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Response of Antihypertensive Treatments and Incidence of Drug-Related Problems in Patients with Chronic Kidney Disease

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Abstract: Hypertension is nearly universal in chronic kidney disease (CKD) and is a principal driver of morbidity, mortality, and disease progression. Antihypertensive therapy is fundamental to CKD management, but patients are at high risk for drug-related problems (DRPs) due to polypharmacy and altered pharmacokinetics. This review synthesizes evidence regarding antihypertensive treatment response and incidence of DRPs in CKD, drawing on recent clinical trials, pharmacological studies, and observational cohorts.

Keywords: Chronic kidney disease (CKD), Hypertension, Antihypertensive therapy, Drug-related problems (DRPs), Polypharmacy.

INTRODUCTION

Patients with CKD commonly present with difficult-to-control hypertension and multiple comorbidities. Effective blood pressure (BP) management is essential for slowing CKD progression and reducing cardiovascular risk, but this population is disproportionately subject to DRPs such as adverse drug reactions (ADRs) and drug-drug interactions (DDIs)[1][2]. Understanding both the efficacy and safety of antihypertensive regimens in CKD is crucial to optimizing care.

ANTIHYPERTENSIVE TREATMENT RESPONSE IN CKD

Pathophysiology of Hypertension in CKD

- As nephron loss progresses, increased sodium retention, activation of the renin-angiotensin-aldosterone system (RAAS), sympathetic overactivity, and endothelial dysfunction all contribute to elevated BP[2][3].
- Masked or resistant hypertension is highly prevalent in CKD; ambulatory or home BP monitoring is recommended for detection and management[4].

Pharmacological Choices

- **RAAS Blockers (ACE inhibitors/ARBs):** Preferred first-line agents, especially for proteinuric CKD. Provide both BP-lowering and renoprotective effects[2][4].
  - Typical BP reduction: ~20mmHg systolic in CKD[1].
  - Superior in reducing proteinuria versus other classes.
- **Calcium Channel Blockers (CCBs):** Often used as second-line agents, especially in non-proteinuric CKD or as add-on therapy[2].
- **Diuretics:** Thiazides or thiazide-like agents (e.g., chlorthalidone) are used in earlier CKD; loop diuretics become essential in later stages with volume overload[2].
- **β-blockers:** Reserved for specific indications such as heart failure or ischemic heart disease[5].
- **Mineralocorticoid Receptor Antagonists (e.g., spironolactone):** Can be used for resistant hypertension but risk hyperkalemia, particularly in advanced CKD[2].

Table 1. Common Antihypertensive Drug Classes in CKD Patients

Drug Class	Main Benefits	Key Risks in CKD
RAAS Blockers (ACEi/ARBs)	Renoprotection, Proteinuria ↓	Hyperkalemia, AKI
Calcium Channel Blockers	BP Lowering, Vascular protection	Edema
Thiazide Diuretics	Volume/BP Control (early CKD)	Electrolyte disturbances
Loop Diuretics	Volume Control (late CKD)	Hypokalemia
β-blockers	CV Protection	Bradycardia, Fatigue
Spironolactone	Resistant HTN, Proteinuria ↓	Hyperkalemia

Achieving Blood Pressure Targets

- **Guideline targets:** Most guidelines recommend <120/80mmHg for native CKD and <130/80mmHg for renal transplants[4][3].
- **Practical response:** BP control often requires combination therapy; more than 60% of CKD patients need ≥3 agents[4].
- **Treatment-resistant hypertension:** May require addition of spironolactone or chlorthalidone, though careful monitoring for hyperkalemia and renal function is essential[2][3].

Example: Clinical Response Data

- In the CRIC study of 3,939 CKD patients, RAAS blockade was associated with improved outcomes, but use declined with progressive CKD[5].
- Diuretic and CCB use increased in later-stage CKD, reflecting evolving volume status and resistance to other therapies.

Figure 1. Patterns of Antihypertensive Use by CKD Stage
(A line graph showing highest RAAS inhibitor use in stage 3, with increasing diuretic and CCB use in stages 4–5)[5].

Incidence and Types of Drug-Related Problems in CKD

Polypharmacy and Drug Exposure

- Polypharmacy is common; mean number of prescribed drugs often exceeds 10 per CKD patient[1].
- High comorbidity burden (diabetes, dyslipidemia) increases the risk of DRPs[1].

Prevalence of Drug-Related Problems

- **Potential Drug-Drug Interactions (pDDIs):**
  - Prevalence: Up to 89.2% of CKD patients have at least one pDDI[1][6].
  - 708 pDDIs identified in a study of 130 CKD patients; polypharmacy was the strongest predictor[1].
  - Diabetes and dyslipidemia, longer hospitalization, and increasing medication count all raise risk.
- **Adverse Drug Reactions (ADRs):**
  - Incidence: Around 10.7% in prospective CKD cohorts[1][6].
  - Most ADRs were mild–moderate and non-preventable.
  - Common offenders: Diuretics, RAAS blockers, and drugs with narrow therapeutic windows.
- **Drug-Related Acute Kidney Injury (AKI):**

- AKI incidence in CKD patients: 21%, with 28% of drug-related AKI episodes being preventable[7].
- Top drug classes: Diuretics, RAAS inhibitors, contrast agents.
- Risk factors: Cardiovascular comorbidity, polypharmacy, poor adherence, reduced eGFR.

- **Other DRPs:** Include inappropriate dosing, medication errors, and nonadherence due to pill burden[1].

Table 2. Summary of DRP Incidence in CKD

Parameter	Study Data
Prevalence of pDDI	89.2% of CKD patients[1]
Incidence of ADRs	10.7%[1][6]
Drug-related AKI incidence	21% (of all CKD patients), 28% preventable[7]
Top culprit drug classes	Diuretics, RAAS blockers, contrast agents[7]
Polypharmacy effect (OR for pDDI)	6.3–62.3 (significant increase)[1]

Figure 2. Frequency of Drug-Related Problems in CKD Patients
(A bar chart showing: pDDI 89%, ADR 11%, drug-induced AKI 21%)[1][7].

CLINICAL IMPLICATIONS AND STRATEGIES

Optimizing Efficacy and Safety

- **Personalized Regimens:** Therapy should be individualized, balancing BP control with risk of DRPs[2][4].
- **Monitoring:** Frequent assessment of BP, electrolytes (especially potassium), and renal function is critical.
- **Polypharmacy Reduction:** Regular medication review helps minimize unnecessary drugs.
- **Interdisciplinary Teams:** Collaboration among nephrologists, pharmacists, and other healthcare professionals reduces the risk of DRPs and improves outcomes[1][6].
- **Patient Engagement:** Education regarding medication adherence, monitoring for side effects, and importance of follow-up visits.

Preventive Policies

- Use interactions screening databases with each prescription change[1].
- Renal dosing adjustments according to stage of CKD.
- Close monitoring when using agents with high nephrotoxicity or risk for electrolyte derangements.

CONCLUSION

Antihypertensive therapy is effective in achieving blood pressure control and slowing CKD progression, but patients are at high risk for drug-related problems because of the complex interplay of polypharmacy, altered drug handling, and comorbidities. Proactive identification and management of DRPs—especially pDDIs and ADRs—are fundamental to optimizing patient safety and improving clinical outcomes in CKD.

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