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SERUM VITAMIN D CONCENTRATIONS ARE ASSOCIATED WITH FALLING AND COGNITIVE FUNCTION IN OLDER ADULTS

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Abstract

Objectives—To elucidate the mechanism through which vitamin D is associated with decreased falls.

Design—This was a convenience sample from a larger observational study examining correlations between vitamin D and 1) falls, 2) motor function, and 3) cognition (n=159).

Setting—Falls data were collected via weekly on-line surveys completed in the participants' homes. Yearly evaluations of motor and cognitive function were conducted in an out-patient setting of a large tertiary medical center.

Participants—Participants from the Intelligent Systems for Assessment of Aging Changes Study (ISAAC), a community-based cohort study of independently living older adults over age 70, who had vitamin D concentration within 6 months of clinical evaluations were included in the analysis.

Results—Participants mean age was 85 years and 74% were women. Fallers (n=37) had significantly lower vitamin D concentration (32.9 ng/ml) compared to non-fallers (39.2 ng/ml) ($p<0.01$). The relationship between vitamin D and falls remained significant after adjusting for age, health status (via CIRS), and supplement use ($p=0.004$). Vitamin D concentration were significantly associated with cognitive impairment (Clinical Dementia Rating = 0.5) ($p=0.02$) and MMSE ($p<0.01$) after adjusting for age, gender, and education. Vitamin D concentrations did not correlate with any motor measures.

Conclusion—Vitamin D concentrations correlated with cognition and falls, but not with motor measures. Further research is needed to demonstrate a causal relationship between vitamin D and cognitive function and determine if cognition plays a role in falls reduction.

Keywords

Accidental falls; cognitive function; vitamin D

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Introduction

Vitamin D is traditionally associated with bone health, but more recent research demonstrates an effect of vitamin D on multiple other organ systems (1). Of particular interest for physicians working with an older population is the fact that vitamin D supplementation greater than 700 IU a day appears to decrease falls by approximately 20% (2). Since one in three adults over age 65 fall annually with a total direct cost for fall injuries expected to climb as high as $54.9 billion by 2020, this has major public health implications (3, 4). The NIH conference “Vitamin D and Health in the 21st Century: an Update” identified determining the mechanism through which vitamin D decreases falls as a key research need (5). We proposed to look for correlations of vitamin D concentration with measures of motor function (gait, balance, and strength) and cognitive function to better inform mechanisms of action for falls reduction. We hypothesized significant correlations between motor function and vitamin D concentration.

Methods

Participants

The Intelligent Systems for Assessment of Aging Changes Study (ISAAC) is a community-based cohort study that examines changes in motor and cognitive function among independently living older adults over age 70. Participants have yearly evaluations and have computer systems in the home to complete questionnaires about falls and other health measures. Inclusion criteria include age of 80 years and older (70 years and older for minorities and spouses of participants), living independently, not demented with a Clinical Dementia Rating score < 0.5, Mini-Mental State Examination (MMSE) score > 24, and being of average health for age. Full details of study enrollment and assessment procedures have previously been described (6). We describe the 159 ISAAC participants with vitamin D concentration (within 6 month of clinical evaluations) and complete clinical data here.

Assessments

Participants were assessed with standardized health and function questionnaires, physical and neurological examinations, and a variety of tests of motor and cognitive function. Motor tests included: Tinetti Gait and Balance Instrument, UPDRS, chair stands, grip strength, and gait speed (7–10). The neuropsychological testing included the following domains and tests: Attention and concentration (Digit Span Forward, Digit-Symbol and Trail Making Part A); Processing speed (Simple & Choice Reaction Time and Crossing-off test); Working memory (Digit Span Backward, Letter-Number Sequencing, and Digit Sequencing); Memory (Logical Memory Delayed Visual Reproduction, CERAD Word List, and CERAD Visual Figures Recall; Language WRAT-R and Boston Naming Test); Executive function (Category Fluency, Trail Making Part B, Stroop Test, Letter Fluency, and Odd Man Out task); and Visuospatial construction (Picture Completion and Block Design) (11–16). Z-normalized scores were calculated for each of the 5 cognitive domains as well as a global score. Falls were self-reported via weekly, computerized questionnaires.

Health status was documented via the modified Cumulative Illness Rating Scale (17). Falls were defined as any fall, including a slip or trip, in which the subject came to rest on the floor, ground or on a lower level (6). The number of falls each subject reported were summed for the 3 months before, and the 3 months after the date of the vitamin D blood draw. Blood draws were non-fasting and were all completed between 9/26/08 and 2/11/09. Ninety percent of plasma collections were done in the Fall. Vitamin D assays were completed in October 2009. Vitamin D was measured as 25-hydroxy vitamin D in the serum using a radioimmunoassay (RIA) from IDS (Immunodiagnostic Systems Inc, Fountain Hills, AZ 85269-7063). The sensitivity, defined as the concentration corresponding to the mean minus 2 standard deviations of 10 replicates of the zero calibrator, is < 1.2 ng/mL. Our in-house laboratory quality control program produces interassay %CV's of 5.1% at 13.7 ng/mL and 9.1% at 51.3 ng/mL. The antibody recognizes 100% of 25 hydroxyvitamin D3 and 75% of 25-hydroxyvitamin D2 when assessed at 50% binding of the zero calibrator according to the manufacturer.

Statistical analysis

Neuropsychological and motor measures obtained at the annual evaluation closest to the vitamin D blood draw date were used. Participant characteristics of fallers and non-fallers were compared using Student's t-test or Wilcoxon Rank Sum Test for continuous variables and Pearson Chi-square test for categorical variables. Multivariate logistic regression was used to estimate risk of falls by vitamin D level, controlling for gender and supplementation use. Interaction terms were introduced to investigate whether the relation between vitamin D and falls risk varied by cognitive status (CDR = 0 vs. 0.5). Analysis of variance was used to compare vitamin D concentration among three fall categories (non-faller, single faller, multiple faller). Correlations between Vitamin D concentration and clinical variables are reported as Spearman's or Pearson's coefficient as appropriate. Multivariate linear regression was used to model the relationships between Vitamin D level and each cognitive domain z-score, after adjusting for age, sex and education. All analyses were performed using SAS 9.2 software (SAS Institute Inc., Cary, NC).

Results

Subject Characteristics

Subjects averaged 85 years old, were generally highly educated (average of 15 years of education), and largely white females (92% and 74% respectively). The mean serum vitamin D level was 37.7 ng/ml (range: 9–90 ng/ml). Twenty-three percent of subjects (n=37) reported at least one fall within 6 months surrounding the vitamin D collection (3 months before and 3 months after date of blood draw) and only 5% (n=8) reported multiple falls. Table 1 presents demographic, clinical, and cognitive characteristics among fallers and non-fallers.

Fallers had lower serum vitamin D

Fallers had a significantly lower vitamin D level (32.9 ng/ml) as compared to non-fallers (39.2 ng/ml) (p=<.01). Fallers had slightly higher cumulative illness ratings (CIRS) at 23.2 compared to 21.6 (p=0.01). There were no statistically significant differences in motor measures or cognitive domain z-scores between groups. The adjusted OR and 95% CI for the association between vitamin D and falls is OR 0.96, 95% CI 0.93 – 0.99, p=0.02. Using logistic regression we modeled the risk of falling by vitamin D after adjustment for covariates: age, health status (via CIRS), and supplement use. Vitamin D remains a significant predictor of falls risk, p=0.004. A 5 ng/ml increase in vitamin D corresponds to a 20% decrease in odds of falling. Looking exclusively at the 111 participants with generally considered sufficient vitamin concentration D (>30 ng/ml) mean vitamin D among fallers was lower at 40.0 ng/ml than non-fallers at 45.1 ng/ml; this did not reach statistical significance possibly due to lower sample size (p=0.07). Vitamin D supplement use (based on patient self-report for the 2 weeks prior to evaluations) did not modify the relationship between vitamin D and falls risk. Cognitive status (CDR=0 vs. 0.5) did not modify the relationship between vitamin D and falls risk (p=0.12). A post-hoc analysis was done for falls and vitamin D including covariates: BMI, depression (GDS), autonomy (FAS), grip strength, and race, although none of these variables were different among fallers and non-fallers (see Table 1). Vitamin D remained the only variable in the model significantly associated with fall status, p=0.01.

Serum vitamin D and motor function

We investigated the relationships between vitamin D and motor measures (see Table 2). There were no significant correlations between vitamin D concentration and the following motor measures: stopwatch walk, Tinetti gait and balance, UPDRS, grip strength, or chair stands.

Vitamin D and cognitive measures

MMSE scores correlated significantly with vitamin D levels (p<0.01). Subjects with very mild dementia (CDR=0.5) had significantly lower vitamin D concentration as compared to cognitively intact subjects (CDR=0), 30.9 vs. 38.8 (p=0.02). These relationships remained significant after adjustment for age, gender, and education (p-values<0.05). There was a trend towards a correlation with the global cognition, as well as the attention and working memory subscores, but these did not reach significance. Multivariate linear regression between vitamin D concentration and each cognitive domain z-score (adjusted for age, gender, and education) did not reach statistical significance.

Discussion

These data are consistent with other studies showing that higher plasma vitamin D concentrations are associated with reduced falls (2). In this group of independently living older adults, fallers had significantly lower vitamin D concentration than non-fallers. Correction for age and health status did not modify this relationship. A “dose response” was also evident, with multiple-fallers having lower serum vitamin D than single fallers and non-fallers. In our study, a 5 ng/ml increase in vitamin D decreased odds of falling by 20%.

One possible mechanism by which vitamin D might reduce fall risk is via a direct effect of vitamin D on muscle, hypothesized because vitamin D receptors are in muscle and severe vitamin D deficiency causes a myopathy (18). However, our data did not show a correlation between vitamin D and strength. It is possible that our measure of muscle function (grip strength) was not sensitive enough or that other mentions of muscle power, such as speed of contraction is more important than absolute strength (19). Central nervous system effects of vitamin D on gait and balance regulation have also been postulated (20). Again, our data did not show a significant correlation between vitamin D and gait or balance measures. Our data did however show a significant correlation of serum vitamin D concentration with MMSE scores and cognitive status. A number of cross-sectional studies show a similar relationship, but none have included falls data (21, 22). Two small, short term intervention studies showed no significant change in cognitive measures (23, 24).

Our data suggest that cognitive effects may play a role in vitamin D’s influence on falls while motor function may play a lesser role. This however does seem to explain the entire mechanism as our data showed the relationship between vitamin D and falls remained after correcting for cognitive status, suggesting there are additional factors at play. There are clear limitations to this study. With a cross-sectional study causality cannot be concluded. Certainly one concern is reverse causation – those that are more cognitively intact remember to take their supplements and those who don’t fall get outside to obtain more sun exposure. This cohort is also particularly healthy so results may not be generalisable to other populations. Season of blood draw may also affect vitamin D concentration, but samples were collected over a relatively narrow window (90% in the Fall) and there was no significant variation by season was seen. This study by no means is conclusive. The relevance of these data is in informing future studies of vitamin D and falls. It is well known that cognitive function plays a role in falls (25, 26). These data suggest that future intervention studies should includ in-depth cognitive measures to properly elucidate the mechanism via which vitamin D results in falls reduction. It adds further supports that intervention studies to specifically look at the effects of vitamin D supplementation on cognitive function, are warranted.

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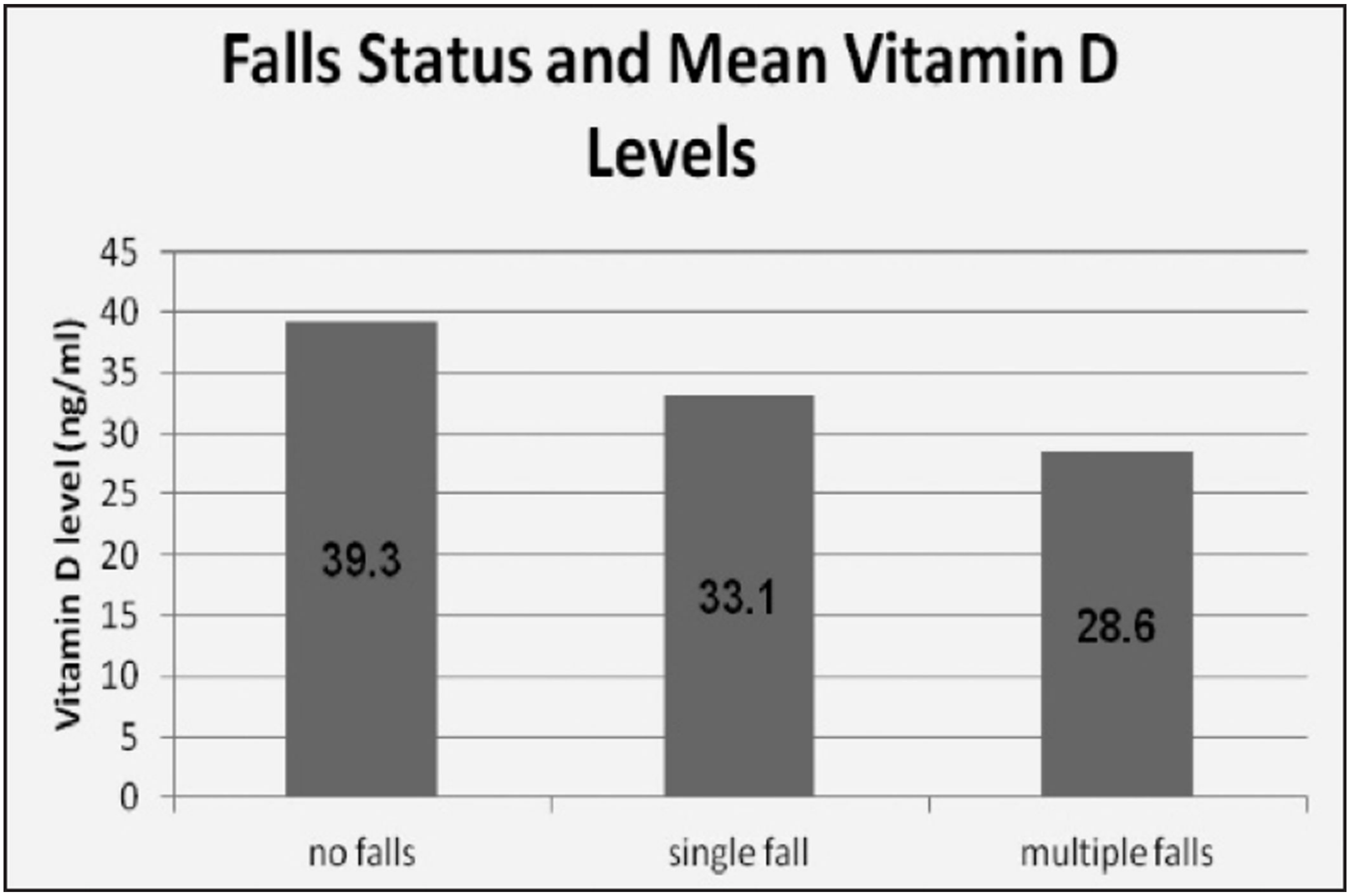

Figure 1.

Presents mean vitamin D concentration for the 122 non-fallers, 29 single fallers, and 8 multi-fallers. There was a significant difference across groups (ANOVA, p=0.0387). Post – hoc pair-wise analysis between each group showed a significant difference in vitamin concentration between non-fallers vs. multiple fallers (p=0.04). Analysis in non-fallers vs. single fallers and single fallers vs. multiple fallers did not reach statistical significant (p=0.08 and p=0.33 respectively)

Table 1

Subject Characteristics

Variables	Total	No Falls	Fallers	p-value
N	159	122	37	
Age (years)	85.5	85.1	86.6	0.09
Gender (% female)	74%	74%	76%	0.82
Education (years)	15.5	15.5	15.4	0.68
Race (% Non-White)	8%	8%	5%	0.73
Cognitive Status (% CDR=0.5)	13%	12%	17%	0.4
Vitamin D (ng/ml)	37.7	39.2	32.9	<0.01**
Vit D supplementation (%)	41%	43%	32%	0.23
Geriatric Depression Score (0–30)	1.6	1.4	2.2	0.39
Functional Assessment Scale (0–30)	0.9	0.8	1.5	0.08
Cumulative Illness Rating Scale (14–70)	22	21.6	23.2	0.01**
MMSE (0–30)	28.4	28.4	28.5	0.85
Cognitive Domain z-scores				
Global Score	−0.12	−0.12	−0.14	0.87
Attention	−0.14	−0.16	−0.1	0.65
Executive Function	−0.03	0.00	−0.13	0.37
Memory	−0.18	−0.16	−0.26	0.62
Working Memory	−0.2	−0.25	−0.04	0.19
Visuospatial	0.01	0.01	0.04	0.82
Motor Measures				
Stopwatch walk	75.8	77	71.3	0.21
Tinetti gait (0–16)	1.2	1.1	1.5	0.08
Tinetti balance (0–16)	4.5	4.2	5.5	0.12
mUPDRS (0–108)	2.3	2.1	3.1	0.11
Grip strength (dynes)	17.7	18.1	16.6	0.32
Chair stands: Unable (%)	23%	19%	33%	0.08

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Table 2

Correlations between clinical variables and vitamin D concentration

Motor Measure	Correlation	p value
Stopwatch walk	−0.08	0.33
Tinetti gait	0.1	0.21
Tinetti balance	0.02	0.89
UPDRS	−0.01	0.88
Grip strength	−0.14	0.09
Chair stands (n=120)	0.04	0.7

Cognitive Measure	Correlation	p value	Regression coefficient**	95% confidence interval	p value
Global Score	0.14	0.07	3.30	−0.50, 7.10	0.09
Attention	0.15	0.06	2.68	−0.68, 6.04	0.12
Executive Function	0.10	0.21	1.73	−1.35, 4.80	0.27
Memory	0.12	0.13	1.35	−0.90, 3.60	0.24
Working Memory	0.14	0.08	2.30	−0.44, 5.04	0.10
Visuospatial	0.08	0.35	1.63	−1.18, 4.44	0.25
MMSE*	0.24	<0.01	1.50	−0.01, 3.01	0.05

Cognitive Status	Mean vitamin D concentration	p value
CDR=0.5	30.9 ng/ml	
		0.02
CDR=0	38.8 ng/ml	

* Spearman's rank correlation coefficient was used since MMSE scores are not normally distributed.

** Individual multivariate linear models for vitamin D adjusted for age, gender, and education.