Adv Ther (2010) 27(4): .
DOI 10.1007/s12325-010-0025-6

ORIGINAL RESEARCH

Serum Vitamin D Concentration and Short-Term Mortality among Geriatric Inpatients in Acute Care Settings

Cédric Annweiler · Sophie Pochic · Bruno Fantino · Erick Legrand · Régis Bataille · Manuel Montero-Odasso · Olivier Beauchet

Received: March 23, 2010 / Published online:

ABSTRACT

Introduction: Vitamin D insufficiency is related to acute medical conditions known to increase the risk of short-term death in older adults. The objective of this study was to determine whether serum 25-hydroxyvitamin D (25OHD) concentrations were associated with the occurrence of in-hospital mortality in geriatric acute care settings while taking into account all characteristics likely to improve the rate of in-hospital mortality. ***Methods:*** Three hundred ninety-nine Caucasian adults admitted between January and October 2009 to the geriatric acute care unit of Angers University Hospital, France were included in this cross-sectional study. The occurrence of all-cause in-hospital death and the measurement of serum 25OHD were assessed. Age, gender, body mass index, supine systolic blood pressure, numbers of acute diseases, chronic diseases, and hospital days, serum albumin, creatinine clearance, and season of hospital admission were used as potential confounders. ***Results:*** Mean serum 25OHD was 34.8±1.7 nmol/L. Seventeen deaths occurred in the acute care unit. Only serum 25OHD concentration was significantly and independently associated with in-hospital death (adjusted odds ratio [OR] 0.65; 95% CI: 0.44, 0.96; *P*=0.029 for full adjusted logistic regression. OR 0.87; 95% CI: 0.76, 0.99; *P*=0.029 for step-wise backward model). ***Conclusion:*** Increased serum 25OHD concentrations were associated with a low in-hospital mortality rate in this cohort of acute care geriatric inpatients. It is not only a new orientation of research, but also an

Cédric Annweiler (✉) · Bruno Fantino · Olivier Beauchet
Department of Internal Medicine and Geriatrics,
Angers University Hospital,
Angers University Memory Center, UPRES EA 2646,
University of Angers, UNAM, 49933 Angers Cedex 9,
Angers, France.
Email: CeAnnweiler@chu-angers.fr

Sophie Pochic
Department of Geriatrics, Saumur Hospital,
University of Angers, UNAM, Angers, France

Erick Legrand
Department of Rheumatology, Angers University
Hospital, University of Angers, UNAM, Angers, France

Régis Bataille
Regional Center of Fight against Cancer,
Angers University Hospital, University of Angers,
UNAM, Angers, France

Manuel Montero-Odasso
Department of Medicine, Division of Geriatric
Medicine, University of Western Ontario,
London, Ontario, Canada

additional argument for prescribing vitamin D in deficient older adults.

Keywords: acute care; older adults; short-term mortality; vitamin D

INTRODUCTION

Vitamin D is a secosteroid hormone; its insufficiency is related to chronic medical conditions in older adults such as cancer or cardiovascular diseases,[1,2] with an impact on long-term mortality.[2,3] It was recently shown that vitamin D insufficiency was also associated with a high number of acute diseases in a geriatric acute care unit, which in turn reflects the risk of unstable health status during hospitalization.[4] We thus hypothesized that serum 25-hydroxyvitamin D (25OHD) concentration could be associated with short-term mortality in acute care settings. The objective of this study was to determine whether serum 25OHD concentration was associated with the occurrence of short-term mortality (ie, in-hospital mortality) among acute care geriatric inpatients, while taking into account all characteristics likely to improve the rate of in-hospital mortality.

MATERIALS AND METHODS

Between January and October 2009, a standardized comprehensive geriatric assessment was obtained from all patients admitted to the geriatric acute care unit of Angers University Hospital, France, after obtaining their informed consent. The study was conducted in accordance with the ethical standards set by the Declaration of Helsinki (1983). The entire study protocol was approved by the local ethics committee.

The number of hospital days between unit admission and discharge, the number of acute (ie, with sudden onset and rapid progression) and chronic conditions (ie, of indefinite duration or running a course with minimal change), and the occurrence of all-cause in-hospital death were assessed. Fasting early morning venous blood was collected from resting subjects on the first day of hospital stay. No subjects were transfused before the blood test. Serum concentrations of 25OHD were measured by radioimmunoassay (Incstar Corp., Stillwater, MN) locally at Angers University Hospital. There is no lipid interference with this method, which is often observed in other nonchromatographic assays of 25OHD. The intra- and interassay precisions were 5.2% and 11.3%, respectively (range 30-125 nmol/L in normal adults aged 20-60 years).

The subjects' baseline characteristics were summarized using means and standard deviations or frequencies and percentages, as appropriate. Normality of data distribution was checked using Skewness-Kurtosis test. As the number of observations was higher than 40, no transform was applied. Adjusted logistic regression analyses (ie, full adjusted and step-wise backward methods) were performed to specify the association between serum 25OHD and in-hospital death. Age, gender, body mass index (BMI), supine systolic blood pressure (SBP), numbers of acute diseases, chronic diseases, and hospital days, serum albumin concentration, creatinine clearance, and season of hospital admission were used as potential confounders. All of these covariates were used without exception in the regression models since covariates should be considered as confounders even when they are not statistically significant by themselves, because they change the effect of the exposure of the secondary outcome to the primary outcome when they are included in the model, or because they are confounders only when included with other covariates.[5] *P* values less than 0.05 were considered as statistically

significant. All statistics were performed using SPSS (version 17.0; SPSS, Inc., Chicago, IL).

RESULTS

Among 399 elderly adults included (mean age 84.5±0.5 years; range 60-100 years; 69.2% women; 100% Caucasian; mean BMI 25.8±0.4 kg/m^2; mean SBP 132.8±1.6 mmHg), mean serum 25OHD was 34.8±1.7 nmol/L, serum albumin 35.8±0.5 g/L, and creatinine clearance 55.9±1.8 mL/min. We found that 46.2% of studied patients had a vitamin D insufficiency (ie, serum 25OHD ≤50 nmol/L),[6] and observed on average 5.9±0.21 acute diseases, 4.0±0.1 chronic diseases, and 10.8±0.4 hospital days. Seventeen patients (4.3%; 10 women; all 25OHD measurements ≤50 nmol/L; none of them had used vitamin D supplements) died in the acute care unit. Multiple logistic regression models showed a significant and independent positive association between increased serum 25OHD concentration and a low in-hospital mortality rate (adjusted odds ratio [OR] 0.65, *P*=0.029 for full adjusted logistic regression. OR 0.87, *P*=0.029 for stepwise backward model) (Table 1).

DISCUSSION

Our results showed that, irrespective of potential confounders, the higher the serum 25OHD concentration was, the fewer in-hospital deaths in acute care geriatric inpatients we observed. These findings could be explained by the fact that low vitamin D status leads to multiple organ dysfunction, often contributing

Table 1. Adjusted logistic regression showing the cross-sectional association between short-term mortality in acute care settings (dependant variable) and serum 25-hydroxyvitamin D concentration (independent variable) adjusted for subjects' baseline characteristics (*n*=399).

	Short-term mortality*					
	Full adjusted model†			Stepwise backward model†		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Age	1.27	0.89, 1.80	0.185	–	–	–
Female	0.01	0.01, 1.79	0.071	–	–	–
Body mass index‡	0.89	0.61, 1.29	0.544	–	–	–
Number of acute diseases‖	0.30	0.07, 1.20	0.089	–	–	–
Number of chronic diseases‖	0.39	0.10, 1.60	0.193	–	–	–
Systolic blood pressure	1.15	0.99, 1.34	0.072	–	–	–
Number of hospital days	0.83	0.64, 1.08	0.166	–	–	–
Serum 25-hydroxyvitamin D	**0.65**	0.44, 0.96	**0.029**	**0.87**	0.76, 0.99	**0.029**
Serum albumin	0.67	0.39, 1.15	0.144	–	–	–
Creatinine clearance§	0.98	0.90, 1.07	0.686	–	–	–

CI=confidence interval; OR=odds ratio (OR significant [ie, *P*<0.05] indicated in bold).

*Defined as in-hospital mortality.

†Adjusted for the effect of season of hospital admission and blood sampling, with no significant effect (overall OR 0.55; 95% CI: 0.15, 1.94; *P*=0.350).

‡Calculated as weight $_{kg}$ / height^2 $_{m2}$.

‖Obtained from a standardized comprehensive geriatric assessment.

§Calculated from the Cockcroft formula ([140-age $_{years}$] / creatinine $_{mmol/L}$) ×1.04 for women, and ×1.25 for men.

to death,[1-4,7] as shown in previous Third National Health and Nutrition Examination Survey (NHANES III) studies, which found an increased hypovitaminosis D-related long-term mortality rate among noninstitutionalized older adults (hazard ratio 0.95; 95% CI: 0.92, 0.98, per 10 nmol/L 25OHD)[2] and representative adults aged 20 and older (mortality rate ratio 1.26; 95% CI: 1.08, 1.46, for 25OHD <44.43 nmol/L compared with 25OHD >80.12 nmol/L).[3] These results were strengthened by a meta-analysis of 18 randomized controlled trials, which highlighted a significant association between the intake of vitamin D supplements (mean 528 IU/day) and a 7% decrease in all-cause mortality.[7] However, to the best of our knowledge, serum vitamin D has not yet been associated with short-term death, especially in acute care settings. In geriatric practice, the challenge lies in the identification of frail older individuals at high risk of death.[8] Therefore, our findings highlighted for the first time that the measure of serum vitamin D concentrations could be an easily accessible and inexpensive strategy to determine the risk of in-hospital death among geriatric inpatients and thus the level of care intervention and monitoring. Along with this primary result, we found that almost half of studied patients had a serum 25OHD concentration lower than 50 nmol/L, which was coherent with previous published studies on medical inpatients,[9] and indicated chronic insufficiency in this older frail population.[6]

The main limitation of our study was the use of a cross-sectional design, which may limit the exploration of the association between serum 25OHD concentration and short-term death, and does not allow any causal inference compared with a prospective cohort design.

In conclusion, this study reports a significant association between increased serum 25OHD concentrations and a low short-term mortality rate in a geriatric acute care unit. Further prospective analyses are needed to corroborate these results on a variety of adult acute care units, and to further clarify the expected effects of vitamin D on mortality risk, especially on cardiovascular mortality. Nevertheless, we describe not only a relevant new orientation of research, but also provide an additional argument for prescribing vitamin D in deficient older adults.

ACKNOWLEDGMENTS

The authors wish to thank Angers University Hospital for technical support.

Prof. Montero-Odasso is the first recipient of the Schulich Clinician Scientist Award (2008-2011) and holds research grants from Drummond Foundation, Physician Services Incorporated Foundation (PSI), Canadian Institutes of Health and Research (CIHR), all in Canada.

Dr. Annweiler serves as a consultant for Ipsen Pharma company. He has no relevant financial interest in this manuscript. Dr. Pochic reports no conflicts of interest. She has no relevant financial interest in this manuscript. Prof. Fantino reports no conflicts of interest. He has no relevant financial interest in this manuscript. Prof. Legrand reports no conflicts of interest. He has no relevant financial interest in this manuscript. Prof. Bataille reports no conflicts of interest. He has no relevant financial interest in this manuscript. Prof. Montero-Odasso reports no conflicts of interest. He has no relevant financial interest in this manuscript. Prof. Beauchet serves as a consultant for Ipsen Pharma company. He has no relevant financial interest in this manuscript.

Annweiler has full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Annweiler,

Beauchet, and Bataille. Acquisition of data: Pochic, Annweiler, and Beauchet. Analysis and interpretation of data: Annweiler, Fantino, Montero-Odasso, Legrand, and Beauchet. Drafting of the manuscript: Annweiler and Beauchet. Critical revision of the manuscript for important intellectual content: Legrand, Bataille, Fantino, Pochic, and Montero-Odasso. Statistical expertise: Beauchet and Annweiler. Administrative, technical, or material support: Annweiler and Beauchet. Study supervision: Beauchet.

REFERENCES

1. Peterlik M, Cross HS. Vitamin D and calcium deficits predispose for multiple chronic diseases. Eur J Clin Invest. 2005;35:290-304.
2. Ginde AA, Scragg R, Scwartz RS, Camargo CA Jr. Prospective study of serum 25-hydroxyvitamin D level, cardiovascular disease mortality, and all-cause mortality in older U.S. Adults. J Am Geriatr Soc. 2009;57:1595-1603.
3. Melamed ML, Michos ED, Post W, Astor B. 25-hydroxyvitamin D levels and the risk of mortality in the general population. Arch Intern Med. 2008;168:1629-1637.
4. Sutra del Galy A, Bertrand M, Bigot F, et al. Vitamin D insufficiency and acute care in geriatric inpatients. J Am Geriatr Soc. 2009;57:1721-1723.
5. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. Epidemiology. 1999;10:37-48.
6. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. Endocr Rev. 2001;22:477-501.
7. Autier P, Gandini S. Vitamin D supplementation and total mortality: a meta-analysis of randomized controlled trials. Arch Intern Med. 2007;167:1730-1737.
8. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. J Gerontol A Biol Sci Med Sci. 2004;59:255-263.
9. Thomas MK, Lyord-Jones MD, Thadhadi RI, et al. Hypovitaminosis D in medical inpatients. N Engl J Med. 1998;338:777-783.