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Vitamins and Sleep: An Exploratory Study

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Keywords

vitamins; insomnia; sleep diary; epidemiology

One-third of the United States population takes a vitamin or mineral supplement daily¹. The booming nutritional supplement industry is predicated on consumers' beliefs that these products produce health enhancement. Claims for sleep improvement have been advanced for a variety of such products as typified by valerian, for which there is evidence of mild efficacy². Little or weak evidence exists to support soporific claims for other nutritional supplements³.

The majority of sleep enhancement products are classified as nutritional supplements. Minerals and vitamins have not been reported to have soporific effects, although B vitamins have been advanced as a preventive for insomnia based on research that suggests deficiencies in vitamin B6 promote psychological distress and ensuing sleep disturbance⁴.

Although the direct link between vitamins and insomnia is unclear, there are studies that show an association between vitamins and other sleep disorders. Studies have reported that B-12 shortens the length of the sleep-wake rhythm⁵ and affects the circadian aspect of sleep propensity⁶. Studies have also identified vitamin B complex as a helpful treatment of nocturnal leg cramps⁷. Deficiencies in iron may be related to restless leg syndrome or periodic leg movement disorder⁸, both of which may have an effect on sleep maintenance. Evidence from these studies points to the possibility that sleep may be affected by vitamin and mineral intake or lack of these substances.

The presence of vitamins and other nutritional supplements has been known to have negative side effects, as well. For example, high doses of vitamin D have led to symptoms such as nausea, vomiting, and depression⁹. High doses of vitamin A have been associated with bone loss¹⁰. The finding of both positive and negative effects associated with vitamin use invites the question: Are there sleep effects associated with vitamins? A literature search revealed no studies addressing this question. Given this research gap, we conducted a preliminary investigation to determine if sleep-promoting or sleep-inhibiting effects are associated with common vitamins.

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Methods

Participants

The current data are from a larger epidemiological survey that utilized random-digit dialing to recruit 772 people, ranging in age from 20 to 98 years, from Shelby County, Tennessee¹¹. That survey recruited at least 50 men and 50 women in each of seven age groups across the adult lifespan. The age groups were divided by decades beginning with 20–29 years and ending with the decade beginning at age 80. No upper age limit was imposed on this last decade. Information on vitamin use was collected from 519 of these participants.

Shelby County is composed of the city of Memphis and its suburbs and has a population of 897,472¹². The population of Shelby County divided nearly equally between men (47.8%) and women (52.2%). The ethnic distribution is predominantly Caucasian and African American, at 47.3% and 48.6%, respectively. Per capita income for Shelby County was most recently listed as \$28,828, which is comparable to the national average of \$28,546¹².

Recruitment eligibility criteria were minimal. Participants were required to be at least 20 years of age and able to speak and read English at approximately a seventh-grade level. In a few cases, potential participants with poor reading skills were allowed to participate if their spouse/partner or adult child agreed to be responsible for collecting their data. Bed partners from the same household were not allowed to participate due to the concern that variability in their sleep data would be constrained. However, non-bed partner members of the same household were eligible if they met all requirements.

To be classified as having insomnia, individuals had to satisfy all of the following standards (see Table 1 for a more detailed list of the criteria): (a) a subjective complaint of insomnia lasting at least six months, (b) report of impaired daytime functioning, and (c) a sleep-onset latency of ≥ 31 minutes or wake time after sleep onset totaling ≥ 31 minutes at least three times per week as assessed by two weeks of sleep diary data. Criteria (a) and (b) are the core diagnostic criteria for insomnia according to the International Classification of Sleep Disorders (ICSD)¹³. These were supplemented in (c) by empirically derived quantitative criteria¹⁴.

The justifications for the cutoffs for the daytime functioning questionnaires have been previously reported¹⁴. The ICSD does not provide quantitative criteria for what constitutes impaired daytime functioning; nor does it specify how qualitatively severe such impairment should be to satisfy the insomnia diagnosis. Using several questionnaires as discussed in the following paragraphs to assess this aspect of insomnia, we resorted to contriving what appeared to us to be reasonable criteria to establish at least minimum daytime impairment.

For the Epworth Sleepiness Scale (ESS), norms are not available; however, information from one study reported the mean to be 4.6 and the standard deviation (SD) as 2.8 for normal sleepers¹⁵. In addition, this study found a correlation between insomnia and scores on the ESS. Based on these data, we used a cutoff of 1 SD above the mean (7.4) to classify significant sleepiness.

The Insomnia Impact Scale does not have standardized norms. We used a cutoff of 125 to identify a significant complaint in daytime functioning. This cutoff is between the mean for individuals with insomnia seeking treatment and college students who report insomnia¹⁶.

The Fatigue Severity Scale also lacks standardized norms. In a sample of persons reporting insomnia, who were seeking treatment, the average score was 6.0, SD = 0.5¹⁷. Based on these data, a cutoff was set at 1 SD below the mean (5.5).

The Beck Depression Inventory is a standardized scale, with a score of 10 indicating mild depression. Scores of 10 or above were considered indicative of daytime impairment¹⁸.

The State-Trait Anxiety Inventory is a commonly used anxiety measure with norms available for psychiatric inpatients and outpatients. We selected a cutoff of 37 which is 1 SD below the mean for psychiatric inpatients who have an anxiety diagnosis¹⁹.

Measures

The study packet for the epidemiological survey contained sleep diaries for two weeks and seven daytime functioning questionnaires. Two measures were particularly salient for the current study: an experimenter-designed health survey that contained questions about vitamin use and the 14-day sleep diary. The portion of the health questionnaire devoted to vitamin use required participants to list the following: all vitamins taken in the last month, frequency with which they were taken, time of day taken, and the purpose of use.

The sleep diary, given elsewhere¹¹, provided a subjective assessment of the following variables: the time each participant entered bed the night before, how long it took to fall asleep, number of nocturnal awakenings, the time spent awake during those awakenings, the time of awakening, the time of rising from bed in the morning, and a sleep quality rating. Information from the completed sleep diary allowed us to compute the following six sleep pattern and quality variables: sleep onset latency (SOL), number of awakenings (NWAK), wake time after sleep onset (WASO), sleep efficiency percent (SE), total sleep time (TST), and sleep quality rating (SQR). SE is TST divided by the amount of time spent in bed $\times 100$. The SQR is a subjective estimate of sleep quality given in a five-point scale ranging from 1 (poor) to 5 (excellent).

Procedure

Random-digit dialing was accomplished by selecting all valid three-digit prefixes in use in Shelby County and pairing them with randomly generated four-digit numbers. This method improved efficiency and cost effectiveness by minimizing the amount of non-working numbers. Research assistants worked their way through these phone lists to solicit participants.

When a potential participant was reached, the research assistant delivered a one-minute pre-specified recruitment protocol. The protocol identified the research assistant and described the study of the experience of sleep that people have. The potential participant was then asked if he or she was interested in taking part and willing to fill out a one-hour packet of questionnaires over a two-week period in their home. Potential participants were informed that the questionnaires focused on sleep habits and related daytime functioning issues and that they would be compensated for their time. Those individuals who were interested were mailed a questionnaire packet. Upon receiving the packet, participants were instructed to fill out the sleep diary for 14 consecutive days and then fill out the set of daytime functioning questionnaires that included vitamin usage. After the diary and questionnaires were complete, the participant was instructed to return the materials to researchers in a postage-paid envelope. More detailed information on the methods of this survey is given elsewhere¹¹. The response rate for the study was 18.3%. This study posed a heavy participant burden, and this response rate is typical of such studies¹¹.

Results

The goal of these analyses was to explore the association between vitamins and sleep. Because this is one of the first investigations in this area, we were more concerned about minimizing Type II error than Type I error. When venturing in a new domain, it is important to be careful

not to close off areas of exploration. As we were interested in detecting any association between vitamins and sleep that might exist, we used several different groupings of vitamins. In addition, we also report marginally significant results ($p < .10$) to highlight areas that may potentially be useful to explore further.

Initially, participants were classified by the type of vitamin they reported taking. There were 10 reported groups: no vitamin, vitamin A, B, C, E, niacin, antioxidants, multivitamin (a single vitamin pill composed of a broad spectrum of vitamins), multiple vitamins (more than one individual vitamin pill), and other. Frequencies were calculated to determine the number of participants in each category. Several of the single-vitamin categories had less than 10 participants and were, therefore, merged into a single vitamin category. This process produced a total of five vitamin groups: no vitamin, multivitamin, single vitamin, multiple vitamins, and vitamin E. A one-factor multivariate analysis of variance (MANOVA) compared these five vitamin groups on the set of sleep variables of interest (SOL, NWAK, WASO, SE, TST, and SQR). This analysis proved non-significant, Wilks' $\Lambda = 0.93$, $F(28, 1833) = 1.37$, *ns*. The means of the sleep variables for each of the vitamin groupings are listed in Table 2. Though nonsignificant, the few individuals taking vitamin E reported the best sleep on every variable.

We intended to explore the possibility that time of day or frequency of vitamin use was associated with sleep effects. However, the uniformity of responses on these two variables did not provide sufficient variability to investigate the potential role of these factors. Eighty-two percent of participants took their vitamins in the morning, and 85% took their vitamins once a day.

After examining the individual means and N's of each vitamin group, it became clear that most vitamin users were congregating in multiple-vitamin categories and it seemed useful to more carefully explore this segment. To maximize statistical power and flesh out the exploratory potential of this study, participants were re-grouped into two vitamin categories. Participants taking single vitamins were excluded from the analyses and participants who were taking multiple or multivitamins were combined into a single group. We contrasted these two vitamin groups (no-vitamin vs. multi-/multiple vitamins) in a MANOVA on our set of sleep variables (SOL, NWAK, WASO, SE, TST, and SQR) and this proved significant, Wilks' $\Lambda = 0.95$, $F(7, 472) = 3.47$, $p < .01$. Univariate follow-up revealed that the groups differed on NWAK and WASO, though the magnitude of these differences was modest (see Table 3). Participants in the multi-/multiple vitamin group reported more awakenings ($M = 1.8$, $SD = 1.1$) than those in the no-vitamin group ($M = 1.4$, $SD = 1.0$), $F(1, 478) = 17.91$, $p < 0.001$, and more time awake after sleep onset ($M = 29.3$, $SD = 30.4$) than those in the no-vitamin group ($M = 24.2$, $SD = 26.9$), $F(1, 478) = 4.21$, $p < 0.05$. See Table 3 for a list of means by vitamin grouping.

The demographic information for participants in the final vitamin grouping is given in Table 4. To assess the association between vitamin use and demographic variables, several analyses were undertaken. We determined that age significantly correlated with vitamin grouping, $r = 0.28$, $p < 0.01$. Second, two separate chi-square tests of independence were conducted to assess the proportional differences between vitamin users and non-vitamin users based on gender and ethnicity. The chi-square tests for gender and ethnicity were both significant $\chi^2(1) = 12.6$ and $\chi^2(1) = 15.6$, respectively, all p 's < 0.01 . We reconsidered the above MANOVA incorporating age as a covariate and ethnicity and gender as blocked factors. The main effect of vitamin group was reduced but marginally significant, Wilks' $\Lambda = 0.98$, $F(6, 462) = 1.89$, $p = 0.08$. Univariate follow-up tests showed that there was only a difference in NWAK between groups, such that those taking vitamins reported more awakenings than those not taking vitamins, $F(1, 467) = 3.93$, $p < 0.05$. Although the omnibus test is marginally significant, it does suggest that vitamin use may be associated with sleep independent of demographic variables.

A chi-square test of independence was conducted to assess whether other medications could account for the difference in sleep variables between the vitamin and no-vitamin groups. Medications that had sleep-promoting effects included hypnotics, over-the-counter medications, herbal supplements, and antidepressants. The chi-square test showed that there was a higher but non-significant proportion of participants in the vitamin group who were taking sleep-promoting medications at bedtime as compared to the no-vitamin group, $\chi^2(1) = 0.09$, *ns*.

A chi-square goodness-of-fit test evaluated whether the proportion of insomniacs in the multi-/multiple vitamin group was significantly different from the proportion of insomniacs in the sample who reported no vitamin use. The chi-square test contrasted the observed proportion of insomniacs in the multi-/multiple group (21.6%) to expected (17.8%), which was marginally significant ($\chi^2(1) = 3.45$, $p = 0.06$). Insomniacs were over-represented in the multi-/multiple vitamin group compared to the no-vitamin group.

A one-way MANOVA tested differences between the insomniacs taking vitamins and insomniacs who were not on the set of sleep variables. The overall model was non-significant, Wilks' $\Lambda = 0.88$, $F(7, 84) = 1.71$, *ns*.

Discussion

Use of a multivitamin or multiple single vitamins was associated with poorer sleep maintenance compared to individuals who did not take vitamin supplements. There was a tendency for vitamin users to have a greater number of awakenings during the night, more total wake time during the night, greater use of sleep medications, and a higher rate of insomnia than non-users. Controlling for age, gender, and ethnicity partially attenuated the sleep-vitamin association. Future research should examine the influence of these variables more closely to better illuminate differential effects vitamins may have on sleep for different populations.

This study was conducted to stimulate a scientific dialogue on the subject of vitamins and sleep, not to resolve the matter, and many questions remain unanswered. There are at least five plausible interpretations for the observed association between vitamin use and disturbed sleep, and the present study cannot assign differential credence to any one. First, vitamin use causes disturbed sleep in some individuals. Second, no single vitamin causes disturbed sleep, but the interaction of some unknown combination of vitamins does cause disturbed sleep. Third, individuals experiencing disturbed sleep are more likely to initiate vitamin use. Fourth, there is no causal link between vitamins and poor sleep, but factors that motivate insomnia, such as anxiety and depression, also invite vitamin use. Fifth, the results of this study are unreliable and unreplicable.

This is one of the first studies to test the association between vitamins and sleep. These data should be considered preliminary, needing replication, and needing clarification, but are nonetheless provocative and worthy of further investigation. Methodological shortcomings and low response rate restricted our ability to tease out potentially important associations in this data set. For example, we could not evaluate dose effects, time of day administration, or duration of use. Dosing may be of particular importance because either toxic or inadequate amounts of vitamins have been shown to affect sleep adversely. In addition, inadequate distribution of sample size prevented analysis of particular vitamins, such as possible beneficial effects of vitamin E. Like all other cross-sectional studies, uncontrolled variables may have corrupted the age influence. Finally, we did not collect data on herbal supplements so their influence in the present study is indeterminate.

For future consideration, one plausible methodological approach that would illuminate salient factors would be to assign vitamin use, singly and in combinations, to normal sleeping

volunteers and observe sleep progress. The inclusion of a placebo vitamin condition would be a valuable feature of such a study. Similarly, this study could be conducted in insomnia patients to determine if these individuals are particularly sensitive to the effects of vitamin and experience further sleep deterioration. Care should also be taken to assess what, if any, other types of herbal or folk remedies may be taken for sleep, as some (e.g., valerian) have been found to have soporific effects.

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Table 1**Diagnostic Criteria for Insomnia**

- (1) Complaint of insomnia
 - Reported current insomnia on health survey
- (2) Poor sleep
 - SOL or WASO ≥ 31 minutes
 - occurring ≥ 3 nights a week, and
 - duration ≥ 6 months
- (3) Impaired daytime functioning on at least one of these:
 - Epworth Sleepiness Scale score ≥ 7.4
 - Fatigue Severity Scale score ≥ 5.5
 - Insomnia Impact Scale score ≥ 125
 - Beck Depression Inventory score ≥ 10
 - State-Trait Anxiety Inventory score ≥ 37

SOL – sleep onset latency; WASO – wake time after sleep onset

Table 2

Sleep Variables by Initial Vitamin Grouping

	No Vitamin N = 262		Multivitamin N = 91		Single Vitamin N = 27		Multiple Vitamins N = 127		Vitamin E N = 12	
	M	SD	M	SD	M	SD	M	SD	M	SD
SOL ^a	23.2	18.5	21.4	16.0	27.3	24.4	24.5	23.6	16.3	10.6
NWAK ^b	1.4	1.0	1.1	1.1	1.8	1.1	1.9	1.1	1.0	0.7
WASO ^a	24.2	26.9	28.9	31.2	27.9	27.3	29.6	29.9	16.4	19.1
TST ^a	426.2	72.0	417.7	65.9	417.2	88.6	421.1	72.5	432.8	64.9
SE ^c	86.1	9.2	85.7	9.5	84.3	11.2	85.2	9.3	89.6	5.2
SQR ^d	3.4	0.6	3.4	0.7	3.3	0.7	3.5	0.7	3.7	0.9

Note 1. Comparisons between groups on all sleep variables were non-significant.

Note 2. SOL – sleep onset latency; NWAK – number of awakenings; WASO – wake time after sleep onset; TST – total sleep time; SE – sleep efficiency; SQR – sleep quality rating

^aUnit of measurement is minutes.

^bUnit of measurement is count of awakenings.

^cUnit of measurement is percentage.

^dUnit of measurement is rating on a 5-point scale

Table 3

Sleep Variables by Final Vitamin Grouping

	No Vitamin		Multi-/Multiple Vitamins	
	N = 263		N = 218	
	M	SD	M	SD
SOL ^a	23.2	18.5	23.2	20.8
NWAK ^{b**}	1.4	1.0	1.8	1.1
WASO ^{a*}	24.2	26.9	29.3	30.4
TST ^a	426.2	72.0	419.7	69.7
SE ^c	86.1	9.2	85.4	9.3
SQR ^d	3.4	0.6	3.4	0.7

* p < .05.

** p < .01.

Note. SOL – sleep onset latency; NWAK – number of awakenings; WASO – wake time after sleep onset; TST – total sleep time; SE – sleep efficiency; SQR – sleep quality rating

^aUnit of measurement is minutes.

^bUnit of measurement is count of awakenings.

^cUnit of measurement is percentage.

^dUnit of measurement is rating on a 5-point scale

Table 4

Demographic Variables by Vitamin Group

	No-Vitamin Group	Vitamin Group
Age **	<i>M</i> = 52.9, <i>SD</i> = 20.6	<i>M</i> = 64.3, <i>SD</i> = 17.2
Gender **	101 females 162 males	119 females 99 males
Ethnicity **	93 African-American 164 Caucasian 5 Asian	42 African-American 172 Caucasian 1 Hispanic
Sleep *	45 insomniacs 208 normal sleepers	47 insomniacs 161 normal sleepers

*
p = .06.**
p < .01.