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Research Article

Mind the Kidney: Assessing Antihypertensive Dose Adjustment Based on Creatinine Clearance and Its Clinical Impact

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ABSTRACT

Hypertension is a disease characterized by continuously elevated blood pressure, which increases pressure in the kidneys and results in nephron damage.Decreased kidney function disturbs the pharmacokinetics of drugs in the body, resulting in toxic effects. In patients with hypertension and chronic kidney disease (CKD), it is necessary to adjust the dose of antihypertensive therapy using the GFR value.The aim of this study is to evaluate the dose regimen adjustment and its clinical outcome (blood pressure) and to analyze the correlation between the two.The study design is cross sectional with retrospective data through medical records of outpatient hypertensive with CKD from 2016-2020 in RSUP Fatmawati Jakarta. The results showed that of the 174 patients who met the inclusion criteria, 343 drugs were prescribed and 139 patients (79.9%) had an appropriate dose adjustment. Of those patients, 53.45% had controlled blood pressure and 26.44% had uncontrolled blood pressure. While 35 patients (20.1%) had an inappropriate dose adjustment, 12.64% of these patients were controlled and 7.47% were uncontrolled. Of the 343 prescribed drugs, bisoprolol has the highest rate of inappropriate dose adjustment. There was no significant correlation between dose adjustment suitability and blood pressure control (p-value = 0.651). However, comorbidities can affect both the suitability of dose adjustment (p-value = 0.024) and blood pressure (p-value = 0.037).

Keywords: Antihypertensive; blood pressure; chronic kidney deseases; dose adjustment

INTRODUCTION

Both chronic kidney disease (CKD) and hypertension are associated with similar complications due to the overactivation of the sympathetic nervous system, such as high blood pressure and impaired renal function. Excessive intravascular volume is a major pathogenic factor of hypertension in patients with CKD. Managing blood pressure is an important part of treating renal failure (Hebert & Ibrahim, 2022). For renal failure testing, glomerular filtration rate (GFR) is the best indicator and helps determine the stage of chronic kidney disease. The earlier it is detected, the better the chances of stopping its progression (Sharma *et al*., 2021). Treatment will be given according to the stage of the disease. CKD is usually symptomatic, so it is often detected at an advanced stage (Pothen *et al*., 2019).

Antihypertensives are a class of drugs excreted by the kidneys. However, in patients with hypertension and chronic kidney disease (CKD), creatinine clearance decreases, affecting metabolic processes. As a result, there will be an accumulation of endogenous or exogenous compounds. This can cause toxic effects, such as hyperkalemia, which often

occurs in patients with kidney failure(Farrell et al., 2024; Georgianos & Agarwal, 2023). When renal function is reduced, drug doses should be adjusted and nephrotoxic drugs should be avoided. To avoid drug-related problems due to kidney disorders, select the right drug and adjust the dose to achieve clinical outcomes, minimize toxicity, and prevent a decrease in kidney function. Drugs with a high renal excretion ratio are more dependent on changes in blood flow rate in the kidneys. In the dosing regimen for renal failure, changes in blood flow rate may be mistaken for changes in GFR(Chikuba et al., 2016; Farrell et al., 2024; Georgianos & Agarwal, 2023).

Dose adjustments were made using the creatinine clearance/SCr/GFR ratio. The following types of antihypertensive drugs require dose adjustments for patients with CKD: ACE inhibitors (captopril, lisinopril, ramipril, benazepril, and enalapril); beta blockers (bisoprolol and atenolol). However, loop diuretics do not require dose adjustments(Bondre et al., 2020; Hebert & Ibrahim, 2022; Očovská et al., 2024; Ohno et al., 2021; Sinha & Agarwal, 2019). Dose adjustments are made based on changes in pharmacokinetics. In kidney disorders, drug absorption decreases due to increased blood urea levels. Drug distribution can be altered by changes in hydration levels or protein binding. Active metabolites can accumulate in kidney disorders, causing clinical problems in drug metabolism. Renal failure decreases clearance of the eliminated drug by 50%, and the drug's half-life becomes longer due to impaired glomerular filtration (Cheng *et al*., 2025).

The suitability of dose regimen adjustments in patients with chronic kidney disease (CKD) greatly affects the desired therapeutic effect and helps avoid toxic effects. However, not all doctors assess a patient's GFR. Sometimes, they only look at creatinine serum levels to estimate the appropriate dose. Therefore, it is necessary to calculate this drug's dose adjustment. Pharmacists can warn doctors about this, ensuring that antihypertensive drugs are effective for patients with chronic kidney disease. However, research on dose adjustments for CKD patients is limited, particularly for antihypertensive drugs used by patients with hypertension and CKD. While research focuses on the rationale behind antihypertensive drugs, it does not detail how to adjust the dosage for patients with hypertension and CKD.

METHODS

Study Design and Inclusion Criteria

This retrospective cross-sectional study used the medical records of outpatients with hypertension and chronic kidney disease at Fatmawati Hospital Jakarta from 2016 to 2020. The study population was all chronic kidney disease outpatients. The selected sample must fulfill the inclusion and exclusion criteria. Purposive sampling was used to collect the sample for this study.

The inclusion criteria consist of hypertensive CKD outpatients who have experienced an increase in serum creatinine (0.3 mg/dL above normal), received oral antihypertensives for at least three months, are at least 20 years old, and have complete medical records Patients undergoing hemodialysis, as well as patients with AIDS, tuberculosis, liver disease, pregnancy, lactation, or psychiatric disorders, are excluded. Of the 618 patients, a total of 174 met the inclusion criteria.

Dose Adjusment and Blood Pressure Parameters.

In this study, the adjustment of antihypertensive doses was to compare the dosage regimen given to patients by the hospital for more than three consecutive months with the dosage regimen listed in the Drug Information Handbook: Renal Pharmacotherapy. This comparison was based on each patient's creatinine clearance value. Later, the dosage regimen will be calculated, as well as the estimated maximum and minimum levels of each dose given by the hospital, compared to the estimated maximum and minimum levels based on the adjusted dosage regimen in the library. The creatinine clearance value will be calculated using the Cockcroft-Gault equation. If the dosage regimen is deemed inappropriate, a calculation will be carried out using the Giusti-Hayton equation to adjust the dosage regimen to the creatinine clearance value of each patient (Chikuba et al., 2016). The adjusted dosage regimen for CKD using Giusti-Hayton can be calculated as follows:

$$G = K^U / K^N = 1 - f(1\text{-}CL^U_R / CL^N_R)$$

$$\text{Adjustment dosage} = DoN \times G$$

$$\text{Adjustment Interval : } \tau U = \tau N \times 1/G$$

Where G is the Giusti-Hayton equation, f is the fraction excreted unchanged, CLUR is the clearance in patients with chronic kidney disease (CKD) or renal dysfunction, CLNR is the clearance in patients with

normal kidney function, DoN is the normal or usual dosage, and ҬU is the adjustment interval in patients with CKD. ҬN is the interval for patients who use drugs administered by the hospital.

In this study, blood pressure monitoring was carried out by measuring the patients' blood pressure for three consecutive months of treatment. The results of the last examination were used as a reference for categorization. There are two categories: controlled and uncontrolled. Blood pressure is considered controlled if the results of the final examination reach the target. The blood pressure target for CKD stages 1–4 is less than 130/80 mmHg, while for stage 5 it is less than 140/90 mmHg. However, these targets are adjusted according to the patient's age.

Data analysis

This study used a univariate analysis to determine the percentage of characteristics, including age, sex, class of antihypertensives, and appropriateness of dose adjustment. Furthermore, a chi-square test was performed to determine the correlation between dose adjustment suitability and blood pressure. Finally, multiple logistic regression analysis was used to determine the correlation between confounding variables and the appropriateness of the dose adjustment and blood pressure.

RESULTS AND DISCUSSION

Of the 618 patients in this study, 174 met the inclusion criteria. Of the 174 patients who underwent antihypertensive therapy at Fatmawati Hospital's Jakarta outpatient facility, each had different baseline characteristics, including age, gender, comorbidities, use of other drugs, and CKD stage (Table 1).

In this study, dose adjustments were made based on each patient's creatinine clearance (ClCr) value. The study yielded the following results: 343 drugs were used by 174 patients. Of the 174 patients, 79.9% used antihypertensive drugs with an appropriate dose adjustment and 20.1% used antihypertensive drugs with an inappropriate dose adjustment. Antihypertensive drugs consist of eight classes of drugs, each with different pharmacological and pharmacodynamic processes(Pugh et al., 2019; Velenosi & Urquhart, 2014).

The results of this study show that the majority of patients received two types of antihypertensives: amlodipine as a single agent and amlodipine with candesartan in combination. Forty-one percent of patients used a combination therapy when their blood pressure had already reached therapeutic goals. Amlodipine and candesartan were the most widely used drugs in single therapy. Amlodipine is an antihypertensive drug that does not significantly affect the angiotensin system; however, it may have a favorable effect on the endothelium in vitro. Combination therapy was more beneficial than monotherapy(Ku et al., 2024; Ohno et al., 2021; Sinha & Agarwal, 2019; Sumathy & Monika, 2017). Calcium channel blockers have been shown to be very effective in treating hypertension with low renin levels, such as in elderly patients. The mechanism of action of an angiotensin receptor blocker (ARB) is that angiotensin II promotes aldosterone secretion and acts as a vasoconstrictor; as a result, it lowers blood pressure. A third option for single therapy is the ACE-I group, which can reduce intraglomerular pressure and proteinuria, thereby preventing further decline in kidney function(Bondre et al., 2020).

Oral antihypertensive regimens widely prescribed for hypertension accompanied by chronic kidney disease (CKD) were combination therapies of two antihypertensives. Other combinations of drugs used include ACE-I or ARB with beta-blockers, as well as CCBs or ARBs with diuretics. Combining ARBs with diuretics is more effective at lowering systolic and diastolic blood pressure than combining CCBs with diuretics. The combination of a CCB and a diuretic has an additive effect, partly due to the two drugs' overlapping pharmacological properties. However, this combination can still be tolerated because diuretics reduce edema caused by CCBs. There will be little therapeutic effect when ACE-I is combined with beta-blockers because the mechanism of action of ACE-I on renin is contrary to the renin inhibition induced by beta-blockers (Agarwal *et al*., 2025; Bondre *et al*., 2020; Fitzpatrick *et al*., 2022; Jo *et al*., 2023; Ku *et al*., 2024; Ohno *et al*., 2021; Rimoldi *et al*., 2015; Sinha & Agarwal, 2019; Suganya *et al*., 2017; Sumathy & Monika, 2017).

Table 1. Baseline Patient Characteristics

Patient characteristics	Amount of patient (n=174)
	n (%)
Age (years)	
26-45	3 (1.7)
46-65	95 (54.6)
> 65	76 (43.7)
Gender	
Men	106 (60.9)
Women	68 (39.1)
Comorbid	
No Comorbid (other than CKD)	16 (9.2)
Obesity	1 (0.6)
Cardiovascular	29 (16.6)
Diabetes mellitus (DM)	65 (37.4)
Hyperuricemia	9 (5.2)
Hyperuricemia and DM	5 (2.9)
Cardiovascular and DM	25 (12.4)
Obesity, DM and Cardiovascular	5 (2.9)
Obesity and DM	7 (4)
Obesity, DM and Dyslipidemia	3 (1.7)
Cardiovascular, DM and Dyslipidemia	1 (0.6)
DM and Dyslipidemia	2 (1.1)
Hyperuricemia and Dyslipidemia	1 (0.6)
Obesity and Cardiovascular	2 (1.1)
Obesity, DM and Hyperuricemia	1 (0.6)
Amount of other medications	
1-5 drugs	155 (89.1)
> 5 drugs	19 (10.9)
Stage of CKD	
Stage 1 (GFR>90 mL/min/1.73m^2)	1 (0.6)
Stage 2 (GFR 60-89 mL/min/1.73m^2)	9 (5.2)
Stage 3 (GFR 30-59 mL/min/1.73m^2)	71 (40.8)
Stage 4 (GFR 15-29 mL/min/1.73m^2)	74 (42.5)
Stage 5 (GFR < 15 mL/min/1.73m^2)	19 (10.9)

A combination of three drugs was used by only 33 patients, while a combination of more than three drugs was used by 10 patients. The blood pressure target cannot be achieved by using only a combination of two classes of antihypertensive drugs(Bondre et al., 2020; Georgianos & Agarwal, 2023; Hebert & Ibrahim, 2022). However, in this combination of three or more drugs, two types of drugs from the same class should not be used. To reduce the overlapping effects that occur, combinations of antihypertensive drugs must come from different drug classes. In the combination of three drugs with the use of 20 patients, the most widely used types of drugs were ARBs, CCBs, and β-blockers. The most widely used ARBs were candesartan and valsartan; the most widely used CCBs were amlodipine and nifedipine; and the most widely used β-blockers were bisoprolol and carvedilol, each used by three patients. β-Blockers are appropriate to add during three-drug combination therapy because they are used as a last resort after first-line antihypertensive therapy fails to reach the target. The combination of two or more antihypertensive drugs is required because achieving therapeutic goals is difficult. Some patients have not achieved therapeutic goals even after being prescribed three to five antihypertensive drugs(Fitzpatrick et al., 2022; Sulochana & Rani, 2019).

Dose Adjusment and Its Correlation with Blood Pressure

Bisoprolol is a drug that requires dose adjustments. Of the 42 uses of bisoprolol, 9 (21.4%) do not match the dose or interval with the literature. First, the patient's creatinine clearance (ClCr) value is calculated using serum creatinine with the Cockcroft-Gault equation. The ClCr value is then used to determine the appropriate dose adjustment based on the values listed in the literature (Table 2).

Dose adjustment for patients with CKD is determined based on the value of the patient's ClCr (Su et al., 2024). The study yielded results showing that 20 types of drugs were used by 13 patients who experienced cases that did not match the dose (Table 3). One example of a case of dose inapproriate is seen in a patient who uses single ramipril, where the patient has a ClCr of 18.99 mL/min/1.73 m^2 receiving a ramipril dose of 10 mg/day. Meanwhile, based on the literature, the dose adjustment of ramipril in patients with CrCl 10-50 ml/min/1.73 m^2 is 2.5-7.5 mg/day. The usual dose of ramipril in normal renal function is 5-10 mg, 1-2 times/day. The dose adjustment of ramipril in this patient should be 3-5 mg/day (according to the dose adjustment range based on the literature).

Therefore, the dose of candesartan that the patient received was appropriate. It matches the ClCr based on the literature. If the patient received a subtherapeutic dose inappropriate for the ClCr range, it would not be possible to achieve the therapeutic effect.Similarly, overdosing can increase the risk of toxicity. In addition to the dose, the interval of administration should also be considered when adjusting the dose. Dose adjustments can be made to either the dose or the interval of administration, or both. An administration interval that is much shorter or longer than it should be may result in blood levels of the drug not reaching the therapeutic range. The same applies to inappropriate dose adjustments.Inappropriate dose adjustments, especially in patients with CKD, can lead to loss of kidney function due to reduced renal blood flow and glomerular filtration rate caused by reduced cardiac output. The risk of an unachieved or adverse therapeutic effect is higher with drugs that are primarily excreted by the kidneys(Kusumawardani et al., 2025; Lea-Henry et al., 2018).

Tabel 2. Distribution of Antihypertensive Based on Dose and Interval Adjusment Suitability

Type of Drug	Dose Adjustment	
	Appropriate (n=301)	Inappropriate (n=42)
	n (%)	n (%)
Captopril	1 (0.3)	1 (2.4)
Lisinopril	3 (1)	0
Ramipril	21 (7)	5 (12)
Diltiazem	13 (4.3)	0
Candesartan	58 (19.2)	3 (7.1)
Valsartan	32 (10.6)	0
Irbesartan	2 (0.7)	1 (2.4)
Losartan	1 (0.3)	0
Amlodipine	68 (22.6)	2 (4.8)
Telmisartan	5 (1.7)	4 (9.5)
Nifedipine	33 (10.9)	2 (4.8)
Hidroclortiazide	3 (1)	0
Furosemid	14 (4.7)	1 (2.4)
Spironolakton	3 (1)	1 (2.4)
Bisoprolol	33 (10.9)	9 (21.4)
Carvedilol	8 (2.7)	7 (16.6)
Clonidine	3 (1)	6 (14.2)

Tabel 3. Category of Inappropriate Adjusment and Dose Adjustment Based on Giusty Hayton

No	Drugs	CLCr (mL/minute/1.73m^2)	Dose adjustment Based on DIH/*Renal Pharmacotherpy* (mg/interval)	Dose adjustment on hospital (mg)	Dose adjustment based on *Giusti Hayton* (mg)	Note
1	Bisoprolol	53.31	5/once daily	10/day	1x4-8	D
2	Bisoprolol	26.57	5/once daily	2.5/day	1x3-6	D
3	Bisoprolol	17.93	2.5-5/once daily	1.25/day	1x3-6	D
4	Ramipril	81.56	5-10/once daily	2.5/day	1x4-9	D
5	Carvedilol	81.56	25-100/twice daily	2x6.25	2x12-48	D
6	Ramipril	23.72	2.5-7.5/once daily	1x10	1x3-5	D
7	Bisoprolol	60.45	5/once daily	1x2.5	1x4-8	D
8	Bisoprolol	32.41	2.5-5/once daily	1x1.25	1x3-7	D
9	Irbesartan	38.78	56.25-225/once daily	1x300	1x66-263	D
10	Ramipril	18.99	2.5-7.5/once daily	1x10	1x3-5	D
11	Carvedilol	26.47	12.5-50/twice daily	2x3.125	2x10-41	D
12	Spironolakton	26.47	Avoid	1x25	1x10-78	D
13	Ramipril	24.43	2.5-7.5/once daily	1x10	1x3-5	D
14	Ramipril	39.54	2.5-7.5/once daily	1x10	1x3-6	D
15	Carvedilol	60.36	25-100/twice daily	2x6.25	2x11-45	D
16	Bisoprolol	37.78	2.5-5/once daily	1x1.25	1x3-7	D
17	Bisoprolol	27.22	2.5-5/once daily	1x10	1x3-6	D
18	Bisoprolol	21.68	2.5-5/once daily	1x10	1x3-6	D
19	Bisoprolol	38.89	2.5/once daily	1x1.25	1x3-7	D
20	Bisoprolol	40.73	2.5-5/once daily	1x1.25	1x4-7	D
21	Candesartan	17.36	1-16/once daily	2x16	1x12-23	I
22	Clonidine	17.36	0.1-2/twice daily	3x0.15	2x0.05-0.6	I
23	Telmisartan	12.25	No adjustment	1x100	3x19-91	I
24	Telmisartan	20.95	No adjustment	1x100	3x21-96	I
25	Telmisartan	34.18	No adjustment	1x100	3x22-103	I
26	Carvedilol	32.1	12.5-50/twice daily	3x12.5	2x5-42	I
27	Nifedipine	40.73	No adjustment	2x30	1x21-63	I
28	Telmisartan	19.61	No adjustment	1x100	3x20-95	I
29	Clonidine	38.89	0.1-2/twice daily	1x2	2x0.06-0.7	I
30	Amlodipine	29.57	No adjustment	2x5	1x1.4-6	I
31	Carvedilol	20	12.5-50/twice daily	1x50	2x10-40	I
32	Clonidine	12.41	0.1-2/twice daily	3x0.15	2x0.04-0.5	I
33	Carvedilol	21.51	12.5-50/twice daily	3x12.5	2x10-40	I
34	Clonidine	10.98	0.1-2/twice daily	3x0.15	2x0.04-0.5	I
35	Furosemid	21.68	No adjustment	2x40	1x8-33	I
36	Clonidine	10.42	0.1-2/twice daily	3x0.15	2x0.04-0.5	I
37	Captopril	64.21	25-50/twice daily	3x20	2x22-45	DI
38	Clonidine	14.2	0.1-2/twice daily	1x25	2x0.05-0.6	DI
39	Candesartan	14.66	2-24/once daily	2x16	1x11-23	DI
40	Carvedilol	18.34	12.5-50/twice daily	1x6.25	2x10-40	DI
41	Clonidine	55.49	1-2.4/twice daily	3x0.15	2x0.07-0.9	DI
42	Candesartan	21.68	2-24/once daily	2x16	1x12-24	DI

Note: This table describes the categories of inappropriate dosage regimen adjustments which are divided into dose or interval adjustment or both. After each drug was categorized, adjustments were made to either the dose only, the interval only, or the dose and the interval was adjusted according to the category dose regimen adjustment to determine the appropriate dose regimen range. The adjustment calculation uses the Giusti Hayton equation by considering the value of creatinine clearance. I: Interval, D: Dose, DI: Dose and Interval.

An inappropriate dose or interval can occur with one antihypertensive drug at the same time. For example, a patient using combination therapy with nifedipine and carvedilol may experience this. After reviewing the patient's ClCr, which was 18.34 mL/min/1.73 m², and comparing it to the recommended dosage of nifedipine, the prescribed dose was 30 mg/day. The carvedilol dose adjustment for a ClCr of 10-50 mL/min/1.73 is 12.5-50 mg twice daily. However, the prescribed dose is only 6.25 mg once daily. Therefore, the patient was given an inappropriate dose and interval. To determine the appropriate dosage regimen, the Giusti-Hayton formula was used to calculate the dosage. The patient's ClCr was 18.34 mL/min/1.73 m², and 25% of the carvedilol was eliminated by the kidneys. The usual dosage is 12.5–50 mg twice daily. Therefore, the dose should be 10–40 mg twice daily.

Accurate dosing is essential to achieving the desired therapeutic outcomes, particularly in patients with chronic kidney disease (CKD). Changes in absorption, distribution, metabolism, and elimination experienced by patients with CKD affect drug processes in the body, resulting in changes in the clinical outcomes of drug therapy. For example, spironolactone therapy is used for patients with a GFR or ClCr of less than 30 mL/min/1.73 m². Chronic kidney disease generally reduces glomerular filtration and active secretion, resulting in decreased drug excretion through the kidneys and a longer elimination half-life(Roberts et al., 2018; Wang et al., 2024).

The results of the blood pressure tests show that most controlled blood pressure is in the appropriate dose adjustment category (53.4%). However, 26.4% of cases are not controlled. In the group that is not yet appropriate for dose adjustment, 7.5% of patients' blood pressure is still not controlled. This distribution may be caused by several factors, including age, comorbidities, the number of drugs used, and drug interactions, which vary from patient to patient. These factors can affect the pharmacokinetics of drugs traveling through the body, thereby affecting outcomes such as blood pressure(Su et al., 2024; Sulochana & Rani, 2019; Sumathy & Monika, 2017).

Age is a determinant of drug disposition; the pharmacokinetic process of drugs changes with age due to changes in physiological function. Subjects who are mostly 46-65 years old experience changes in their bodies, such as decreased gastric emptying time, increased body fat, and decreased enzyme activity, which can affect a drug's clinical outcome(Aymann et al., 2010). Most subjects have comorbidities, which result in polypharmacy and increase the risk of drug interactions. If a drug interaction occurs during the ADME process, the drug level will be higher than the minimum therapeutic level. This puts the drug at risk of toxicity, which can prevent the desired clinical outcomes from being achieved(Sharma et al., 2021). Several factors influence clinical outcomes, which can result in patients receiving inappropriate doses having their blood pressure controlled or patients experiencing uncontrolled blood pressure despite accurate dose adjustments.

Judging from the chi-square results, there is no correlation between dose adjustment suitability and blood pressure (p-value = 0.651; see Table 4). The correlation between dose adjustment and blood pressure involves pharmacokinetics and pharmacodynamics. There is large variability in plasma drug levels and response between patients taking each antihypertensive drug. The presence of comorbid factors can affect drug pharmacokinetics and clinical outcomes(Geerts et al., 2012). A hypothesis regarding the relationship between dose suitability and clinical outcomes shows that higher doses produce higher clinical outcomes until the maximum drug effect is achieved. However, the dose must also be adjusted according to the patient's age, weight, and any existing disorders(Via-Sosa et al., 2013). This should be considered when determining the appropriateness of the dosage and frequency of drug administration. If the dosage and frequency are not appropriate, the drug levels in the blood may exceed the therapeutic range, which can cause clinical outcomes to exceed the target goals of each individual's therapy. Treatment for hypertension varies from patient to patient. Treatment is individualized, considering that drug effects are not always the same for everyone (Su et al., 2024).

The Chi-Square test revealed no significant relationship between dose adjustment suitability and clinical outcome. This may be due to other suspected contributing factors. It appears that comorbidities have a significant relationship with clinical outcomes (p-value = 0.037). Meanwhile, other variables, such as gender, age, polypharmacy, and chronic kidney disease stage, showed no significant relationship with clinical outcomes.

Tabel 4. Correlation of Dose Adjustment Suitability with Blood Pressure

Dose adjusment suitability	Blood Pressure		*p-value*
	Controlled n (%)	Uncontrolled n (%)	
Appropriate	93 (53.45)	46 (26.44)	0.651
Inappropriate	22 (12.64)	13 (7.47)	

Although the results indicated that only comorbidities were significantly related to clinical outcomes and drug adjustment suitability, other factors needed to be considered, such as polypharmacy due to other patient complications. Polypharmacy can significantly increase the risk of drug interactions and decrease the likelihood that patients will adhere to treatment, which can affect the achievement of the desired blood pressure outcome. Patients usually avoid taking their medications due to the long duration of treatment and lack of symptoms of hypertension, and the most common cause of uncontrolled hypertension is lack of adherence to the treatment regimen. Comorbidities make treatment more complex because drug administration must consider the patient's condition(Beygi et al., 2017; Mallamaci et al., 2024). Administering the correct drug with the appropriate dosage regimen greatly affects clinical outcomes and the achievement of therapeutic goals, especially with regard to blood pressure in patients with hypertension. As can be seen, comorbidity is correlated with blood pressure (p-value = 0.037).

CONCLUSION

Of the 174 patients taking 343 oral antihypertensives, 139 patients (79.9%) took 301 drugs with an appropriate dose regimen adjustment, while 35 patients (20.1%) took 42 drugs with an inappropriate adjustment. The antihypertensive with the highest percentage of appropriate dose adjustments was amlodipine (22.6%), while the antihypertensive with the highest percentage of inappropriate adjustments was bisoprolol (21.4%). The blood pressure of 53.4% of patients was controlled, while 26.4% had uncontrolled blood pressure. There was no correlation between dose adjustment suitability and blood pressure, but there was a correlation with comorbidities. Accurate dose adjustments are crucial for achieving therapeutic effects. Although there is no statistical correlation, it has a clinical impact, especially on blood pressure in CKD patients.

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CONFLICT OF INTEREST

There was no conflict of interest in this manuscript.

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