in the middle belt of Nigeria. *Ann Afr Med* 2004;3:177-80.
15. Adigun AQ, Ishola DA, Akintomide AO, Ajayi AA. Shifting trends in the pharmacologic treatment of hypertension in a Nigerian tertiary hospital: A real-world evaluation of the efficacy, safety, rationality and pharmaco-economics of old and newer antihypertensive drugs. *J Hum Hypertens* 2003;17:277-85.
16. Etuk E, Isezuo SA, Chika A, Akuche J, Ali M. Prescription pattern of anti-hypertensive drugs in a tertiary health institution in Nigeria. *Ann Afr Med* 2008;7:128-32.
17. Major cardiovascular events in hypertensive patients randomized to doxazosin vs. chlorthalidone: The antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). ALLHAT Collaborative Research Group. *JAMA* 2000;283:1967-75.
18. Saunders E, Weir MR, Kong BW, Hollifield J, Gray J, Vertes V, *et al.* A comparison of the efficacy and safety of a beta-blocker, a calcium channel blocker, and a converting enzyme inhibitor in hypertensive blacks. *Arch Intern Med* 1990;150:1707-13.
19. Ernst S. Hypertension guideline adherence of private practitioners and primary health care physicians in Pretoria. *SA Fam Pract* 2005;47:51-4.
20. Heart Outcomes Prevention Evaluation Study Investigators, Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, *et al.* Effects of an angiotensin-converting-enzyme inhibitor, Ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 2000;342:145-53.
21. National Collaborating Centre for Chronic Conditions. Hypertension: Management in Adults in Primary Care: Pharmacological Update. London: Royal College of Physicians; 2006.
22. Douglas JG, Bakris GL, Epstein M, Ferdinand KC, Ferrario C, Flack JM, *et al.* Management of high blood pressure in African Americans: Consensus statement of the Hypertension in African Americans Working Group of the International Society on Hypertension in Blacks. *Arch Intern Med* 2003;163:525-41.
23. Ma J, Lee KV, Stafford RS. Changes in antihypertensive prescribing during US outpatient visits for uncomplicated hypertension between 1993 and 2004. *Hypertension* 2006;48:846-52.
24. Whitworth JA; World Health Organization, International Society of Hypertension Writing Group. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. *J Hypertens* 2003;21:1983-92.
25. Hyman DJ, Pavlik VN. Self-reported hypertension treatment practices among primary care physicians: Blood pressure thresholds, drug choices, and the role of guidelines and evidence-based medicine. *Arch Intern Med* 2000;160:2281-6.