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# A pharmaceutical case of hypertension management with adverse reactions to medications

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## *ABSTRACT*

Hypertension is a significant public health concern due to its high prevalence and association with cardiovascular diseases and other complications. A client with a long history of hypertension presented with adverse reactions to prescribed medications, including headaches, tension, and moderate dull headache, during a hypertensive urgency event. Pharmaceutical care was tailored to address lifestyle and social factors, as well as drug interactions, to improve medication outcomes. Through optimized medication scheduling and stress management, the client achieved improved outcomes and enhanced quality of life. This case demonstrates the positive impact of pharmaceutical intervention on disease management and client well-being.

**KEYWORDS**: Hypertension, Antihypertensive Medications, Drug Interactions, Pharmaceutical Care, Adverse Reactions

## INTRODUCTION

Hypertension is a major risk factor for cardiovascular disease, and its effective management is crucial for reducing cardiovascular morbidity and mortality [1]. Lowering blood pressure to less than 130 mmHg has been shown to prevent complications in clients with heart failure, diabetes, coronary artery disease, stroke, and other cardiovascular conditions [2]. However, adverse reactions to antihypertensive medications can pose significant challenges to management [3, 4]. Despite this, there is a paucity of literature reporting on adverse reactions to antihypertensives in pharmaceutical case studies. The primary objective of antihypertensive treatment is to reduce renal and cardiovascular morbidity and mortality [5]. To achieve this, clients must adhere to both pharmacologic and non-pharmacologic management strategies, emphasizing the importance of client education and compliance (6)."First-dose reactions are ADEs that occur with the initial dose or when the dosage is increased. First-dose reactions have been described with the use of α-receptor blockers, calcium channel blockers, ACE inhibitors, and β-blockers [7]. These reactions are frequently dose related and may result from an abrupt lowering of blood pressure, causing postural hypotension, dizziness, syncope, headaches, lethargy, or other symptoms.

This case study aims to present a detailed report of a client who experienced adverse reactions to antihypertensive medications, despite diligent adherence, and investigate the impact of lifestyle and social factors on drug efficacy and toxicity. By examining the interplay between pharmacological and non-pharmacological factors, this study seeks to provide valuable insights into optimizing hypertension management and improving client outcomes.

## METHODOLOGY/OBSERVATIONS

### Nature of Encounters

A multi-visit case study of a 50-year-old female client, referred to as ND, is presented.

### Medical History

The client, ND, a 50-year-old female with a body mass index (BMI) of 26.4, has been managed for hypertension for 15 years. Her medical history reveals multiple hospitalizations, each lasting at least a week, for various conditions including anemia and hepatitis-related complications. Currently, she is experiencing recurrent and severe hypertensive episodes, accompanied by debilitating headaches and tension.

### Medication History

ND has a significant medication history dating back to her childhood, during which she received frequent courses of antimalarial drugs. Additionally, she was consistently prescribed hematinics, suggesting a history of anemia or iron deficiency. This extensive medication history may have potential implications for her current health status and medication management.

### History of Present Illness

The client reported a deliberate weight loss of 20 kg over the past year, with no experience of fever, night sweats, or gastrointestinal symptoms. However, she acknowledged experiencing a persistent cough, dyspnea, and exertional shortness of breath. Her visit to the pharmacy was prompted by a perceived destabilization of her overall metabolic health, which she described as feeling unwell and disconnected from her body.

### Current Complaint or Presentation

The client presented with uncontrolled hypertension, despite compliance with her prescribed antihypertensive regimen, and reported symptoms of moderate dull headaches and tension, indicating potential treatment resistance or underlying cardiovascular complications.

### Other Diseases/Co-morbidity

The client did not report any noticeable symptoms or indications of other underlying diseases or co-morbidities, suggesting a relatively isolated presentation of hypertension and related symptoms.

### Familial and HEAD-SU

The client's family medical history reveals no instances of hypertension or epilepsy, but does show a history of other health conditions: a maternal uncle who passed away due to complications from asthma and diabetes, and paternal relatives who suffered from peptic ulcers. This suggests a potential genetic predisposition to certain health conditions, which may be relevant to the client's current health status and future risk factors.

### Surgical History

The client has a history of surgical intervention, having undergone an appendectomy approximately 5 years ago, and also underwent dental restoration procedures last year, indicating a history of gastrointestinal and dental issues, respectively.

### Allergies

He has a known allergy to sulphonamide agents. No recorded experience of disturbance with food or the environment.

**Client's Current Medications:** Currently taken medications

***Synthetics***

Amlodipine Norvasc®, 5 mg tablet once daily, Hydrochlorothiazide (HCTZ, 25 mg once daily)

***Natural Products***

None reported.

### Client's Nutritional Intake

***Special intake***

Client is on a vegetarian diet

***Regular intake***

ND reported consuming carbonated beverages more frequently than hot drinks, indicating a preference for

fizzy drinks over warm or hot beverages like tea, coffee, or hot chocolate.

### *Occasional intake*

ND reported consuming mayonnaise and butter as spreads on bread, indicating a preference for rich and savory condiments as part of her dietary habits.

## Client's Lifestyle

### *Professional*

The patient is employed at a cookie bakery, indicating occupational exposure to sweet treats and potentially influencing her dietary habits and health status.

### *Social*

The patient is married and has three children, and is in a monogamous relationship. She also reported a significant history of smoking, having previously consumed 30 cigarettes per day, but successfully quit two years ago, indicating a notable achievement in overcoming nicotine addiction.

### *Religious*

She reported that she is a nominal Christian

## Social and Family History

The patient has experienced significant loss and bereavement, with the passing of her husband four years ago and both parents in a car accident less than a year ago. Following this tragic event, she has become increasingly withdrawn and isolated, avoiding social gatherings and activities that she previously enjoyed, indicating a potential struggle with grief and emotional distress.

## Physical Examination:

### *Vital signs*

Blood Pressure; 140/95**(90-120/60-80);** Respiration rate 21 breaths/min **(12-18);** Heart rate 86 **(60-100);** Body temperature 37.1$^{o}$C **(36.5-37.3);** BMI 28 **(20-24.9).**

### *General Examination*

ND presented with visible signs of distress, appeared with tearful eyes and an unsteady gait, suggesting emotional turmoil and potential physical instability or imbalance.

### *Cardiovascular system*

Cardiovascular examination revealed no abnormalities

### *Respiratory system*

Not remarkable

### *Gastrointestinal system*

Physical examination of the client did not reveal any significant or remarkable abnormalities in the gastrointestinal system, suggesting that her symptoms are not likely related to any obvious gastrointestinal issues.

## Laboratory Investigations: (Pharmacist ordered)

### *Imaging tests*

Chest X-ray revealed mild interstitial pneumonitis

### *Biochemical tests*

Biochemical test results for the client are as follows: AST 90 IU/ml (0-45); ALT 112 IU/ml (0-45); Total protein test 79g/L **(60-83);** ALP 67 IU/ml **(30-120)** ; AFP 10 ng/mL(**0-10**); GGT 45IU/L **(0-50);** Pancytopenia with platelet count of 52,000 per mm3 **(150-450,000)**, RBC 4.1 x $10^{6}$ cells/ml **(4.7-6.1 x $10^{6}$)** : WBC 3.5 x $10^{3}$ /ml **(5.0-11.0 x 10 $^{3}$);** Haemoglobin 8.3 g/dl **(12-16);** LDL 112 mg/dL **(<100); HDL76** mg/dL **(>60);** TT 169 mg/dL **(<150);** TC187mg/dL **(<200).**

### *Microbiological tests*

Negative blood cultures to infectious agents

## Pharmaceutical Audit

### *Drug-Disease Audi*

Drug is appropriate for the disease condition and level

### *Drug-Drug Audit*

The patient's current medication regimen does not indicate any potential drug-drug interactions, suggesting that the medications are compatible and can be safely co-administered without significant risk of adverse interactions.

### *Drug-Food Audit*

The patient's medication regimen does not show any significant interactions with their diet or special foods they are consuming, indicating that their medications can be safely taken with their usual food and beverages without any harmful effects.

### *Drug Laboratory Test-Outcome Audit*

The laboratory test results suggest that the client has suffered some degree of liver damage, which is not being adequately addressed by their current medication regimen. Elevated levels of AST and ALT enzymes indicate liver dysfunction, necessitating a reevaluation and adjustment of their medication dosages to mitigate potential harm.

## Decision to Dispense/Refill or otherwise of Drugs: a – Dispense/Refill- reasons or b. Hold back - reasons

The prescription will be dispensed. Reducing the effect of raised blood pressure on the renal and cardiovascular

## Drug Therapy Problem Observed

This case presents several actual and potential drug therapy issues. Notably, certain essential medications have been overlooked in the prescription. Additionally, the patient has exhibited a reaction to hydrochlorothiazide, which is a concern given the reported associations between antihypertensive drugs and adverse reactions, particularly during the initial stages of treatment.

## Pharmaceutical Intervention: Reasons for intervention/Suggestion for resolution)

In light of the elevated liver enzyme levels revealed by the laboratory results, it is necessary to discontinue the use of hydrochlorothiazide. Furthermore, based on the laboratory diagnosis of Peptic Ulcer Disease (PUD), alternative medications will be recommended to manage this condition.

## Pharmaceutical Care Goals

To enhance medication effectiveness and promote better health outcomes, our goal is to identify and address both actual and potential drug-related issues in our client's treatment plan, thereby resolving any potential problems and optimizing their medication regimen for improved results.

## Pharmaceutical Care Plans

To supplement the original prescription with the necessary medications that were initially overlooked, and to schedule follow-up appointments with the client to monitor and evaluate the effectiveness and outcomes of the revised medication regimen.

## Ensuing Drug Recommendations and Prescription

Livercap one capsule twice daily x 30 days
Cimetidine 400 mg tablet twice daily x 30 days
Lansoprazole 20 mg tablet twice daily x 30 days

# DISCUSSIONS

## Biopharmaceutics and Pharmacology

### *Amlodipine*

Amlodipine is a medication that relaxes blood vessels by directly targeting vascular smooth muscle, leading to decreased peripheral vascular resistance and lower blood pressure. As a dihydropyridine calcium channel blocker, it works by inhibiting the entry of calcium ions into both vascular smooth muscle and cardiac muscle cells. By binding to specific sites on cell membranes, amlodipine selectively blocks calcium ion influx, thereby relaxing muscle cells. This effect is more pronounced in vascular smooth muscle cells than cardiac muscle cells, making amlodipine an effective vasodilator [9]. Amlodipine has a vasodilatory effect on peripheral arterioles, which decreases the total peripheral resistance, reducing the workload of the heart. This leads to a decrease in myocardial energy consumption and oxygen demand, without affecting heart rate. Additionally, amlodipine dilates main coronary arteries and arterioles, increasing myocardial oxygen supply, particularly in individuals with coronary artery spasm or variant angina. This also counteracts coronary vasoconstriction caused by smoking, further contributing to its blood pressure-lowering effects [10].

Amlodipine is absorbed slowly but extensively from the gastrointestinal tract, reaching peak plasma concentrations between 6-12 hours after oral administration. Its bioavailability ranges from 64-90%. Steady-state levels are achieved within 7-8 days of continuous daily dosing. Food does not affect its absorption. Amlodipine has a large volume of distribution (21 L/kg) and is highly protein-bound (approximately 98%). It undergoes extensive hepatic metabolism, with nearly 90% converted to inactive metabolites, and is primarily excreted in the urine (60% as metabolites, 10% as unchanged drug). In hypertensive patients, approximately 93% of circulating amlodipine is bound to plasma proteins, as shown in ex vivo studies [11].

Amlodipine is eliminated from the plasma in a two-phase process, with a terminal half-life of 30-50 hours. Steady-state plasma levels are achieved within 7-8 days of continuous daily dosing. Only 10% of amlodipine is excreted unchanged in the urine, while the remainder is metabolized. Notably, amlodipine can be administered at standard doses in patients with renal failure, without the need for dose adjustment [11].

In patients with impaired hepatic function, the plasma elimination half-life of amlodipine is prolonged to 56 hours, requiring cautious titration in severe cases. In healthy individuals, total body clearance is approximately 7 ml/min/kg, but elderly patients exhibit reduced clearance, leading to a 40-60% increase in AUC, suggesting a lower initial dose may be necessary [12]. Overdose can result in profound peripheral vasodilation, potentially causing reflex tachycardia, severe hypotension, shock, and even fatal outcomes. Amlodipine's pharmacologic profile is characterized by near-complete absorption, delayed peak plasma concentrations, high bioavailability, and slow hepatic metabolism, resulting in extensive conversion to inactive metabolites, with primarily renal excretion [12].

### *Hydrochlorothiazide*

Hydrochlorothiazide and similar thiazide diuretics are considered a first-line, cost-effective treatment option for uncomplicated hypertension. Initially developed to enhance carbonic anhydrase inhibitors, they were found to have a distinct mechanism of action. Unlike carbonic anhydrase inhibitors, which primarily increase sodium bicarbonate excretion, thiazides were discovered to predominantly increase sodium chloride excretion, an effect that occurs independently of carbonic anhydrase inhibition, making them a valuable class of antihypertensive drugs [13].

The use of thiazide diuretics raises concerns about hypokalemia, impaired glucose tolerance, and increased serum cholesterol and uric acid levels [14]. Like loop diuretics, the most severe adverse events are related to fluid and electrolyte imbalances. Common side effects include vertigo, headache, paresthesias, vision changes, weakness, anorexia, nausea, vomiting, cramping, diarrhea, constipation, and skin rashes. The exact mechanism behind impaired glucose tolerance is unclear but may involve reduced insulin secretion and altered glucose metabolism, potentially unmasking latent diabetes. Thiazide diuretics may also increase LDL cholesterol, total cholesterol, and triglyceride levels. Rarely, hydrochlorothiazide therapy can cause hepatotoxicity, a serious but uncommon adverse event that has only been reported in a few clinical cases [14]. The exact mechanism by which thiazides lower blood

pressure remains unclear. However, hydrochlorothiazide is known to act on the distal renal tubules, influencing electrolyte reabsorption. It increases sodium and chloride excretion in roughly equal amounts, leading to natriuresis, which may be accompanied by minor losses of potassium and bicarbonate. Following oral administration, diuresis begins within 2 hours, reaches its peak in approximately 4 hours, and persists for 6-12 hours. Hydrochlorothiazide is not metabolized and is rapidly eliminated by the kidneys, with a plasma half-life ranging from 5.6 to 14.8 hours. At least 61% of the oral dose is excreted unchanged within 24 hours. Additionally, hydrochlorothiazide crosses the placental barrier and is excreted in breast milk, but does not penetrate the blood-brain barrier [15].

Hydrochlorothiazide directly blocks the sodium chloride co-transporter in the distal convoluted tubules of the kidney, leading to natriuresis and diuresis. In contrast, aldosterone, a mineralocorticoid hormone, regulates sodium reabsorption and potassium excretion in the collecting ducts. When sodium levels rise in the collecting duct, aldosterone binds to its receptor, triggering the expression of ion transport channels. This results in sodium reabsorption through epithelial sodium channels in principal cells and potassium excretion in intercalated cells. However, hydrochlorothiazide therapy counteracts this aldosterone-mediated effect, promoting sodium excretion and diuresis, ultimately leading to a decrease in blood pressure [16].

### Pharmacist's Subsequent Assessment

The investigation revealed that certain lifestyle and social factors were contributing to the adverse reactions observed. To address these issues and ensure the client's safety and optimal hypertension management, a comprehensive pharmaceutical care plan was developed and proposed as a follow-up care plan, targeting drug therapy problems and promoting overall well-being.

### Comment/Laboratory Outcome

Subsequent test on the triglyceride levels132mg/dl and the previously elevated transaminase levels AST 29IU/L and ALT 31 IU/L have shown reduced values.

### Client's Self Evaluation Report

The client reported a significant improvement in her overall health, which was supported by notable enhancements in clinical outcomes, quality of life (humanistic outcomes), and cost-effectiveness (economic outcomes), as demonstrated in this case study.

### Non-Pharmacological Advice

#### *Lifestyle counseling*

To manage gastrointestinal ulcers, it's essential to avoid harmful substances like aspirin, alcohol, tobacco, and caffeine. Additionally, eating smaller, more frequent meals and reducing consumption of milk and dairy products can help minimize acid production. By focusing on nutrition, fitness, behavioral changes, and support, lifestyle therapy empowers individuals to make informed choices that prevent, manage, and improve chronic conditions like gastrointestinal ulcers, leveraging clinical expertise to promote overall well-being.

#### *Monitoring of parameters for progress*

After completing treatment, microbiological tests or a urea breath test can be used to detect the presence of Helicobacter pylori, serving as an indicator of treatment outcome and confirming whether the infection has been successfully eradicated.

#### *Seeking medical Advice/Attention*

The client's condition did not require a referral for additional medical treatment, and their care was effectively managed without the need for further intervention.

## CONCLUSION:

This case highlights the crucial role of lifestyle and social factors in managing hypertension, demonstrating that personalized pharmaceutical care interventions can significantly enhance patient outcomes and safety, underscoring the importance of a comprehensive approach to hypertension management.

## ETHICAL CONSIDERATIONS

### Data Availability

For additional information or data related to this study, please contact the corresponding author."**Conflict of Interest:**

None declared.

### Compliance with Ethical Guidelines

This study and related cases received ethical approval from the University of Uyo Health Research Ethics Committee, ensuring that the research was conducted in accordance with ethical standards and principles.

### Authors' Contributions

The authors confirm contributions as follows: study conception and design EEE and MAO; data collection ASM; Analysis and interpretation of results ASO; Draft manuscript preparation AS and EEE; All authors reviewed the result and approved the final version of the manuscript.


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