

Original Research

Vitamin B₆ Is Associated with Depressive Symptomatology in Massachusetts Elders

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Objective: We examined the cross-sectional relationship between dietary vitamin B₆ and plasma pyridoxyl-5'-phosphate concentrations (PLP) with depressive symptomatology among a representative sample of 618 elderly Caribbean Hispanics, and a neighborhood based comparison group of 251 non-Hispanic white (NHW) older adults in Massachusetts.

Methods: Depressive symptomatology was assessed with the Center for Epidemiologic Studies Depression Scale (CES-D). 41% of Hispanics and 22.6% of NHWs had CES-D scores greater than 16, indicating depressive caseness. Dietary intake was calculated from a semi-quantitative food frequency questionnaire (FFQ) designed for this population.

Results: PLP was significantly associated with CES-D score and depressive caseness in the total sample and in non-supplement users. Deficient levels of plasma PLP (plasma PLP < 20 nmol/L) approximately doubled the likelihood of depressive caseness. Total intake (diet + supplement) of vitamin B₆ was not associated with these outcomes. However, dietary vitamin B₆ was significantly associated with CES-D score and depressive caseness.

Conclusion: Longitudinal studies are needed to clarify the direction of causality between vitamin B₆ and depressive symptoms.

INTRODUCTION

B vitamins play a central role in the regulation of psychological states [1–4]. Vitamin B₆, folate and vitamin B₁₂ are involved in a series of methylation reactions that produce monoamine neurotransmitters, phospholipids, and nucleotides. Vitamin B₆ in its active form, pyridoxal 5'-phosphate (PLP), plays a role in the control of plasma homocysteine concentration, which is a risk factor for vascular disease [5–8] and cognitive decline in old age [9–12].

PLP is a necessary cofactor in decarboxylation reactions in tryptophan metabolism, which result in the conversion to the monoamine neurotransmitter, serotonin [13]. Regulation of mood, specifically depression, is highly dependent on tryptophan metabolism and serotonin production. Treatment of depression, therefore, often involves the use of selective serotonin re-uptake inhibitors (SSRIs) [14,15]. In comparison to non-depressed patients, depressed patients have been shown to be deficient in vitamin B₁₂ and folate [1,3,16]. Low plasma PLP has also been inversely associated with depressive symptoms [17–19]. A few intervention trials have shown beneficial effects

of treatment with Vitamin B₆ alongside anti-depressive medications among schizophrenic and depressed patients [20,21].

The effects of dietary vitamin B₆ on depression have been relatively unexplored in the literature [1]. Diet may contribute to the regulation of affective disorders, such as depression, by improving plasma B vitamin status. A recent randomized controlled trial (RCT) of B vitamin fortified cereals versus placebo found significant increases in plasma B vitamin (folate, vitamin B₁₂ and vitamin B₆) status among adults aged 50–85 years old [12]. However, little is known about the relationship between dietary intake of vitamin B₆ and depression.

In particular, the literature lacks studies on ethnic minority groups that may have higher than average prevalence of depression, including older Hispanics. The 2001 US Surgeon General's report on mental health in ethnic minorities noted that Hispanics were less likely to receive treatment for mental illnesses and often received poorer treatment and misdiagnosis [22]. Hispanics aged 55 and over make up 10.6% of the Hispanic US population [23]. It is projected that by the year 2050, Hispanics will make up approximately 24% of the population [24]. B vitamin deficiencies are relatively common in

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elders [2,25]. We have previously reported that Puerto Rican (44%) and Dominican (32%) elders had a higher prevalence of depressive caseness than did a neighborhood-based comparison group of non-Hispanic white elders (22%) [26]. In the current study, we examine the cross-sectional relationship between plasma PLP, dietary intake of Vitamin B₆ and depressive symptomatology among a representative sample of elderly Hispanics and non-Hispanic whites in Massachusetts.

MATERIALS AND METHODS

The data used in this analysis were gathered from the Massachusetts Hispanic Elderly Study (MAHES). This study includes a representative cross-sectional sample of Hispanic elders in Massachusetts and a neighborhood based comparison group of non-Hispanic white elders (NHW). Data collection began in 1993 and was completed in 1997. This sample has been previously described [26]. Briefly, a two-stage cluster sampling technique was used, with sampling proportionate to the size of the Hispanic population, aged 60 and older [27]. Massachusetts counties and census blocks served as the two levels of hierarchy. Census blocks drawn into the sample were enumerated and respondents were chosen randomly. We completed a total of 1,033 home interviews including 475 Puerto Ricans, 143 Dominicans, 161 of other Hispanic origin, and 251 non-Hispanic whites. During home interviews, participants completed a detailed questionnaire, which included modules on social and economic background, migration, health history, physical functioning, depression, cognitive function, dietary intake, and prescription drug use. Height, weight, blood pressure and fasting blood samples were obtained. Puerto Ricans and Dominicans possess socio-cultural similarities due to their Caribbean origin, therefore, only Puerto Ricans and Dominicans were included as Hispanics in our sample. The sample used in our analysis consisted of 618 Caribbean origin Hispanics and 251 neighborhood-based Non-Hispanic whites (60% female and 40% male).

Dependent Variables

To measure symptoms of depression, all subjects completed the Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D is a widely used instrument that has established itself as a useful and valid tool in population studies, including older Hispanic groups [7,28–30]. CES-D assessments of depressive symptomatology strongly correlate with the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) categories of depression [31]. We have shown that the CES-D exhibited high reliability ($\alpha = 0.90$) in the population under study and that this high reliability did not differ by subgroup [26]. The scale includes 20 items, of which 16 measure symptoms in the negative direction and 4 in the positive direction. The questions in the scale refer to symptoms during

the week prior to the interview. Once the positive scores are reversed in value for consistency, the sum of the scale values for the CES-D score can range from 0 to 60. Respondents with a score of 16 points or higher are seen as exhibiting symptoms of clinical depression [32–34].

Dietary Intake

Dietary intake of vitamin B₆ was calculated from a specifically designed food frequency questionnaire (FFQ). The FFQ is a semi-quantitative dietary history which allows for quantification of serving sizes, and also provides detailed information on frequency of food intake, summary questions and supplement use. Vitamin B₆ intake from supplements, including from multivitamins, was added to dietary intake of vitamin B₆ to derive total intake of vitamin B₆ in mg/day. A dichotomous variable for supplement use (Y/N) was included in models with dietary intake of vitamin B₆. This FFQ contained 118 food list items. Development of the food list followed the procedures used for the National Cancer Institute/Block FFQ, using dietary recall data from the Puerto Rican subset of the Hispanic Health and Nutrition Examination Survey (HHANES) as well as the 2nd National Health and Nutrition Examination Survey (NHANES II) [35]. Because the Puerto Rican and Dominican populations have a typical diet that differs considerably from both the general US population and from Mexican Americans, foods like plantains, and specific soup and rice-dish recipes were added. Quantification of nutrient intake was conducted with the Minnesota Nutrient Database System, Program 2.8, Version 25 (NDS, University of MN, Minneapolis, MN).

Plasma PLP

Subjects fasted overnight after which a phlebotomist collected a 12 hour fasting blood sample. Plasma analyses were performed at the Nutrition Evaluation Laboratory located in the Jean Mayer USDA Human Nutrition Research Center of Aging at Tufts University in Boston, Massachusetts. Plasma PLP was measured with a radioenzymatic assay (CV = 15%) [36]. Plasma PLP below 30 nmol/L has been used as an indicator of inadequate status [17,37–39] while a cutoff of 20 nmol/L indicates deficient concentrations [37,40,41]. Both cutoffs have been widely used in the literature and demonstrate utility in assessing adequacy of vitamin B₆ intake.

Statistical Analyses

To explore the relationship between dietary intake of vitamin B₆ and plasma PLP with CES-D score, multivariate regression models were fit. Logistic regression models were used to explore the relationship between the exposures of interest and the presence of depressive caseness (CES-D \geq 16).

There were no significant interactions (at the $\alpha < 0.05$ level) between ethnicity and any indicator of vitamin B₆ status

with depressive outcome measures. We therefore present analyses for the combined sample. Because few studies exist with Hispanics, we repeated analyses with this subset. These results did not differ greatly from those of the full sample, and we, therefore, do not present them here. Analyses were repeated among the subset of our sample who were not using vitamin B₆ supplements (82% of Hispanics and 70% of NHWs).

Dietary vitamin B₆ models were adjusted for age, sex, total energy intake, ethnicity, and where appropriate, for supplement usage. Plasma PLP was logarithmically transformed to improve normality. Plasma PLP models were adjusted for age, sex, ethnicity and plasma folate. Age, education, and sex have been shown to be associated with depressive symptomatology and were therefore included as covariates. Adjustment for plasma creatinine did not change the point estimate for plasma PLP in either the full model or in a model including just plasma vitamin B₆ and creatinine, and so this variable was dropped from the final model. Statistical analyses were conducted with SAS statistical software, version 9.1 (Cary, NC).

RESULTS

The mean age in our sample of Caribbean Hispanics was 70 ± 7.6 years. Mean years of education were 6.6 ± 5.0 , ranging from 0 to 21 years. As previously reported, Caribbean origin Hispanic elders had a higher mean CES-D score as well as almost twice the prevalence of depressive caseness (CES-D ≥ 16); 41% versus 23% compared to NHWs (Table 1). Low plasma PLP (<30 nmol/L) was common in both Hispanics (30%) and NHWs (28%). Sixteen percent of NHWs had plasma PLP concentrations below 20 nmol/L compared to 11% of Hispanics. Vitamin B₆ intakes from food were also similar. However, NHWs were more likely to use vitamin supplements, and total vitamin B₆ intake was therefore higher among NHWs than among Hispanics (4.71 ± 1.26 mg). In this sample, significantly more Hispanics (39%) than NHWs (32%) reported daily intakes that did not meet the Recommended Dietary Allowance (RDA) (Table 2). Of those that met the RDA, 9% and 25% had plasma PLP concentrations less than 20 nmol/L and 30 nmol/L, respectively. Dietary intake ($\beta = 0.30$, SE = 0.05, $P < 0.0001$), as well as total intake ($\beta = 0.43$, SE = 0.04, $P < 0.0001$), of vitamin B₆ were each significantly associated with plasma status.

After adjusting for covariates, plasma PLP was significantly associated with lower CES-D score in the full sample and

among non-supplement users (Table 3). Plasma PLP was significant against depressive caseness in the folate adjusted model for the total sample, and in the basic model for non-supplement users. However, these were attenuated with further adjustment for education. Deficient concentrations of plasma PLP (plasma PLP < 20 nmol/L) approximately doubled the likelihood of depressive caseness in the total sample and in non-supplement users, although again, initially significant results were attenuated to only approach significance after adjustment for education.

Total intake of vitamin B₆ (dietary + supplements) was not significantly associated with CES-D score or with depressive caseness (Table 4). However, dietary vitamin B₆ was significantly associated with both measures of depressive symptoms for both the total sample, where supplement use was adjusted, and in non-supplement users ($p < 0.01$). These remained significant after adjustment for folate intake and education level. After full adjustment, each log unit of dietary vitamin B₆ intake was associated with an approximately 40% lower likelihood of depressive caseness.

DISCUSSION

In this sample of Caribbean Hispanic and non-Hispanic white elders in Massachusetts, dietary vitamin B₆ intake and plasma PLP were significantly associated with lower CES-D score and likelihood of depressive caseness. Folate has previously been linked with depression [1,3,16] and the fact that its adjustment did not change our results suggests that vitamin B₆ is independently associated with depressive symptomatology. The prevalence of depressive symptomatology in these Caribbean Hispanic elders was higher (41%) than that reported in the literature for other Hispanic subgroups. The Hispanic EPESI study found a prevalence of 26% among Mexican Americans aged 65 and older using the same CES-D cutoff as in our study [28]. This is similar to the prevalence of depressive symptomatology among the non-Hispanic whites in our sample (22%). Gonzalez et al. (2001) also found a similar prevalence of depression (25%) in the SALSA study, a population-based prospective study of Latinos aged 60 and older [34]. Mexican Americans and Caribbean Hispanics are distinctively different cultural groups. Krause compared Mexican Americans, Cubans and Puerto Ricans and found that Puerto Ricans experienced more depressive affect than other groups [42].

Few studies have examined the relation between vitamin B₆ and depression, but at least two groups have reported significant associations between low plasma PLP and higher depressive symptomatology [17,18]. The first [17] examined this in a group deficient in vitamin B₁₂; while the latter [18] was in a population of men in a bereavement support intervention group. Our results are consistent with these studies and add credibility to the importance of dietary vitamin B₆.

Table 1. Depressive Symptomatology

	Caribbean Hispanics (N = 566)	NHW (N = 238)
CES-D score (Mean \pm SE)	15.4 \pm 0.51***	10.0 \pm 0.63
Caseness % (CES-D ≥ 16)	41.3***	22.6

*** $P < 0.0001$.

Table 2. Vitamin B₆ Status

	Hispanics	NHW
Plasma PLP ^a (M ± SE, nmol/L)	52.1 ± 2.2	64.0 ± 2.1*
% Plasma PLP < 30 nmol/L	30.4	28.1
% Plasma PLP < 20 nmol/L	11.3	16.0†
Dietary vitamin B ₆ intake (M ± SE, mg)	1.96 ± 0.04	2.05 ± 0.06
Total vitamin B ₆ intake (diet + supplement, M ± SE, mg)	2.46 ± 0.11	4.66 ± 1.23**
% not meeting the RDA for dietary vitamin B ₆ intake ^b	38.9	31.6*
% using B ₆ supplement	18.0	29.9***

† P < 0.1.

* P < 0.05.

** P < 0.001.

*** P < 0.0001.

^a PLP, pyridoxyl-5'-phosphate.

^b The Recommended Dietary Allowance (RDA) for vitamin B₆ is 1.7 mg/d for men and 1.5 mg/d for women, aged 51 and older [52].

Table 3. Association of Plasma PLP^a with Depression Score^b and Depressive Caseness^c

	Model	β (SE)		OR (95% CI)	
		Total sample (N = 602)	Non-supplement users (N = 475)	Total sample (N = 602)	Non-supplement users (N = 475)
PLP (nmol/L) ^d	1	-0.12* (0.06)	-0.14* (0.07)	0.79† (0.61, 1.02)	0.71* (0.52, 0.98)
	2	-0.13* (0.06)	-0.18* (0.08)	0.74* (0.56, 0.99)	0.76† (0.55, 1.05)
	3	-0.11† (0.06)	-0.15* (0.08)	0.78† (0.58, 1.04)	0.77 (0.55, 1.06)
PLP < 20 nmol/L	1	0.29* (0.12)	0.27* (0.12)	1.71* (1.02, 2.89)	1.78* (1.03, 3.09)
	2	0.29* (0.12)	0.30* (0.13)	1.75* (1.01, 3.03)	1.84* (1.04, 3.27)
	3	0.25* (0.12)	0.26 (0.13)	1.61† (0.93, 2.79)	1.70† (0.96, 3.03)

† P < 0.10.

* P < 0.05.

^a PLP, pyridoxyl-5'-phosphate, log transformed.

^b Center for Epidemiologic Studies Depression Score (CES-D), log transformed.

^c Model 1: Adjusted for age, sex, and ethnicity.

Model 2: Model 1 plus plasma folate.

Model 3: Model 2 plus education.

^d PLP < 30 nmol/L versus higher was not significantly associated with depressive caseness in any model.

Intervention studies have shown mixed results on the improvement of depressive symptoms upon administration of vitamin B₆ [20,43–45]. Most of the literature on vitamin B₆ and depression focuses on randomized controlled trials (RCTs) among women who suffer from pre-menstrual syndrome (PMS) [43,44]. Depression is among the many reported pre-menstrual symptoms [46,47]. It has also been suggested that use of oral contraceptives worsens depressive symptoms [13,48–50]. We found that dietary intake of vitamin B₆ was more strongly associated with depressive symptoms in an older cohort than total intake or plasma PLP. However, the majority of intervention trials observed a younger cohort of women and did not measure dietary intake of vitamin B₆.

Among five randomized, double-blind, placebo controlled trials of vitamin B₆ supplementation reviewed by Wyatt et al. (1999), the overall odds ratio for improvement of depressive symptoms in premenstrual women was 1.69 (95% CI: 1.39, 2.06) compared to placebo [43]. Weizman et al. (1999) found a decrease in depressive symptomatology (measured by the

Hamilton Depression Rating Scale) after administration of 150 mg/day of B₆ for a month in a psychiatric population [20]. Weizman et al.'s (1999) study, despite lacking a placebo comparison group, is qualitatively important in that it demonstrates positive results among psychiatric patients. Commonly used dosages of vitamin B₆ supplementation in trials range from 50 mg [44] to 150 mg [20,45]. A 150 mg/d supplement of vitamin B₆ exceeds the tolerable upper limit (TUL = 100 mg/day) and may cause nerve damage [51]. It is unlikely that population groups will consume such a high intake of vitamin B₆ in their diet or through supplements.

In a cross-over study, vitamin B₆ did not show a significant independent effect on depressive symptoms; however, in combination with Mg²⁺, vitamin B₆ reduced anxiety and craving-related symptoms [44]. Another study, among Mexican women using oral contraceptives, found no differences in depressive symptoms between those taking vitamin B₆ or placebo [45]. Variation in findings may result from differences in dose or form of the supplement as well as the population under study.

Table 4. Association of Total Vitamin B₆ Intake, and Dietary Vitamin B₆ with Depression Score^{a,b} and Caseness^{b,c}

	Model	β (SE)		OR (95% CI)	
		Total Sample (N = 791)	Non-supplement users (N = 623)	Total Sample (N = 791)	Non-supplement users (N = 623)
Total vitamin B ₆ (mg, log)	1	-0.09 (0.06)	—	0.88 (0.64, 1.19)	—
	2	-0.15 (0.09)	—	0.85 (0.52, 1.37)	—
	3	-0.12 (0.09)	—	0.88 (0.54, 1.44)	—
Dietary vitamin B ₆ (mg, log)	1	-0.34** (0.12)	-0.36** (0.14)	0.54* (0.31, 0.94)	0.50* (0.27, 0.94)
	2	-0.33* (0.14)	-0.42** (0.16)	0.58† (0.30, 1.09)	0.52* (0.27, 0.99)
	3	-0.30* (0.14)	-0.39* (0.16)	0.60 (0.32, 1.14)	0.57† (0.29, 1.10)

† P < 0.10.

* P < 0.05.

** P < 0.01.

^a Center for Epidemiologic Studies Depression Score (CES-D), log transformed.^b Model 1: Adjusted for age, sex, ethnicity and total energy intake.Model 2: Model 1 plus adjusted for dietary folate intake in dietary vitamin B₆ models and total folate intake (diet + supplement) in total vitamin B₆ models.

Model 3: Model 2 plus adjusted for education.

All dietary vitamin B₆ models were adjusted for vitamin B₆ supplement intake (Y/N).^c CES-D \geq 16.

In our sample of Massachusetts elders, intakes of total vitamin B₆ ranged from 2.5 mg among Caribbean origin Hispanics to 4.7 mg among NHWs. Because our analysis is cross-sectional, our finding that total intake of vitamin B₆, which includes supplement doses, was not significantly associated with depressive outcomes may be affected by self-use of vitamin supplements by depressed individuals. The relative benefits of supplements versus dietary intake of vitamin B₆ and their effect on depressive symptoms deserves further study.

Our results show that the prevalence of low vitamin B₆ status is high in both Caribbean origin Hispanic elders and neighborhood-based NHWs (Table 2). Inadequate vitamin B₆ status appears to be widespread. A non-institutionalized sample in the National Diet and Nutrition Survey in Britain showed 24.5% with plasma PLP < 20 nmol/L and 47.7% with plasma PLP < 30 nmol/L [37]. The proportion of those with plasma < 20 nmol/L in our sample is comparable with a population-based study of Dutch adults, aged 50–79 (men: 16%, women: 7%, plasma < 19 nmol/L) [41].

Mean plasma PLP concentrations in this population ranged from 53 nmol/L in Hispanics to 64 nmol/L in NHWs. These are similar to the mean plasma PLP concentrations reported in the Framingham Heart study for participants without elevated C reactive protein (56 nmol/L) and are higher than reported values of non-institutionalized adults, aged 65 and older, in the National Diet and Nutrition Survey in mainland Britain (mean range: 29–47 nmol/L) [6,37].

Bates et al. (1999) noted that ‘adequate’ vitamin B₆ intake does not always result in adequate plasma status and explored the percentages of those with low plasma concentrations who also met the dietary recommendations [37]. In our sample, 9% and 25% of those who reported intakes greater than the RDA had plasma PLP less than 20 nmol/L and 30 nmol/L respectively, suggesting that intakes higher than the current RDA may be advisable for older adults.

There are several limitations in our study. Because of the cross-sectional design, the direction of causality between depression and dietary intake of vitamin B₆ is unknown. Unexpectedly, use of supplements containing vitamin B₆ was not associated with risk of depressive caseness in our sample. It is possible that those who were depressed were more likely to take supplements. This theory is supported by the observation that plasma PLP was significantly inversely associated with CES-D score depressive caseness (Table 3) among non-supplement users, but not among supplement users. If supplements were taken due to the presence of depressive symptoms, this would dilute our ability to see an effect for both total intake of vitamin B₆ and current plasma PLP.

CONCLUSIONS

Hispanic elders are understudied in the literature. In particular, Puerto Ricans and Dominicans have lifestyles, including dietary intake patterns, that differ from other groups and may contribute to their higher than average prevalence of depression. Caribbean origin Hispanic adults had lower mean vitamin B₆ intakes and plasma concentrations than their non-Hispanic white comparison group. However, the prevalence of low plasma concentrations did not differ greatly across groups, suggesting that differences in vitamin B₆ status may contribute to, but do not explain, the large disparity in depressive caseness. Further, there was no interaction by ethnicity and vitamin B₆ in relation to depressive symptomatology, suggesting similar mechanisms for both groups.

Both depression and low vitamin B₆ status are prevalent in this population of Caribbean origin Hispanic elders, and although less so, in a low-income comparison group of NHWs. Improved intake of vitamin B₆ may be useful in reducing

depressive symptomatology. However, longitudinal studies are needed to clarify the direction of the association between intake of vitamin B₆ and depression and to better understand the role of dietary intake versus supplements in this association.

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