

Adverse Effects of Antihypertensive Medication and Their Impact on Therapeutic Adherence in the Moroccan Population: A Case Series

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Abstract

Background:

Therapeutic adherence is crucial for effective high blood pressure control and reducing cardiovascular risk. Nevertheless, adverse effects associated with antihypertensive medications are common and often underestimated, potentially leading to non-adherence and pseudo-resistance. Despite the clinical significance of this issue, evidence exploring the relationship between drug-related adverse effects and therapeutic adherence remains limited. Therefore, this study aims to assess the adverse effects of antihypertensive medications and evaluate their impact on patient adherence among Moroccan patients with hypertension.

Methods:

We retrospectively gathered clinical and treatment data from adult patients with hypertension who were receiving antihypertensive therapy and were followed at our outpatient cardiology center. Data on antihypertensive medications, treatment-related adverse effects, treatment interruptions, and therapeutic adherence were collected at baseline and at 3-, 6-, 9-, and 12-month follow-up visits. Adherence was evaluated by Pill Count Adherence Ratio.

Results:

A total of 105 patients were included in the final analysis, with a mean age of 55 years and a male predominance (58%). The majority of patients (89%) were on combination therapy, while 8% were on monotherapy, and 3% were on a single-pill triple combination. The most frequently reported adverse effects were cardiopulmonary (ankle and foot edema, cough, palpitations and dyspnea), genitourinary (polyuria, erectile dysfunction, decreased libido, and nocturia), gastrointestinal (dyspepsia, vomiting, and nausea), constitutional and neuropsychiatric symptoms (asthenia, insomnia, and depression). Notably, 57% of patients experienced temporary discontinuation of their antihypertensive therapy due to these side effects, while 4% permanently discontinued their regimen. Patients experiencing two or more adverse effects had higher odds of treatment interruption than those reporting a single adverse effect (aOR, 1.44; 95% CI, 1.08–1.93, $p < 0.05$).

Conclusions:

Adverse effects of antihypertensive medications represent a significant clinical challenge, contributing substantially to therapeutic non-adherence. Addressing these adverse effects is essential for optimizing patient outcomes.

1. Introduction

Hypertension is still the leading modifiable risk factor for cardiovascular morbidity and mortality worldwide, impacting about one-third of the adult population [1]. According to recent estimates from the World Health Organization, nearly 1.4 billion adults aged 30–79 years are affected by hypertension globally, with two-thirds of these individuals residing in low- and middle-income countries. In spite of substantial advances in diagnosis and management of hypertension, its burden continues to increase, particularly in resource-limited countries where rates of awareness, treatment, and blood pressure control remain insufficient [2]. Despite wider availability of antihypertensive medications in recent years, several studies have shown that half of treated patients had uncontrolled blood pressure levels. Poor therapeutic adherence has been identified as one of the key factors of uncontrolled hypertension, greatly influencing the persistence of elevated cardiovascular risk and its associated complications. Among the factors influencing adherence, adverse effects related to antihypertensive medications represent a frequent, yet often underestimated cause of treatment discontinuation, dose reduction, or irregular drug intake [3]. Adverse effects associated with antihypertensive medications are common, ranging from 20% to 40%, while serious adverse drug reactions requiring hospitalization are uncommon, less severe symptoms including peripheral edema, dizziness, fatigue, headache, flushing, dry cough, increased urinary frequency, gastrointestinal disturbances and erectile dysfunction may considerably impair patients' willingness to continue long-term therapy. [4–7]. Despite the documented frequency of these treatment-related adverse effects, most studies have primarily described their occurrence, their influence on therapeutic adherence has received comparatively less attention, particularly in North African and Moroccan populations. To address this gap, we conducted this study to characterize adverse effects associated with antihypertensive medications and assess their impact on therapeutic adherence in a cohort of Moroccan adults receiving antihypertensive treatment.

2. Methods

Study design

A single-center retrospective study conducted at Mohammed V Military Instruction Hospital of Rabat. Clinical and treatment data were retrospectively reviewed for the period from August 1, 2022, to July 30, 2023. Data recorded at baseline and during follow-up visits at 3, 6, 9, and 12 months were retrieved from the patients' medical records.

Inclusion and exclusion criteria

Adult Moroccan patients with a confirmed diagnosis of essential hypertension, who had been receiving at least one antihypertensive medication for a minimum of three months and were regularly followed in the outpatient cardiology clinic during the study period, were eligible for inclusion in the study. Patients with secondary hypertension, symptoms known to have preceded antihypertensive treatment or related to other causes, and patients with incomplete follow-up data were excluded.

Adherence was evaluated by Pill Count Adherence Ratio (PCAR), defined as the proportion of pills taken of the total number of pills prescribed between consecutive follow-up visits, expressed as a percentage. Patients were considered non-adherent if they took less than 80% of the prescribed number of pills.

Statistical analysis

Values were stated as mean ± standard deviation or median and interquartile range for continuous variables, while categorical variables were presented as frequencies and percentages. Between the different groups, continuous variables were compared with the Student t-test, and the chi-square test for categorical variables. Multivariable logistic regression analysis was performed to identify factors independently associated with treatment interruption. A two-sided P value < 0.05 was considered statistically significant.

According to institutional policy, ethical approval and informed consent were not required for retrospective studies using anonymized data and not involving direct patient contact.

3. Results

A total of 105 patients were included in the final study. The mean age was 55.7 ± 8.1 years (range, 43–71 years). There was a male predominance, with men accounting for 58% of the study population (male-to-female ratio, 1.3:1). The majority of patients lived in urban areas and were married. (Table 1).

Table 1
Baseline characteristics of the study population.

Characteristics	
Age Mean (± standard deviation)	55.7 (8.1)
Sex N (%)	
Male	54 (51%)
Residence N (%)	
Urban	72 (68%)
Familial Status N (%)	
Married	89 (85%)
Single	10 (9%)
Widowed	6 (6%)
Diabetes N (%)	28 (26%)
Smoking Status N (%)	12 (11%)
Other medication use N (%)	31 (29%)

Regarding baseline hypertension severity, 57 patients (54%) had grade 1 hypertension, 24 (23%) had grade 2 hypertension, 8 (8%) had grade 3 hypertension, and 16 (15%) presented with isolated systolic hypertension.

Most patients (89%) were receiving dual antihypertensive therapy, whereas 8% were treated with monotherapy and 3% with triple-drug therapy. The most frequently prescribed combination was an angiotensin-converting enzyme inhibitor (ACEI) plus a calcium channel blocker (CCB) (29%), followed by a thiazide diuretic plus an angiotensin II receptor blocker (ARB) (20%), a thiazide diuretic plus an ACEI (16%), an ARB plus a CCB (15%), an ACEI plus a beta-blocker (6%), and a beta-blocker plus a CCB (5%). Triple-drug therapy accounted for 3% of all treatment regimens (Fig. 1).

The most commonly reported adverse effects were cardiopulmonary, including ankle and foot edema (26%), cough (23%), palpitations (21%), and dyspnea (3%). Genitourinary adverse effects included polyuria (16%), erectile dysfunction (11%), decreased libido (9%), and nocturia (8%), whereas gastrointestinal symptoms consisted mainly of dyspepsia (12%), vomiting (6%), and nausea (3%). Constitutional and neuropsychiatric symptoms were presented by fatigue (16%) insomnia (13%), and depression (9%) (Fig. 2).

Overall, 61% of patients a PCAR lower than 80%, thus considering them non- adherent, Among these patients, 57% experienced a temporary interruption because of adverse effects. The median duration of treatment interruption was 44 days (interquartile range [IQR], 28–66 days). In 80% of cases, treatment was resumed within two months following improvement or resolution of symptoms. By contrast, 4% of patients permanently discontinued antihypertensive therapy, with adverse effects representing the primary reason for treatment cessation.

Within the study cohort, 48 patients (46%) reported a single adverse effect, whereas 57 (54%) experienced two or three adverse effects. Multivariable analysis demonstrated that patients reporting two or more adverse effects had higher odds of treatment interruption than those reporting a single adverse effect (aOR 1.44, 95% CI 1.08–1.93, $p < 0.05$) (Fig. 3).

4. Discussion

The present study investigated the impact of antihypertensive treatment-related adverse effects on therapeutic adherence among Moroccan patients with hypertension. Our findings indicate that adverse effects were associated with poorer therapeutic adherence, with more than half of the study population (61%) demonstrating poor adherence and 4% of patients permanently discontinuing antihypertensive therapy because of treatment-related symptoms.

We also observed a significant association between the burden of adverse effects and treatment interruption during follow-up. Patients reporting two or more adverse effects had 44% higher odds of treatment interruption than those experiencing a single adverse effect, suggesting that the cumulative

impact of multiple symptoms may substantially influence patients' willingness to maintain long-term therapy.

These findings are consistent with previous reports highlighting the contribution of treatment-related adverse effects to poor adherence among patients receiving antihypertensive therapy [4, 8–11]. A Canadian study reported that patients who attributed symptoms to their antihypertensive medications were nearly twice as likely to discontinue their initial treatment as those who did not report adverse effects [12]. Similarly, Grassi et al. estimated that more than half of antihypertensive treatment discontinuations could be attributed to medication-related adverse effects [13].

Cardiopulmonary symptoms were the most frequently reported adverse effects in our cohort, predominantly ankle edema, cough, and palpitations. These were followed by genitourinary symptoms, including polyuria, nocturia, and erectile dysfunction, while gastrointestinal complaints, mainly heartburn and vomiting, were reported less frequently. Comparable findings have been described in a systematic review, in which fatigue, increased urinary frequency, ankle edema, asthenia, and erectile dysfunction were identified as among the most troublesome adverse effects experienced by patients receiving antihypertensive therapy [14].

Although adverse effects represented a major determinant of treatment interruption in the present study, they are unlikely to be the sole explanation for poor therapeutic adherence. Previous studies have identified additional contributing factors, including forgetfulness, fasting, and lack of motivation, all of which remain common barriers to sustained adherence among hypertensive patients [8, 15, 16].

Only 8% of patients were treated with antihypertensive monotherapy, whereas the vast majority received dual- or triple-drug therapy. Although our study was not designed to evaluate the relationship between treatment complexity and adherence, several reports have suggested that an increasing number of prescribed antihypertensive medications may adversely affect adherence by complicating treatment regimens [9, 10]. In contrast, other studies have failed to demonstrate a significant association between the number of antihypertensive agents and medication adherence. Despite these inconsistent findings, fixed-dose combination therapy is increasingly recognized as an effective strategy to simplify treatment, improve tolerability, and ultimately enhance long-term adherence [17, 18].

Optimizing adherence to antihypertensive therapy remains a major clinical priority because of its well-established prognostic implications. Poor adherence has consistently been associated with increased all-cause mortality and a higher risk of hospitalization for cardiovascular events [19]. These observations underscore the importance of implementing strategies aimed at improving long-term adherence, with particular attention to the early recognition and management of treatment-related adverse effects.

5. Study limitations

This study has several limitations that should be considered when interpreting its findings. First, its retrospective single-center design and relatively small sample size may limit the generalizability of the

results to the broader Moroccan population and to other healthcare settings. The study was conducted in a tertiary-care cardiology center, thus the characteristics of patients attending this setting may differ from those of patients managed in primary care or other regions. Secondly, adverse effects were based primarily on patient-reported symptoms and their association with antihypertensive treatment; therefore, misclassification and recall bias cannot be excluded. Third, although adherence was assessed using pill counts during follow-up, this method reflects medication use rather than objectively confirming medication ingestion and may therefore overestimate adherence. Finally, residual confounding by comorbidities, treatment complexity, concomitant medications, and other factors influencing adherence cannot be completely excluded. Nevertheless, the availability of 12 months follow-up data and repeated assessment of treatment-related symptoms and adherence provide useful real-world data on the relationship between antihypertensive treatment tolerability and treatment interruption.

6. Conclusion

In this series of Moroccan patients with hypertension, adverse effects of antihypertensive medications were frequently associated with treatment interruption and reduced therapeutic adherence. The likelihood of interrupting treatment increased with the number of adverse effects reported, emphasizing the cumulative burden of treatment-related symptoms rather than the occurrence of a single adverse event.

These findings reinforce the importance of routinely assessing treatment tolerability during follow-up visits. Early identification of troublesome adverse effects and timely adjustment of therapy may help limit unnecessary treatment interruption and improve long-term blood pressure control. Further studies involving larger and more diverse patient populations are needed to determine whether these findings can be generalized to routine clinical practice.

Abbreviations

aOR

Adjusted Odds Ratio

ACEI

Angiotensin-Converting Enzyme Inhibitor (ACEI)

ARB

Angiotensin II Receptor Blocker

CCB

Calcium Channel Blocker

PCAR

Pill Count Adherence Ratio

Declarations

Author Contribution

A.B. – Conceptualization, Methodology. A.B., O.L., N.B. – Writing. N.M., Z.L., A.B. – Review and editing. All authors have read and approved the manuscript.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

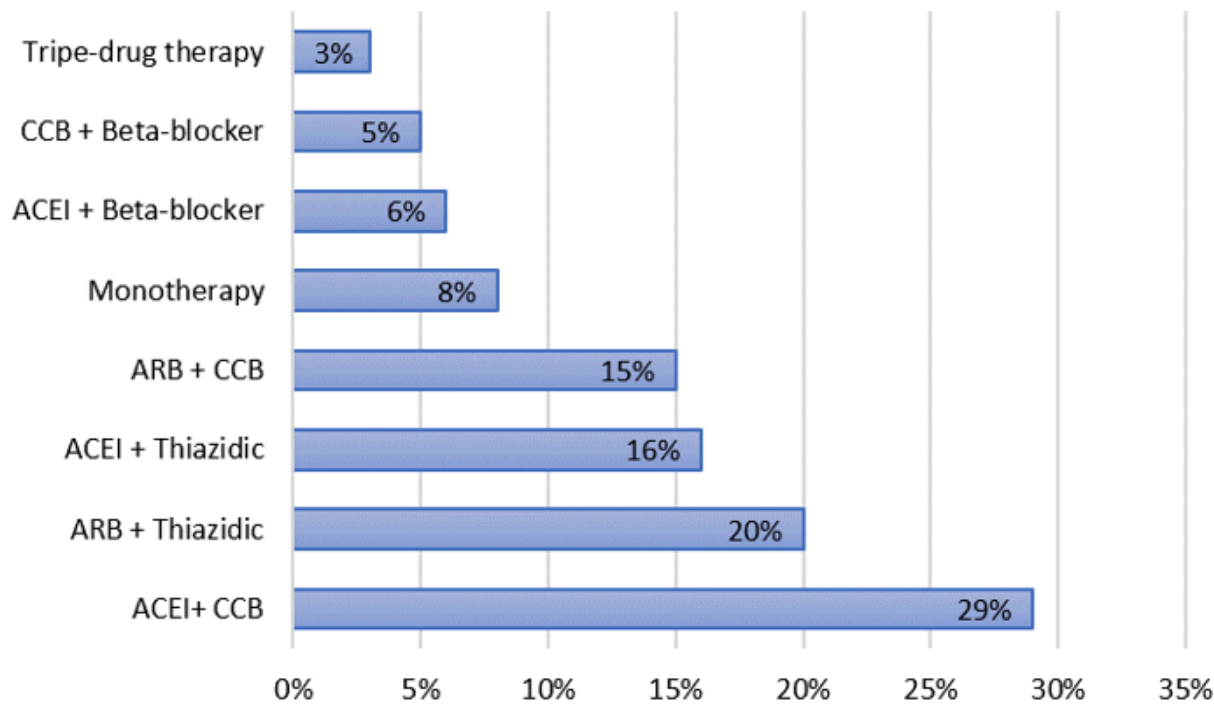


Figure 1

Distribution of antihypertensive treatment regimens among the study population.

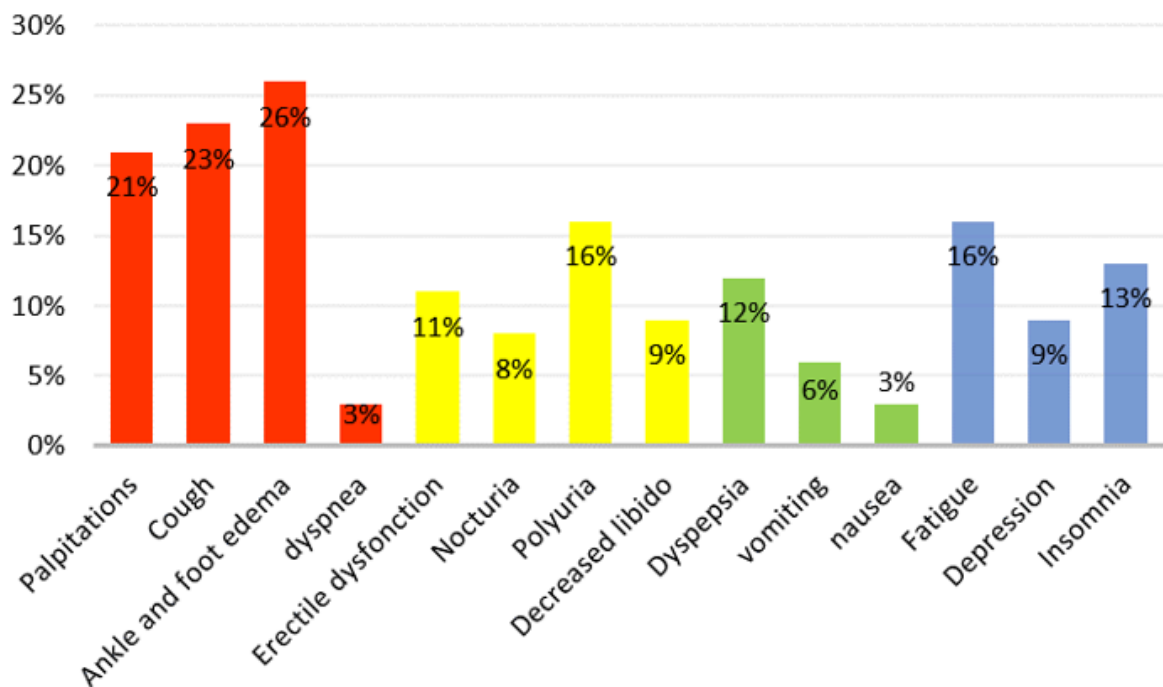


Figure 2

Profile of adverse effects reported by patients receiving antihypertensive medications

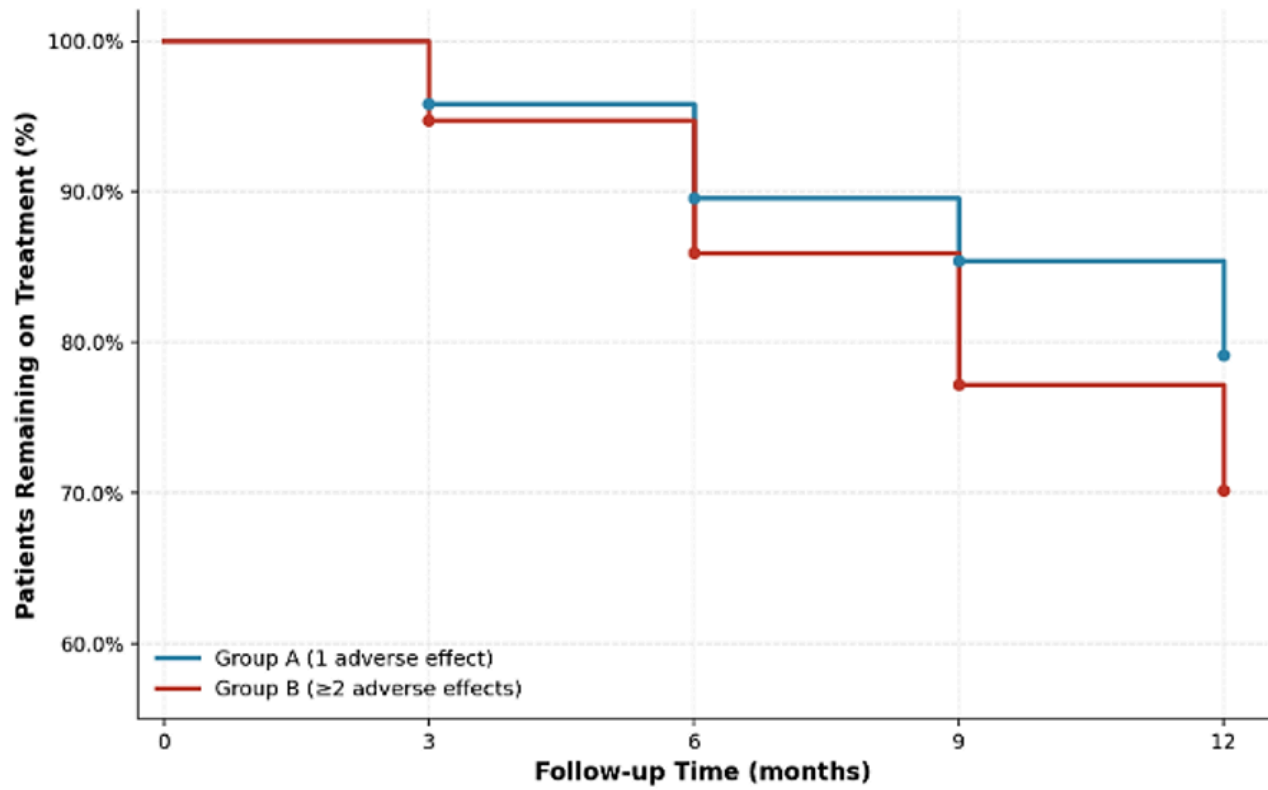


Figure 3

Treatment continuation during follow-up.