

5. Evens AM, Sweetenham JW, Horning SJ. Hodgkin lymphoma in older patients: An uncommon disease in need of study. *Oncology* (Williston Park) 2008;22:1369–1379.

COMMENTS/RESPONSES

ANALYSIS OF GAIT SPEED AND VITAMIN D DEFICIENCY

To the Editor: With great interest, I read the article, “C-Reactive Protein, Vitamin D Deficiency, and Slow Gait Speed,” by Kositsawat, Barry, and Kuchel, in which the effect of vitamin D (25(OH)D) levels and those of C-reactive protein (CRP) on gait speed of people aged 50 and older was studied. The study found that low levels of 25(OH)D and high levels of CRP had an outcome of gait speeds less than 0.8 m/s. This suggests “that evaluation and correction of vitamin D levels may be especially important in individuals with high CRP levels.”¹ I found this fascinating because, as a future physical therapy professional with a concentration in geriatrics, one of my future duties will be increasing gait speeds of elderly adults recuperating from falls and surgeries. This information is significantly relevant within the healthcare community.

With increased use of evidence-based practice, it is important for clinicians to be current with the latest research in all areas of health care. Physical therapists who encourage adequate vitamin D intake can expect to see greater improvement with their treatments with regard to gait speed. Raising vitamin D levels to recommended concentrations may lead to an associated increase in an individual’s trabecular bone strength, skeletal musculature, and gait speed.

Studies have found that limitations on mobility are more likely to occur with inadequate vitamin D levels. Individuals who had 25(OH)D in concentrations lower than 75 nmol/L had an approximately 30% greater risk of developing limitations in mobility later in life, although individuals who had blood concentrations of vitamin D of less than 50 nmol/L were two times as likely as those with ample levels to develop limitations on mobility.² By increasing intake of 25(OH)D, an individual’s limitations may be reduced.

Vitamin D levels have also been proven to have positive effects with regard to confidence in completing specific physical tasks. A study conducted in Amsterdam used 20 ng/mL as a cutoff for vitamin D concentrations in the blood. Participants were asked to answer questions related to activities of daily living. Those with levels below the cutoff were significantly more likely to report a limitation in at least one task than those with levels above the cutoff.³ Studies have also shown that adequate levels of 25(OH)D can contribute to maintenance of muscle strength in proximal areas of all extremities, which provides individuals with the confidence to perform activities of daily living. Clinicians can use this information to improve the overall health of their patients and to achieve better treatment outcomes.

Limitations of this study include a small variation in testing methods. The only method used for measurement was a physical examination of the participant being timed walking 20 feet. Other possible tests could include the

Timed Up and Go (TUG) test, which would test the individual’s ability to stand up and walk, or the 6-minute walk test, which tests endurance. Another possible limitation could be the use of canes or walkers during the examination. Walkers and canes could hinder the observation of the potential benefits of adequate vitamin D in the diet by allowing the individual to rely on these devices for strength and stability.

This research study could be expanded to determine which of the two important forms of vitamin D (ergocalciferol (vitamin D₂) or cholecalciferol (vitamin D₃)) has a stronger effect along with CRP on gait speeds. Future research could also include studies on the effects of other vitamins or micro- and macronutrients with regard to gait speed.

This article provided information about how I could improve my future patients’ treatments. It inspired me to look more closely at different areas of health care because many aspects play a critical role in the healing process. Along with observing the effects of physical treatment, clinicians need to be able to look past the mechanical approach and take into account the nutritional effects on one’s performance.

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ACKNOWLEDGMENTS

Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the author and has determined that the author has no financial or any other kind of personal conflicts with this paper.

Author Contributions: I am the sole author of this article.

Sponsor’s Role: None.

REFERENCES

1. Kositsawat J, Barry L, Kuchel G.C-reactive protein, vitamin d deficiency, and slow gait speed. *J Am Geriatr Soc* 2013;61:1574–1579.
2. Houston DK, Neiberg RH, Toozé JA et al. Low 25-hydroxyvitamin D predicts the onset of mobility limitation and disability in community-dwelling older adults: The Health ABC Study. *J Gerontol A Biol Sci Med Sci* 2013;68A:181–187.
3. Are you getting enough vitamin D to prevent disability? *Tufts Univ Health Nutr Lett* 2013;31:3.

RISK OF PROTON PUMP INHIBITOR-INDUCED MILD HYPONATREMIA IN OLDER ADULTS

To the Editor: I read the article by Buon et al.,¹ “Risk of Proton Pump Inhibitor-Induced Mild Hyponatremia in Older Adults,” with interest.

They reported that 24 of 145 included individuals (16.6%) had moderate hyponatremia, and 48 (33.1%) had been taking proton pump inhibitors (PPIs) for longer than 1 year, 31.3% of whom (95% confidence interval (CI) = 18.7–46.3%) had moderate hyponatremia, versus

9.3% (95% CI = 14.3–16.9%) in the rest of the population (odds ratio (OR) = 4.4, 95% CI = 1.8–11.1, $P = .001$). Individuals taking PPIs and tramadol had a significantly higher risk of hyponatremia than those taking neither (OR = 7.7, 95% CI = 1.9–31.2).¹

They concluded that the association between PPIs and tramadol appears to potentiate the risk of hyponatremia, but when the table in the article was analyzed, the use of two more drugs—namely first-generation neuroleptics ($P = .01$) and corticosteroids ($P = .004$) with PPIs—was also associated with higher risk of hyponatremia, even more significantly than use of tramadol and PPIs ($P = .04$). The authors should have analyzed the association between tramadol and PPI use and hyponatremia using a multivariate regression analysis including use of corticosteroids plus PPIs and first-generation neuroleptics plus PPIs as independent variables to find whether the association between tramadol plus PPIs and hyponatremia would remain significant after excluding the hyponatremic effects of corticosteroids plus PPIs and first-generation neuroleptics plus PPIs. The table clearly demonstrates that all three individuals undergoing corticosteroid therapy were also taking PPIs.¹ The hyponatremia might have been related to use of corticosteroids rather than use of PPIs. The hyperglycemic effects of corticosteroids are well known, and physiological calculations suggest that the serum sodium concentration should fall by 1.6 meq/L for every 100-mg/dL (5.5 mmol/L) rise in serum glucose concentration,² although antipsychotic drugs are also a well-known cause of hyponatremia.³ With their published analysis limited with univariate associations, it cannot be concluded that the association between PPIs and tramadol appears to potentiate the risk of hyponatremia.

The authors also concluded that their study demonstrates that the chronic use of PPIs increases the risk of hyponatremia in older adults. The authors should also have analyzed the association between PPI use and hyponatremia using a multivariate regression analysis to determine whether the association between PPI and hyponatremia would remain significant after excluding the hyponatremic effects of corticosteroids. What would have been better would have been if they had made this adjustment using multivariate regression analysis including all drugs with known hyponatremia side effects. Their study should be evaluated in light of this limitation.

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ACKNOWLEDGMENTS

Conflict of Interest: None.

Author Contribution: All work was performed by Gulistan Bahat.

Sponsor's Role: No sponsor.

REFERENCES

1. Buon M, Gaillard C, Martin J et al. Risk of proton pump inhibitor-induced mild hyponatremia in older adults. *J Am Geriatr Soc* 2013;61:2052–2054.

2. Katz MA. Hyperglycemia-induced hyponatremia—calculation of expected serum sodium depression. *N Engl J Med* 1973;289:843.
3. Meulendijks D, Mannesse CK, Jansen PA et al. Antipsychotic-induced hyponatremia: A systematic review of the published evidence. *Drug Saf* 2010;33:101–114.

RESPONSE TO BAHAT

To the Editor: According to the letter of Bahat,¹ we should have analyzed the association between the use of tramadol and PPI and hyponatremia using multivariate regression analysis.²

Five risks factors with $P < .25$ were entered into a forward multivariate logistic regression model with maximum likelihood estimation. Before the multivariate analysis, it was verified that none of the five drugs used in the univariate analysis were correlated.

Only proton pump inhibitors (PPIs) remained as a risk factor using a forward logistic model (odds ratio (OR) = 4.44, 95% confidence interval (CI) = 1.77–11.13, $P = .001$).

To assess the effect of synergy, a backward logistic regression model was used to identify the drugs that could potentiate the effect of PPIs. This analysis showed $P = .06$ for kaliuretic diuretic and $P = .08$ for tramadol. Therefore, it was decided to assess the potentiating effect of kaliuretic diuretic and tramadol with PPIs by testing the association between PPIs and kaliuretic diuretics in a univariate logistic model and the association between PPIs and tramadol. This second analysis is similar to testing in a univariate logistic regression the effect of taking a PPI plus tramadol or a PPI plus a kaliuretic diuretic on hyponatremia, versus another scheme of treatment for the sample tested. The univariate logistic regression showed that taking a PPI plus tramadol was a risk factor for hyponatremia (OR = 7.70, 95% CI = 1.90–31.25, $P = .004$). Univariate logistic regression showed that taking a PPI plus a kaliuretic diuretic was not a risk factor for hyponatremia because the association was not significant (OR = 2.85, 95% CI = 0.78–10.27, $P = .11$).

Knowing that, the real effect of the synergy had to be assessed by comparing the risk of hyponatremia in two groups (PPI plus tramadol ($n = 9$) vs PPI alone ($n = 39$)). This analysis showed that there was no greater risk of hyponatremia when tramadol was taken in addition to PPI (OR = 3.62, 95% CI = 0.81–16.22, $P = .09$).

The univariate and multivariate logistic regression models were not the first statistical analyses used because of low enrollment for certain risk factors such as corticosteroids. The use of the Fisher exact test was preferable because a multivariate model would need at most two covariates to explain hyponatremia because there were only 24 cases. By taking into account risk factors present in the sample, PPI remains a risk factor for hyponatremia in elderly adults.

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