

Thiazide-Induced Hyponatremia Presenting as a Fall in an Older Adult

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Background: Regardless of age, first-line therapy for uncomplicated hypertension includes thiazide diuretics, long-acting calcium channel blockers, and renin-angiotensin system inhibitors. Even though older adults are often at increased risk of adverse drug events, specific guidelines for choosing between different classes of antihypertensives are lacking. Given the prevalence of hypertension in older adults, clinicians should be aware of the increased risk of electrolyte disorders after the initiation of thiazide diuretics in this population.

Case Presentation: A patient aged > 90 years fell getting out of his bed 2 weeks following initiation of hydrochlorothiazide

25 mg daily medication therapy. Laboratory tests revealed a urine sodium of 35 mmol/L most consistent with hypovolemic hyponatremia secondary to thiazide initiation. Hydrochlorothiazide was discontinued and sodium gradually normalized over the next 2 weeks without any other intervention.

Conclusions: Despite being recommended as first-line therapy for uncomplicated hypertension, thiazide diuretics may cause more harm than good in older adults with risk factors for thiazide-induced hyponatremia, which should be considered before initiation.

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Hypertension is a major risk factor for heart disease, stroke, and kidney disease. The prevalence of hypertension increases with age, primarily due to age-related changes in arterial physiology.¹ For older adults, current guidelines regarding blood pressure (BP) treatment goals vary. The American Heart Association/American College of Cardiology 2017 clinical practice guidelines recommend a systolic BP (SBP) treatment goal of < 130 mm Hg for community-dwelling, ambulatory, noninstitutionalized adults aged ≥ 65 years; whereas the American College of Physicians/American Academy of Family Physicians recommend a goal of < 150 mm Hg for those aged ≥ 60 years without comorbidities and < 140 mm Hg for those with increased cardiovascular risk.¹⁻³ Regardless of the specific threshold, agreement that some degree of BP control even in those with advanced age improves outcomes.²

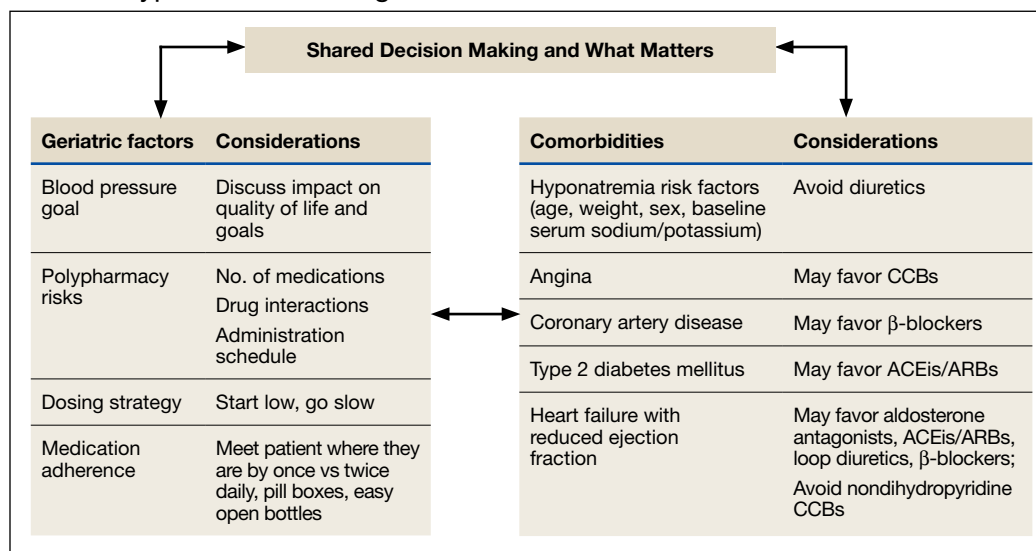
First-line therapy for uncomplicated hypertension includes thiazide diuretics, long-acting calcium channel blockers, and renin-angiotensin system inhibitors. When choosing between these options, it is recommended to engage in shared decision making and to consider the patient's comorbidities. Among patients who are likely to require a second agent (eg, if initial BP is > 20/10 mm Hg above goal), it is recommended to begin both drugs at the same time, preferably benazepril plus amlodipine due to the reduction in cardiovascular events reported in

the ACCOMPLISH trial.⁴ If BP remains elevated despite 2 agents at moderate to maximum doses, it is important to investigate for secondary hypertension causes and to explore medication adherence as possible etiologies of treatment failure. Older adults are often at higher risk of adverse drug events due to age-related changes in pharmacodynamics. Despite this, there are no guidelines for choosing between different classes of antihypertensives in this population. We present a case of thiazide-induced hyponatremia in an older adult and review the risks of thiazide use in this population.

CASE PRESENTATION

A man aged > 90 years was admitted to the hospital after a syncopal episode. His history was significant for hypertension, hyperlipidemia, and vitamin D deficiency. At the time, his home medications were amlodipine 5 mg daily, atorvastatin 40 mg daily, ergocalciferol 50,000 IU weekly, and polyethylene glycol 17 g daily as needed. His syncope workup was unremarkable and included negative orthostatic vital signs, normal serial troponins, an electrocardiogram without ischemic changes, normal serum creatinine, sodium, and glucose, and a head computed tomography without any acute abnormality. Throughout the patient's hospital stay, he had multiple elevated SBP readings, including many > 200 mm Hg. On discharge, in addition to continuing his home medica-

FIGURE Hypertension Management Considerations in Older Adults



Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blocker.

tions, he was started on valsartan 20 mg daily and enrolled in a remote BP monitoring program.

Three weeks later, the patient was seen by their primary care practitioner for follow-up. He reported adherence to his antihypertensive regimen. However, his remote BP monitoring revealed persistently elevated BPs, with an average of 179/79 mm Hg, a high of 205/85 mm Hg, and a low of 150/67 mm Hg over the previous 7 days. Laboratory tests obtained at the visit were notable for serum sodium of 138 mmol/L and potassium of 4.1 mmol/L. His weight was 87 kg. Given persistently elevated BP readings, in addition to continuing his amlodipine 5 mg daily and valsartan 20 mg daily, he was started on hydrochlorothiazide 25 mg daily, with plans to repeat a basic metabolic panel in 2 weeks.

Two weeks later, he fell after getting out of his bed. On examination, he was noted to have dry mucous membranes, and although no formal delirium screening was performed, he was able to repeat the months of the year backward. Vital signs were notable for positive postural hypertension, and his laboratory tests revealed a normal serum creatinine, serum sodium of 117 mmol/L (reference range, 135-145 mmol/L), serum potassium of 3.2 mmol/L (reference range, 3.0-5.0 mmol/L), a low serum osmolality, and urine sodium of 35 mmol/L most consistent with hypovolemic hyposmotic hypona-

tremia secondary to thiazide initiation. The patient's hydrochlorothiazide was discontinued, and he was admitted to the hospital for close monitoring. His sodium levels gradually normalized over the next 2 weeks without any other intervention.

DISCUSSION

Although thiazide diuretics are recommended as first-line therapy for uncomplicated hypertension, they are known to cause electrolyte abnormalities, including hypomagnesemia, hypokalemia, and hyponatremia.⁴ These metabolic derangements are more likely to occur in older adults. One study of adults aged ≥ 65 years found that at 9 months of follow-up, 14.3% of new thiazide users had developed a thiazide-related metabolic adverse event (hyponatremia < 135 mmol/L, hypokalemia < 3.5 mmol/L, and decrease in estimated glomerular filtration rate by > 25%) compared with 6.0% of nonusers ($P < .001$; number needed to harm [NNH] = 12).⁵ In addition, 3.8% of new thiazide users had an emergency department visit or were hospitalized for complications related to thiazides compared with only 2.0% of nonusers ($P = .02$; NNH = 56).⁵ Independent risk factors for thiazide-induced hyponatremia include high-comorbidity burden, low body weight, low-normal or unmeasured serum sodium, low potassium, and

aged > 70 years.⁵⁻⁷ Each 10-year increment in age is associated with a 2-fold increase in risk, suggesting that older adults are at a much higher risk for hyponatremia than their younger peers.⁶

Despite their designation as a first-line option for uncomplicated hypertension, thiazide diuretics may cause more harm than good in some older adults, especially those with additional risk factors for thiazide-induced hyponatremia. In this population, these adverse effects should be discussed before starting thiazides for the treatment of hypertension. If thiazides are initiated, they should be started at the lowest possible dose, and plans made to monitor bloodwork within 1 to 2 weeks of initiation or dose change and periodically thereafter while the patient remains on the therapy.

Medication Management in Older Adults

Due to the risks of medication use in older adults, the phrase “start low, go slow” is commonly used in geriatric medicine to describe the optimal method for initiation and up-titration of new medication with the hope of mitigating adverse drug events. In our case, we started valsartan at 20 mg daily—one-fourth the recommended initial dose. Although this strategy is reasonable to “start low,” we were not surprised to find that the patient’s BP did not markedly improve on such a low dose. The team could have increased the valsartan dose to a therapeutically efficacious dose before choosing to add another hypertensive agent. In alignment with geriatric prescribing principles, starting at the lowest possible dose of hydrochlorothiazide is recommended.⁵ However, the clinician started hydrochlorothiazide at 25 mg daily, potentially increasing this patient’s risk of electrolyte abnormalities and eventual fall.

Managing hypertension also invites a discussion of polypharmacy and medication adherence. Older adults are at risk of polypharmacy, defined as the prescription of 5 or more medications.⁸ Polypharmacy is associated with increased hospitalizations, higher costs of care for individuals and health care systems, increased risks of adverse drug events, medication nonadherence, and lower quality of life for patients.⁹ In some situations, the risks of polypharmacy may

outweigh the benefits of using multiple antihypertensives with different mechanisms of action if patients can reach their BP goal on the maximum dose of a single agent. For patients taking multiple antihypertensives, it is important to routinely monitor BP and assess whether deprescribing is indicated. Cognitive impairment and decreased social support may affect medication adherence for older adults.⁶ Clinicians should be aware of strategies, such as medication reminders and pillboxes, to increase antihypertensive medication adherence. Polypills that contain 2 antihypertensives can be another tool used to manage older adults to increase adherence and decrease health care costs.¹⁰

A current strategy that encompasses discussing many, if not all, of these noted elements is the Institute for Healthcare Improvement’s Age-Friendly Health System. This framework uses evidence-based tools to provide care for older adults across all clinical settings and highlights the 4Ms: what matters, medication, mentation, and mobility.¹¹ Medication considers whether a medication is necessary, whether its use has benefits that outweigh the risks, and how it interacts with what matters, mentation, and mobility. In particular, what matters plays an important role in hypertension management in older adults given the recommended target BP differs, depending on which specialty organization guideline is followed. By better understanding what matters to patients, including their goals and priorities, clinicians can engage patients in shared decision making and provide individualized recommendations based on geriatric principles (eg, start low, go slow, principles of medication adherence) and patient comorbidities (eg, medical history and risk factors for hyponatremia) to help patients make a more informed choice about their antihypertensive treatment regimen (Figure).

CONCLUSIONS

This case illustrates the need for a specialized approach to hypertension management in older adults and the risks of thiazide diuretics in this population. Clinicians should consider BP goals, patient-specific factors, and principles of medication management in older adults. If initiating thiazide therapy, discuss the risks associated with use, start at the lowest possible dose, and monitor bloodwork

within 1 to 2 weeks of initiation/dose change and periodically thereafter while the patient remains on the therapy to decrease the risk of adverse events. Finally, the Institute for Healthcare Improvement's Age-Friendly Health System framework can be a useful when considering the addition of a new medication in an older adult's treatment plan.

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Ethics and consent

This manuscript has been reviewed by the Veterans Affairs Boston Privacy Office prior to submission. We have received written consent and release of information from this veteran to use details of their case for this manuscript.

References

- Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2018;71(19):e127-e248. doi:10.1016/j.jacc.2017.11.006
- Davis LL. Hypertension: how low to go when treating older adults. *J Nurse Pract*. 2019;15(1):1-6. doi:10.1016/j.nurpra.2018.10.010
- Qaseem A, Wilt TJ, Rich R, et al. Pharmacologic Treatment of Hypertension in Adults Aged 60 Years or Older to Higher Versus Lower Blood Pressure Targets: A Clinical Practice Guideline From the American College of Physicians and the American Academy of Family Physicians. *Ann Intern Med*. 2017;166(6):430-437. doi:10.7326/M16-1785
- Aronow WS, Fleg JL, Pepine CJ, et al. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus documents developed in collaboration with the American Academy of Neurology, American Geriatrics Society, American Society for Preventive Cardiology, American Society of Hypertension, American Society of Nephrology, Association of Black Cardiologists, and European Society of Hypertension. *J Am Coll Cardiol*. 2011;57(20):2037-2114. doi:10.1016/j.jacc.2011.01.008
- Makam AN, Boscardin WJ, Miao Y, Steinman MA. Risk of thiazide-induced metabolic adverse events in older adults. *J Am Geriatr Soc*. 2014;62(6):1039-1045. doi:10.1111/jgs.12839
- Chow KM, Szeto CC, Wong TY, Leung CB, Li PK. Risk factors for thiazide-induced hyponatremia. *QJM*. 2003;96(12):911-917. doi:10.1093/qjmed/hcg157
- Clayton JA, Rodgers S, Blakey J, Avery A, Hall IP. Thiazide diuretic prescription and electrolyte abnormalities in primary care. *Br J Clin Pharmacol*. 2006;61(1):87-95. doi:10.1111/j.1365-2125.2005.02531.x
- Shah BM, Hajjar ER. Polypharmacy, adverse drug reactions, and geriatric syndromes. *Clin Geriatr Med*. 2012;28(2):173-186. doi:10.1016/j.cger.2012.01.002
- Benetos A, Petrovic M, Strandberg T. Hypertension management in older and frail older patients. *Circ Res*. 2019;124(7):1045-1060. doi:10.1161/CIRCRESAHA.118.313236
- Sherrill B, Halpern M, Khan S, Zhang J, Panjabi S. Single-pill vs free-equivalent combination therapies for hypertension: a meta-analysis of health care costs and adherence. *J Clin Hypertens (Greenwich)*. 2011;13(12):898-909. doi:10.1111/j.1751-7176.2011.00550.x
- Mate K, Fulmer T, Pelton L, et al. Evidence for the 4Ms: interactions and outcomes across the care continuum. *J Aging Health*. 2021;33(7-8):469-481. doi:10.1177/0898264321991658