

The Reply



We thank Prof. Messerli and his co-authors for their letter concerning our recent publication on risks of electrolyte disorders, syncope, and falls in patients taking thiazide (-like) diuretics.¹

By no means did we intend to question the role of thiazides in the treatment of arterial hypertension. In fact, only recently, a small prospective randomized controlled trial confirmed the key role of chlorthalidone, a thiazide-like diuretic, in difficult-to-treat arterial hypertension in patients with chronic kidney disease.² Nevertheless, even current practice guidelines do clearly mention potential unwanted effects of thiazides and thiazide-like diuretics in patients treated for arterial hypertension.³ Thiazide-associated and thiazide-induced electrolyte disorders are well known and a common problem, especially in vulnerable patient populations such as the elderly or postmenopausal women.⁴ Furthermore, there is solid evidence that hyponatremia itself is associated with an increased likelihood of falls, a finding that is even more significant given the fact that hyponatremia induces osteoporosis and increases risk of fracture.⁵ This vicious circle consisting of an increased risk of falls paired with decreased bone mineralization and a higher fracture risk is especially harmful for the elderly patient. Moreover, also, hypokalemia was shown to be independently associated with falls.⁶

We agree that the groups of thiazide and non-thiazide users differed in their baseline characteristics. Still, the increased risk of hyponatremia and hypokalemia was not only significantly more common in the group of thiazide users—even in the multivariate model correcting for various cofactors—but it was also clearly dose dependent. This finding implies causality and not a pure association.

In the above-mentioned study on chlorthalidone in patients with chronic kidney disease and difficult-to-treat

hypertension, a total of (only) 160 patients were randomized, and a weight loss of -1.2kg was reported in the chlorthalidone group.² Furthermore, dizziness was significantly more common and orthostatic hypotension was reported in 10% of patients in the chlorthalidone group.²

All of the evidence listed suggests that thiazide (-like) diuretics clearly have the potential for unwanted side effects, ranging from the induction of electrolyte disorders to an increased likelihood of falls and associated complications. Thus, our conclusion that “a more careful approach to prescribing thiazides in the older adult seems wise” appears to be justified and valid.

Gregor Lindner, MD
Svenja Ravioli, MD

Department of Internal and Emergency Medicine, Buegerspital Solothurn, Solothurn, Switzerland

<https://doi.org/10.1016/j.amjmed.2022.01.027>

References

1. Ravioli S, Bahmad S, Funk GC, Schwarz C, Exadaktylos A, Lindner G. Risk of electrolyte disorders, syncope, and falls in patients taking thiazide diuretics: results of a cross-sectional study. *Am J Med* 2021;134(9):1148–54.
2. Agarwal R, Sinha AD, Cramer AE, et al. Chlorthalidone for hypertension in advanced chronic kidney disease. *N Engl J Med* 2021;385(27):2507–19.
3. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J* 2018;39(33):3021–104.
4. Filippone EJ, Ruzieh M, Foy A. Thiazide-associated hyponatremia: clinical manifestations and pathophysiology. *Am J Kidney Dis* 2020;75(2):256–64.
5. Corona G, Norello D, Parenti G, Sforza A, Maggi M, Peri A. Hyponatremia, falls and bone fractures: a systematic review and meta-analysis. *Clin Endocrinol (Oxf)* 2018;89(4):505–13.
6. Tachi T, Yokoi T, Goto C, et al. Hyponatremia and hypokalemia as risk factors for falls. *Eur J Clin Nutr* 2015;69(2):205–10.

Funding: None.

Conflicts of Interest: None of the authors has a conflict of interest.

Authorship: All authors had access to the data and a role in writing the manuscript.

Requests for reprints should be addressed to Gregor Lindner, MD, Department of Internal and Emergency Medicine, Buegerspital Solothurn, 4500 Solothurn, Switzerland.

E-mail address: lindner.gregor@gmail.com