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Review Article

Management of Resistant Hypertension in Canada: Physician and Clinical Pharmacist Perspectives Across Ambulatory and Hospital Care

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Abstract

Resistant hypertension is associated with substantial cardiovascular, cerebrovascular, and renal risk and requires careful confirmation before therapy is intensified. In Canada, the 2025 Hypertension Canada primary care guideline defines hypertension as blood pressure (BP) >=130/80 mm Hg when measured under optimal conditions and generally recommends a systolic BP target <130 mm Hg when tolerated. True resistant hypertension should be considered when BP remains above target despite adherence to maximally tolerated therapy with an ACE inhibitor or angiotensin receptor blocker (ARB), a thiazide or thiazide-like diuretic, and a long-acting dihydropyridine calcium-channel blocker. Management requires exclusion of pseudoresistance, assessment for secondary causes, optimization of diuretic therapy, and usually addition of spironolactone as fourth-line treatment when renal function and potassium permit. From the physician perspective, priorities include confirming the diagnosis, evaluating secondary hypertension and comorbidity, individualizing treatment, and distinguishing chronic resistance from hypertensive emergency. Clinical pharmacists complement this work through medication reconciliation, adherence assessment, identification of BP-raising drugs, dose optimization, laboratory monitoring, patient education, and post-discharge follow-up. A coordinated physician-pharmacist model can strengthen Canadian hypertension care while reducing both undertreatment and avoidable overtreatment.

Keywords: resistant hypertension; Canada; Hypertension Canada; physician; clinical pharmacist; spironolactone; chronic kidney disease; inpatient hypertension

1. Canadian Context and Definition

Hypertension affects approximately one in four Canadian adults and remains a major modifiable cardiovascular risk factor. The 2025 Hypertension Canada guideline recommends defining hypertension as BP >=130/80 mm Hg using validated devices and standardized measurement, with a general systolic treatment target <130 mm Hg when well tolerated.[1]

Within this framework, resistant hypertension is BP that remains above target despite confirmed adherence to maximally tolerated treatment with three complementary drug classes: an ACE inhibitor or ARB, a thiazide or thiazide-like diuretic, and a long-acting dihydropyridine calcium-channel blocker.[1] Before labeling a patient resistant, clinicians should exclude inaccurate measurement, white-coat effect, nonadherence, inadequate doses, inappropriate combinations, and insufficient diuretic therapy.[1,2] Out-of-office confirmation with ambulatory BP monitoring or validated home BP monitoring is especially important before adding further medication.

2. Physician Perspective: Confirm the Diagnosis Before Escalating Therapy

For physicians in family medicine, internal medicine, cardiology, nephrology, or hypertension clinics, the first task is to establish whether treatment resistance is genuine. A single high office reading should not trigger another drug. Measurement technique, cuff size, rest period, repeated readings, home values, adherence, and actual medication use should be reviewed first.[1,2]

The physician must also identify conditions in which the therapeutic target or sequencing requires individualization. Orthostatic symptoms, frailty, chronic kidney disease (CKD), coronary disease, heart failure, bradyarrhythmia, pregnancy, and previous drug intolerance may alter the balance between BP reduction and harm. Once true resistance is confirmed, physicians should actively consider secondary hypertension, particularly primary aldosteronism, obstructive sleep apnea, renal parenchymal disease, renovascular hypertension, thyroid disease, and medication-induced hypertension.[1,2] Aldosterone and renin testing should ideally be obtained before spironolactone when primary aldosteronism has not been assessed.[1]

3. Pharmacological Strategy in Canadian Practice

The foundational regimen should be optimized before additional agents are added. Long-acting thiazide-like diuretics such as chlorthalidone or indapamide are often useful when greater or more sustained diuresis is required. Volume and sodium excess are common drivers of apparent resistance, making diuretic selection a central treatment decision.[1,2]

When BP remains above target despite optimized triple therapy, Hypertension Canada suggests adding spironolactone, provided kidney function and serum potassium permit.[1] PATHWAY-2 demonstrated greater BP reduction with spironolactone than with bisoprolol or doxazosin as fourth-line therapy.[3] A practical starting dose is 12.5-25 mg once daily, titrated according to response and tolerability. Potassium and renal function should be reassessed after initiation and dose changes; Hypertension Canada advises potassium reassessment within approximately 2-4 weeks.[1]

CKD requires particular attention. The CLICK trial demonstrated that chlorthalidone can lower ambulatory BP even in stage 4 CKD, although hypokalemia, dizziness, hyperuricemia, and reversible creatinine increases require monitoring.[4] If spironolactone is limited by hyperkalemia, selected patients may benefit from specialist review and, in some circumstances, potassium-lowering strategies, but these should not replace careful laboratory surveillance.[5]

If BP remains uncontrolled after spironolactone, later-line therapy should be individualized according to comorbidity and physiology. Options may include a beta-blocker, alpha-blocker, central alpha2-agonist, hydralazine, or minoxidil. Beta-blockers are especially useful when another indication exists, such as ischemic heart disease, heart failure with reduced ejection fraction, or tachyarrhythmia.

4. Clinical Pharmacist Perspective

Clinical pharmacists are particularly valuable in resistant hypertension because apparent resistance frequently reflects medication-use problems rather than failure of pharmacology. Pharmacist assessment can determine what the patient is actually taking, how doses are timed, whether prescriptions are being refilled, whether adverse effects are driving nonadherence, and whether over-the-counter or prescription products are raising BP.

High-yield pharmacist interventions include medication reconciliation, refill-history review, adherence counselling, simplification to once-daily or single-pill combinations when feasible, identification of NSAIDs, corticosteroids, stimulants, decongestants and other BP-raising agents, optimization of diuretic dosing, and monitoring after ACEI/ARB, diuretic, or mineralocorticoid receptor antagonist changes. Pharmacists can also educate patients on validated home BP technique and help distinguish persistent hypertension from isolated office elevation.

In a collaborative model, the physician remains responsible for diagnostic synthesis, assessment of secondary hypertension, comorbidity management, and complex treatment decisions, while the clinical pharmacist provides repeated medication-focused surveillance between physician encounters. This division of work is particularly useful in Canadian primary care and hospital transitions, where continuity and timely laboratory follow-up may determine whether an evidence-based regimen is sustained safely.

5. Hospitalized Patients: Avoid Treating the Number Alone

Markedly elevated BP during hospitalization should not automatically be interpreted as resistant hypertension. Pain, anxiety, sleep disruption, urinary retention, hypoxemia, missed home medication, corticosteroids, intravenous fluids, withdrawal, and acute kidney injury can all produce transient elevations. The first question is whether there is new or worsening target-organ injury.[6]

Hypertensive emergency requires controlled BP reduction with intravenous therapy in a monitored setting. In contrast, severe asymptomatic inpatient hypertension generally calls for repeat measurement, correction of reversible triggers, review of volume status and omitted medications, and cautious restoration of appropriate long-acting oral therapy rather than reflexive PRN intravenous hydralazine or labetalol.[6]

Here physician-pharmacist collaboration is particularly useful. Physicians determine whether acute target-organ injury or another urgent diagnosis is present. Clinical pharmacists can identify interrupted chronic therapy, duplication, interacting agents, inappropriate short-acting medications, and monitoring requirements. Before discharge, the team should reconcile the chronic regimen with Canadian outpatient recommendations and arrange timely follow-up with primary care, pharmacy, or a hypertension specialist.

6. A Practical Collaborative Canadian Approach

A concise approach to suspected resistant hypertension is:

- Confirm standardized BP measurement and out-of-office hypertension.
- Assess adherence and the actual medication regimen.
- Remove or reduce medications and substances that increase BP when possible.
- Screen for secondary causes, especially primary aldosteronism, obstructive sleep apnea, CKD, and renovascular disease.
- Optimize ACEI/ARB + thiazide/thiazide-like diuretic + long-acting dihydropyridine calcium-channel blocker.
- Add spironolactone when appropriate and monitor potassium and kidney function.
- Individualize later-line therapy and refer confirmed refractory or complex cases.
- Use physicians and clinical pharmacists collaboratively for diagnosis, medication optimization, monitoring, education, and continuity.

7. Conclusion

Resistant hypertension in Canada should be diagnosed only after standardized BP measurement, confirmation of adherence and out-of-office hypertension, and optimization of the Hypertension Canada-recommended three-drug regimen. Spironolactone is the preferred evidence-supported fourth-line therapy when renal function and potassium permit, while CKD and secondary hypertension require individualized evaluation.[1-4]

The physician perspective is essential for diagnostic accuracy, assessment of secondary causes, individualized risk-benefit decisions, and recognition of hypertensive emergencies. The clinical pharmacist perspective strengthens treatment by identifying adherence barriers, optimizing medication use, monitoring safety, educating patients, and improving transitions of care. Combining both perspectives provides a practical Canadian model for improving BP control while minimizing polypharmacy, adverse effects, and inappropriate treatment of transient inpatient BP elevations.

Declarations

Ethics Approval and Consent to Participate

Not applicable. This study did not involve human participants, animal experimentation, or confidential patient clinical data.

Consent for Publication

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Conflicts of Interest

The authors declare that they have no competing financial or non-financial interests.

Data Availability

Data sharing is not applicable to this article as no new datasets were generated or analyzed during the current study.

Author Contributions

All authors contributed equally to the conceptualization, study design, methodology, literature search, data collection, analysis, interpretation of findings, manuscript drafting, critical revision, and final approval of the manuscript. The authors accept full responsibility for the accuracy and integrity of the work.

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