Patient-reported adverse events associated with use of anti-hypertensive drugs in a tertiary hospital in southern Nigeria

Chibuike Eze Nwafor 1, * and Marvis Somtochukwu Muo 2

1 Cardiology Unit, Department of Medicine, University of Port Harcourt and University of Port Harcourt Teaching Hospital, Nigeria.
2 Research unit, GoodHeart Medical Consultants Hospital, Port Harcourt, Rivers State, Nigeria.

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Abstract

Background Hypertension is a leading cause of cardiovascular morbidity and mortality worldwide especially in sub-Saharan Africa. Adverse events with use of antihypertensive medications deter patients’ adherence. This study is aimed at evaluating the adverse events and comorbidities associated with the use of antihypertensive as seen in a tertiary hospital in southern Nigeria.

Method This retrospective cross-sectional study was conducted at a tertiary healthcare hospital in southern Nigeria. Data was collected for a period of six months from 194 patients who attended cardiac clinic with demographic details, blood pressure values, antihypertensive drugs in use, level of medication adherence, adverse events, and co-morbidities.

Result Antihypertensive medications were prescribed according to their classes. Telmisartan (ARB) being the most prescribed one. Fixed dose single pill combination was more preferred. Adverse events such as dry cough, peripheral neuropathy, dizziness, peripheral edema, and erectile dysfunction were recorded. Major comorbidities are diabetes mellitus, dyspepsia and hyperlipidemia. Findings revealed gender disparities with males experiencing erectile dysfunction and more.

Conclusion This analysis pinpoints the need for prompt identification of comorbidities and side effects when treating hypertension. Patients’ compliance to treatment and therapy effectiveness is largely dependent on the provision of patient-specific treatment plan.

Keywords; Adverse effects; Adverse drug reactions; ADR; Comorbidities; Antihypertensives; Drugs; South-south; Nigeria
as 46% of adults aged 25 years and above have a raised blood pressure (2,4), and a study in Southern Nigeria found a prevalence of 40.8% (5). The primary goal of antihypertensive therapy is to prevent morbidity and mortality associated with hypertension (6–8).

Many studies have demonstrated that lifestyle modifications and compliance to appropriate drug treatments are sufficient to maintain blood pressure at optimal levels (2). However, available evidence has also shown that about 75% of hypertensive patients do not have optimal blood pressure control (2,9).

Various classes of antihypertensive drugs are used in the management of hypertension, and they include diuretics (D), beta-blockers (BB), calcium channel blockers (CCB), angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin II receptor blockers (ARBs) (2,9). Under Joint National Committee (JNC 8), in all cases, goal blood pressure targets should be reached within a month of starting treatment either by increasing the dose of an initial drug or by using a combination of medications (10). However, recent published data showed an increase in the use of the more expensive CCBs and ACEIs despite the inadequate evidence to support their superiority to diuretics and BB in reducing morbidity and mortality of cardiovascular diseases (4).

According to the World Health Organization (WHO) definition, an adverse drug reaction (ADR) is ‘a response to a drug that is noxious and unintended and occurs at doses normally used in human for the prophylaxis, diagnosis, and treatment of disease, or for modification of physiological function’ (11). ADR can also be defined as ‘an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product’ (11).

Adverse reactions in outpatient care have been estimated to occur in about 25% of patients and factors associated with adverse reactions include, number of medicines taken by the patient, genetic disposition, age, pregnancy, and exogenous factors such as food and interactions with other medicines (5,12,13). This study is geared towards understanding the adverse effects and co-morbidity of these antihypertensives thereby establishing the clear and contrast superiority in each class of antihypertensive under review for antihypertensive prescriptions at a tertiary healthcare hospital in southern Nigeria.

2. Material and Methods

A pro forma was designed which included, patients’ demographic data (age, gender, Blood pressure values, antihypertensive medications, adverse reactions and morbidities, prognosis of hypertension, and treatment received).

2.1. Study period and setting

This is a retrospective cross-sectional study of patients receiving antihypertensive medications at the Goodheart Medical Consultant Hospital, Port Harcourt, Rivers State, Nigeria over a period of 3 months from 194 patients (1 November 2023 to January 2024).

2.2. Inclusion criteria

The patients who visited the center diagnosed with hypertension and taking antihypertensive medicines.

2.3. Exclusion criteria

Non-hypertensive patients treated with non-antihypertensive agents, unconscious patients (patients depending on other people for medicine administration), and drug addicts.

2.4. Ethics approval

Ethical clearance was obtained from the research ethical review committee of the Goodheart Medical Consultant Hospital.

2.5. Statistical analysis

Antihypertensive medications were classified into different classes: (angiotensin converting enzyme inhibitors [ACEI], beta-blockers, calcium channel blockers [CCBs], diuretics, centrally acting agents, and angiotensin receptor blockers [ARBs]). Data were analyzed.
3. Results

The prescriptions from 194 patients were analyzed. 52% of the patients were female and 45% male (figure 1), all were hypertensive. The blood pressure of patients was grouped into two (group 1=bp levels are≥140/90mmhg; group 2= bp levels are ≤ 140/90mmhg) as seen in figure 2 showing controlled or good hypertension in group 2 according to JNC 8 guidelines. The ages of these patients range from 16 to 94 years with a mean ± SD of 55±15. 20 (20.4%) of these prescriptions were monotherapy while 78 (79.6%) were combination therapy prescription. The drugs commonly prescribed include; (Telmisartan and hydrochlorothiazide), (perindopril and amlodipine), spironolactone, clopidogrel, methyldopa, rabeprazole, esomeprazole. This also includes the drugs used in treating the co morbidities and adverse effects associated with hypertension and antihypertensive agents such as Oral hypoglycemic agents. Telmisartan was the most prescribed antihypertensive drug in the hospital.

Telmisartan and Hydrochlorothiazide, perindopril and amlodipine, spironolactone, carvedilol, metoprolol, bisoprolol, and amlodipine was the most prescribed combination therapy.

Other commonly prescribed drugs were including nifedipine, lisinopril, zopiclone and aspirin. Other prescribed combination therapy consists of amlodipine, perindopril, indapamide, while the least frequently combined therapy is methyldopa, labetalol.

Bisoprolol, methyldopa, amlodipine, nifedipine and frusemide, (telmisartan and Hydrochlorothiazide) and zopiclone were the major monotherapy prescriptions. Good blood pressure control was found to be associated with the combined therapy involving Nifedipine, (telmisartan and Hydrochlorothiazide) (perindopril, indapamide and amlodipine) (perindopril and amlodipine) and clopidogrel.

3.1. Comorbidities and adverse drug reactions experienced

The effects of diagnostic indices revealed that morbidities and adverse effects were observed in all classes of hypertension. The highest morbidities and adverse effects were associated with patients with moderate and severe hypertension. The presenting adverse effects were peripheral neuropathy, dizziness, peripheral edema and erectile dysfunction. The major co morbidities were; diabetes mellitus, hyperlipidemia, arrythmias, angina and, peptic ulcer.

In this study, male patients were associated with erectile dysfunction. The incidence of diabetes mellitus was higher in female patients. Good hypertension controls were experienced by more males than the female patients. Other adverse effects include dry cough and abdominal pain with patients on angiotensin converting enzyme inhibitors (ACEI), headaches and excessive micturition for patients on diuretics, dizziness for patients on beta blockers, alpha blockers and centrally acting anti-hypertensive drugs(13).
Figure 2 Blood Pressure of Patients (Group 1= Bp Levels Are ≥ 140/90 mmHg; Group 2= Bp Levels Are ≤ 140/90 mmHg)

Figure 3 Presenting Adverse Effects

Figure 4 Major Adverse Effects According to Their Gender
4. Discussion
The adverse effects and co-morbidities associated with anti-hypertensive drugs in south-south Nigeria reveals a variety of the antihypertensive medications being prescribed, with Telmisartan being the most referred to. This is due to the independent reno-protective effect and effective cardiovascular and blood pressure control (10, 11). Combination therapies are often practiced in this context as several randomized clinical trials have proven the efficacy of combination therapy to be superior to monotherapy as initial treatment for timely and adequate BP control (16). There are specific combinations that have shown to successfully control blood pressure levels as seen in some studies (13). This study also analyzes the use of these drugs, their side effects and co-morbidities describing the benefits and ease of use to the patient thereby increasing compliance (16, 17).

The results of diagnostic indices showed that morbidities and adverse effects were pervasive throughout the various classes of hypertension, with the highest rate of incidence identified in patients with moderate and severe hypertension. These adverse events were prevalent in patients using fixed dose combinations than those on monotherapy. Common adverse effects reported by patients were dry cough, peripheral neuropathy, dizziness, peripheral edema, and erectile dysfunction which is also seen in other studies (12, 18). Among the major comorbidities encountered in the study population were diabetes mellitus and peptic ulcer.

On the other hand, male patients had a erectile dysfunction, whereas female patients were more prone to diabetes mellitus agreeable to some studies (19). Lastly, good hypertension control was more possible among men than among women. Different classes of antihypertensive medicines were found to induce unique adverse effects. On the other hand, ACEI users experienced dry cough and abdominal pain, diuretic users had headaches and polyuria, and patients using beta blockers, alpha blockers and central antihypertensive drugs reported dizziness. This leads to changes in the prescription such as discontinuation of drug, switching the drugs to a more tolerable agent in the class such as; perindopril and moving the medications to be taken only at night by the physicians because of non-adherence to therapy (20). These patients were advised to adhere to the switched dose. In the case of dizziness and hypotension, patients were advised to sit before standing while getting up to avoid postural hypotension.

Collectively, these outcomes reinforce the necessity of taking comorbidities and possible side effects into account in the management of hypertension. Treatment approaches, which consider not only patient characteristics but also preferences, are vital for achieving both optimal therapy results and higher treatment compliance.

5. Conclusion
There is a relatively high prevalence of adverse reactions experienced by patients on antihypertensive therapy (13, 21). The Notable reactions experienced by the patients include dry cough to ACEIs, excessive micturition to diuretics, and frequent micturition in patients on CCBs. Medication compliance with antihypertensive therapy closely correlates with
the experience of side effects in this study. There is a call to increase the follow up on patients with these medications and good pharmaceutical care and nursing care practices are advised.

Recommendation

Further studies can be done using special population such as pregnant women to review measures for side effects reduction and blood pressure management.

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Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from Goodheart Medical Research unit.

References


