

Prevalence of thiamine deficiency in older hospitalized patients

Maryam Pourhassan¹
Hans Konrad Biesalski²
Bjoern Angersbach¹
Gero Lueg¹
Christiane Klimek¹
Rainer Wirth¹

¹Department of Geriatric Medicine, Marien Hospital Herne, Ruhr-University Bochum, Herne, Germany; ²Institute of Biological Chemistry and Nutritional Science, University of Hohenheim, Stuttgart, Germany

Purpose: Despite some reports of high prevalence of thiamine deficiency in elderly people, the reported prevalence is controversial mainly due to the methods used in assessing thiamin concentrations. In this study, we sought to investigate the prevalence of vitamin B1 deficiency, using the high-performance liquid chromatography (HPLC) method, among older hospitalized patients.

Patients and methods: This cross-sectional study retrospectively analyzed the results of routine measurements of vitamin B1 of 238 older patients who were consecutively hospitalized to a geriatric acute care ward. Whole blood vitamin B1 concentrations were measured using the HPLC method at hospital admission, and the whole blood vitamin B1 level of <20 ng/mL was considered as deficiency.

Results: Of 238 patients, with a mean age of 82.1±7.1 years, 63% of patients were women. In total, the mean whole blood vitamin B1 level was 66.1±24.8 ng/mL (range 29.5–215 ng/mL), indicating no vitamin B1 deficiency in the entire population. In addition, no significant differences in the mean whole blood vitamin B1 concentrations between sexes were observed ($P=0.356$).

Conclusion: This study indicates that the mean whole blood vitamin B1 concentrations using the HPLC method were within the normal range in older hospitalized patients suggesting that thiamine deficiency appears to be rather uncommon among these patients.

Keywords: vitamin B1, thiamine deficiency, older people

Introduction

Thiamine (vitamin B1), a water-soluble vitamin, is a fundamental coenzyme in macronutrient oxidation and transketolase reaction.^{1,2} Human body storage of thiamine is relatively small (25–30 mg); therefore, the requirement (1.0–1.2 mg/day) should be regularly provided by ingestion through diet.^{1–3} The main manifestations of vitamin B1 deficiency in human beings comprise Wernicke's encephalopathy, peripheral edema (wet beriberi), peripheral neuropathy (dry beriberi) and heart failure.^{2,4} In addition, a review of previous literature indicates that thiamine deficiency has been usually found in alcoholics^{2,5} and in patients with renal failure,⁶ with chronic use of diuretics,^{7,8} with dietary imbalance (ie, high carbohydrate intake)⁹ and with a history of gastric bypass surgery¹⁰ or gastrectomy¹¹ which results in inadequate thiamine absorption. In addition, older individuals are also prone for developing thiamine deficiency due to nutritional difficulties and many underlying comorbidities.¹² A previous systematic review and meta-analysis of micronutrient intake in community-dwelling older adults¹³ showed thiamine inadequacy in food intake of older individuals. The inadequacy might also depend on several factors such as absorption and utilization, vitamin supplementation, method used to assess dietary thiamine intake and use of reference values. In addition, despite some reports of high prevalence of thiamine deficiency in elderly people,^{12,14,15}

Correspondence: Maryam Pourhassan
Department of Geriatric Medicine,
Marien Hospital Herne, Ruhr-University
Bochum, Hölkeskampring 40, D-44625
Herne, Germany
Email mpourhassan1918@gmail.com

the reported prevalence is controversial mainly due to the methods used in assessing thiamin concentrations.

The erythrocyte transketolase activity (ETKA) assay is a traditional and most widely used method in determining vitamin B1 deficiency which measures the changes in transketolase activity by adding thiamine pyrophosphate (TPP) known as TPP effect.^{16,17} Unfortunately, this indirect way of assessing nutritional status of thiamine is not a very reliable method since various factors, other than the level of TPP, may impact the activity of erythrocyte transketolase. Some of these influencing factors include a fall in transketolase activity, lower level of transketolase activity with advancing age, variation in the interpretation of ETKA due to poor inter-assay precision and difficulty in standardization.^{14,18,19} Therefore, the direct measurement of thiamine status in red blood cells or whole blood by using high-performance liquid chromatography (HPLC)²⁰ may be precise, rapid and less susceptible to factors that alter enzyme activity and a more sensitive assay in screening the thiamine deficiency in clinical practice and for research purposes.^{21,22} Accordingly, in this study, we sought to investigate the prevalence of vitamin B1 deficiency, using the HPLC method, among older hospitalized patients.

Patients and methods

This cross-sectional study retrospectively analyzed the results of routine measurements of vitamin B1 of 238 older patients who were consecutively hospitalized between January 2018 and May 2018 to geriatric acute care ward at Marien Hospital, Herne, Germany. Whole blood vitamin B1 concentrations were obtained from the local laboratory database. The measurements were performed at hospital admission with the HPLC-based method from whole blood vitamin B1 with the reference range of normality as 20–100 ng/mL^{23,24} according to our local laboratory, and the whole blood vitamin B1 level of <20 ng/mL (=59.30 nmol/L) was considered as deficiency. According to previous older patients admitted to geriatric acute care ward at hospital,^{25,26} the participants of the current study represented a population of frail older hospitalized patients. Patient data were managed with confidentiality according to the Declaration of Helsinki, and the study was approved by the ethics committee of Ruhr-University Bochum (ethic number: 18-6335-BR). The participant consent is not applicable due to the retrospective methodology.

Statistical analyses

The statistical analyses were performed with SPSS statistical software (SPSS Statistics for Windows, version 23.0; IBM Corporation, Armonk, NY, USA). Results are reported as mean and SD. Comparison between females and males was

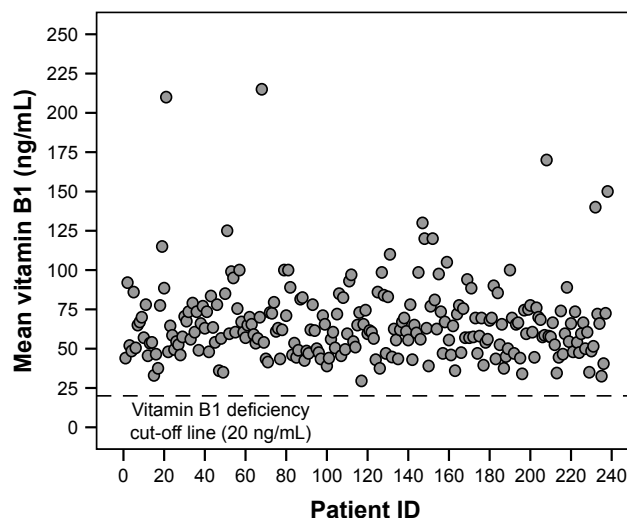


Figure 1 Distribution of vitamin B1 concentrations among total population (n=238).

performed using the unpaired *t*-test for continuous data with normal distribution. A *P*-value of <0.05 was considered as the limit of significance.

Results

Of 238 patients, with a mean age of 82.1 ± 7.1 years (age range between 60 and 100 years), 63% of patients were women and 37% of patients were men. In total, the mean whole blood vitamin B1 level was 66.1 ± 24.8 ng/mL (range 29.5–215 ng/mL), indicating no vitamin B1 deficiency in the entire population (Figure 1). In addition, no significant differences in the mean whole blood vitamin B1 concentrations between sexes were observed (64.2 ± 2.4 ng/mL in males vs 67.2 ± 2.1 ng/mL in females, $P=0.356$). Furthermore, there was no evidence of taking thiamin-containing supplements in the form of multivitamins in the study population, although this could not be individually excluded.

Discussion

The findings of the current study confirm that the mean whole blood vitamin B1 concentrations using the HPLC method were within the normal range in older hospitalized patients suggesting that thiamine deficiency appears to be rather uncommon in this population. However, our results are not consistent with previous reports of thiamine deficiency in the elderly population. In the study of 75 geriatric nursing home patients admitted to an emergency department, Lee et al¹² indicated that, by using HPLC and a very high cut-off values of 10 µg/dL (=100 ng/mL), 14% were thiamine deficient. By measuring ETKA, thiamin deficiency has also been demonstrated to be common in 17 out of 36 consecutive non-demented, community-dwelling elderly patients admitted to hospital in which 76% of thiamine-deficient patients developed delirium.²⁷ In another

study of a large group of older individuals from New Zealand, by using HPLC, 43% of the elderly subjects indicated TPP concentrations below the fifth percentile of the younger subjects (140 nmol/L = 47 ng/mL) and these differences were irrelevant to common illness and medications, body mass index (BMI) and grip strength.¹⁵ In addition, the mean TPP levels of the elderly subjects in that study were lower compared to our study population (152 nmol/L [=51 ng/mL] vs 66.1 ng/mL, respectively). Nonetheless, our results are in line with the recent study of 475 older patients (mean age: 80±7 years) admitted to the geriatric outpatient department showing that only few patients (n=20; 5%) were found to be deficient in thiamine status based on the cutoff values of <90 nmol/L (≤30 ng/mL).²⁸

Low vitamin B1 concentration has been found in many populations of older people in different countries, although the reported prevalence differs between the studies. The discrepancy might be as a result of different cutoff values used to define thiamine deficiency and methods performed in assessing thiamin concentrations. In the study of hospitalized patients with congestive heart failure¹ and other studies in elderly people,^{15,28,29} using HPLC method, thiamine deficiency was defined as an erythrocyte TPP of <78 ng/mL¹, <47 ng/mL (=140 nmol/L)^{15,29} and <90 nmol/L (≤30 ng/mL),²⁸ which was not comparable to our cutoff values. By using our reference value (<20 ng/mL) and HPLC method, no evidence of vitamin B1 deficiency in older hospitalized patients was observed. However, it is worth mentioning that whole blood thiamine concentrations might not sufficiently reflect thiamine deficiency. A recent cross-sectional study of older adults (aged 55–85 years) demonstrated that despite the normal to high thiamine blood levels of all study participants, insufficient metabolism of thiamine could result in an effective thiamine metabolite deficiency in the target tissue (ie, brain).³⁰

Furthermore, there is no consensus concerning the best method to be used in evaluating thiamine status. Due to the limitation of indirect assessment of ETKA,^{14,18,19} the direct measurement of thiamine concentrations in red blood cells or whole blood has been suggested in several previous studies.^{19,21,31} Indeed, the determination of erythrocyte TPP concentrations by using the HPLC method, as used in the current study, is considered to be more precise, reliable and sensitive index of thiamine levels compared to ETKA.^{19,21,31} Accordingly, lower reference limits used for concentrations of vitamin B1 in the current study compared to the aforementioned studies^{1,12,14,15,28} and using the high-sensitivity HPLC method may explain our findings.

Some limitations of this study bear mention. Because of the retrospective design, we did not estimate usual thiamin intake in our study population. Although, the data regarding

no evidence of taking thiamin-containing supplements were derived from the patients' medical records, it cannot be excluded that some subjects had previous vitamin B1 supplementation without respective information in the record. Since, there is a large difference in the prevalence of vitamin B1 deficiency based on the cutoff values used in the literature, it is difficult to ascertain the relevant cutoff values of low thiamine. Consequently, more research data are needed to determine clinically significant cutoff point of vitamin B1 deficiency.

Conclusion

This study indicates that the mean whole blood vitamin B1 concentrations using the HPLC method were within the normal range in older hospitalized patients suggesting that thiamine deficiency appears to be rather uncommon among these patients.

Acknowledgement

The study received no financial support.

Author contributions

The study was designed by all the authors. Data were obtained by RW. Statistical analysis was performed by MP. MP, HKB and RW prepared the manuscript. All authors contributed toward data analysis, drafting and revising the paper and agree to be accountable for all aspects of the work. All the authors read and approved the final manuscript.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Hanninen SA, Darling PB, Sole MJ, Barr A, Keith ME. The prevalence of thiamin deficiency in hospitalized patients with congestive heart failure. *J Am Coll Cardiol*. 2006;47(2):354–361.
2. O'Keeffe ST. Thiamine deficiency in elderly people. *Age Ageing*. 2000; 29(2):99–101.
3. Jain A, Mehta R, Al-Ani M, Hill JA, Winchester DE. Determining the Role of Thiamine Deficiency in Systolic Heart Failure: A Meta-Analysis and Systematic Review. *J Card Fail*. 2015;21(12):1000–1007.
4. Hammond N, Wang Y, Dimachkie MM, Barohn RJ. Nutritional neuropathies. *Neurol Clin*. 2013;31(2):477–489.
5. Torvik A, Lindboe CF, Rogde S. Brain lesions in alcoholics. A neuropathological study with clinical correlations. *J Neurol Sci*. 1982;56(2–3): 233–248.
6. Descombes E, Dessibourg CA, Fellay G. Acute encephalopathy due to thiamine deficiency (Wernicke's encephalopathy) in a chronic hemodialyzed patient: a case report. *Clin Nephrol*. 1991;35(4):171–175.
7. Zenuk C, Healey J, Donnelly J, Vaillancourt R, Almalki Y, Smith S. Thiamine deficiency in congestive heart failure patients receiving long term furosemide therapy. *Can J Clin Pharmacol*. 2003;10(4):184–188.
8. Seligmann H, Halkin H, Rauchfleisch S, et al. Thiamine deficiency in patients with congestive heart failure receiving long-term furosemide therapy: a pilot study. *Am J Med*. 1991;91(2):151–155.

9. Koike H, Iijima M, Mori K, et al. Postgastrectomy polyneuropathy with thiamine deficiency is identical to beriberi neuropathy. *Nutrition* (Burbank, Los Angeles County, Calif). 2004;20(11–12):961–966.
10. Worden RW, Allen HM. Wernicke's encephalopathy after gastric bypass that masqueraded as acute psychosis: a case report. *Curr Surg*. 2006;63(2):114–116.
11. Koike H, Misu K, Hattori N, et al. Postgastrectomy polyneuropathy with thiamine deficiency. *J Neurol Neurosurg Psychiatry*. 2001;71(3):357–362.
12. Lee DC, Chu J, Satz W, Silbergleit R. Low plasma thiamine levels in elder patients admitted through the emergency department. *Acad Emerg Med*. 2000;7(10):1156–1159.
13. Ter Borg S, Verlaan S, Hemsworth J, et al. Micronutrient intakes and potential inadequacies of community-dwelling older adults: a systematic review. *Br J Nutr*. 2015;113(8):1195–1206.
14. O'Rourke NP, Bunker VW, Thomas AJ, Finglas PM, Bailey AL, Clayton BE. Thiamine status of healthy and institutionalized elderly subjects: analysis of dietary intake and biochemical indices. *Age Ageing*. 1990;19(5):325–329.
15. Wilkinson TJ, Hanger HC, George PM, Sainsbury R. Is thiamine deficiency in elderly people related to age or co-morbidity? *Age Ageing*. 2000;29(2):111–116.
16. Gibson RS. *Principles of Nutritional Assessment*. Oxford: Oxford University Press; 2005.
17. Shils ME, Shike M. *Modern Nutrition in Health and Disease*. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.
18. Markkanen T, Heikinheimo R, Dahl M. Transketolase activity of red blood cells from infancy to old age. *Acta Haematol*. 1969;42(3):148–153.
19. Talwar D, Davidson H, Cooney J, St JO'Reilly D. Vitamin B(1) status assessed by direct measurement of thiamin pyrophosphate in erythrocytes or whole blood by HPLC: comparison with erythrocyte transketolase activation assay. *Clin Chem*. 2000;46(5):704–710.
20. Lynch PL, Young IS. Determination of thiamine by high-performance liquid chromatography. *J Chromatogr A*. 2000;881(1–2):267–284.
21. Baines M, Davies G. The evaluation of erythrocyte thiamin diphosphate as an indicator of thiamin status in man, and its comparison with erythrocyte transketolase activity measurements. *Ann Clin Biochem*. 1988;25(Pt 6):698–705.
22. Herve C, Beyne P, Delacoux E. Determination of thiamine and its phosphate esters in human erythrocytes by high-performance liquid chromatography with isocratic elution. *J Chromatogr B Biomed Appl*. 1994;653(2):217–220.
23. Lu J, Frank EL. Rapid HPLC measurement of thiamine and its phosphate esters in whole blood. *Clin Chem*. 2008;54(5):901–906.
24. Itokawa Y, Hashizume N, Asano M, et al. Proposed standard for human blood vitamin B1 value using HPLC. The Committee for Vitamin Laboratory Standards, Japan. *Biofactors*. 1999;10(2–3):295–299.
25. Pourhassan M, Cuvelier I, Gehrke I, et al. Risk factors of refeeding syndrome in malnourished older hospitalized patients. *Clin Nutr*. 2018;37(4):1354–1359.
26. Pourhassan M, Wirth R. Seasonal Variation in Vitamin D Status among Frail Older Hospitalized Patients. *J Frailty Aging*. 2018;7(2):95–99.
27. O'Keeffe ST, Tormey WP, Glasgow R, Lavan JN. Thiamine deficiency in hospitalized elderly patients. *Gerontology*. 1994;40(1):18–24.
28. Kurkcu M, Meijer RI, Lonterman S, Muller M, de van der Schueren MAE. The association between nutritional status and frailty characteristics among geriatric outpatients. *Clin Nutr ESPEN*. 2018;23:112–116.
29. Wilkinson TJ, Hanger HC, Elmslie J, George PM, Sainsbury R. The response to treatment of subclinical thiamine deficiency in the elderly. *Am J Clin Nutr*. 1997;66(4):925–928.
30. Jannusch K, Jockwitz C, Bidmon HJ, Moebus S, Amunts K, Caspers S. A Complex Interplay of Vitamin B1 and B6 Metabolism with Cognition, Brain Structure, and Functional Connectivity in Older Adults. *Front Neurosci*. 2017;11:596.
31. Warnock LG, Prudhomme CR, Wagner C. The determination of thiamin pyrophosphate in blood and other tissues, and its correlation with erythrocyte transketolase activity. *J Nutr*. 1978;108(3):421–427.

Clinical Interventions in Aging

Publish your work in this journal

Clinical Interventions in Aging is an international, peer-reviewed journal focusing on evidence-based reports on the value or lack thereof of treatments intended to prevent or delay the onset of maladaptive correlates of aging in human beings. This journal is indexed on PubMed Central, MedLine,

CAS, Scopus and the Elsevier Bibliographic databases. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <http://www.dovepress.com/clinical-interventions-in-aging-journal>

Dovepress