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Original Research Article

The Link between Potassium and Mild Cognitive Impairment in Mexican-Americans

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Keywords

Hispanic population · Cognition · Memory · Electrolytes

Abstract

Background: Recent evidence suggests that increasing dietary intake of minerals reduces the risk of dementia. This study aimed to examine the relationship between potassium and diagnosis of mild cognitive impairment (MCI) in a sample of older Mexican-Americans from rural and urban populations. ***Methods:*** The sample was formed of a total of 139 participants with MCI and 371 normal controls from two independent cohorts: a rural cohort (Facing Rural Obstacles to Healthcare Now through Intervention, Education and Research [Project FRONTIER]) and an urban cohort (the Health and Aging Brain among Latino Elders [HABLE] study). Serum electrolytes examined were sodium and potassium. Age and education were entered in the model as covariates. ***Results:*** Across both cohorts, the Project FRONTIER (OR = 3.1; p = 0.01) and the HABLE Project (OR = 2.0; p = 0.04), the results indicated that serum potassium levels significantly increased the risk of diagnosis of MCI. ***Conclusion:*** Our finding suggested a link between serum potassium levels and a diagnosis of MCI in Mexican-Americans. The results of this study support a previous research which has suggested that the risk factors for MCI may vary by ethnicity.

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Introduction

Alzheimer disease (AD), the most common form of dementia, affects more than 5 million Americans, placing a tremendous strain on our healthcare system [1]. Due to the severity of the problem, research on potentially modifiable risk factors has increased, including the investigation of the role of diet in the onset and prevention of AD [2]. Recent guidelines [3] for AD prevention addressed such dietary factors as saturated fat and trans fat intake, vitamins (especially vitamins E and B_{12}), and the intake of vegetables, legumes, and fruits. Higher levels of the minerals iron and copper were identified as being related to increased risk for AD but the role of other minerals (such as potassium) in cognitive decline was not addressed. The literature on minerals and cognitive impairment associated with dementia is limited. Ozawa et al. [4] studied a community-based Japanese cohort investigating the relationship of self-reported dietary intake of potassium, calcium, and magnesium and the occurrence of dementia over a 17-year period. They found that increased dietary intake of potassium, calcium, and magnesium reduced the risk of all-cause dementia especially vascular dementia. The risk of AD tended to decrease with higher reported dietary mineral intake, but there was no significant linear progression. In another study assessing potassium and cognitive abilities, Cisternas et al. [5] used an animal model of AD to find that increased potassium yielded reduced markers of oxidative stress and inflammation and improved cognition. Additionally, potassium was related to a change in the aggregation pattern of Aβ peptide and a reduction in tau phosphorylation. Mielke et al. [6] investigated the relationship between potassium and Aβ42, a cerebrospinal fluid marker that was decreased in AD in a prospective population-based study of 1,622 women over a 24-year period. An association was found between higher serum potassium and higher levels of Aβ42 in 1968 and 1974, but not in later years, suggesting that potassium is associated with dementia in midlife but not late life. Similar patterns have been found in studies of other vascular risks, such as hypertension [7], high cholesterol [8], and obesity [9]. Despite the growing literature on the relationship of potassium to AD, there has been little research on the relationship of potassium to mild cognitive impairment (MCI). MCI is defined as a decline in cognition that does not meet criteria for dementia but is not normal for the individual's age and does not significantly impair daily functioning [10] and frequently progresses to dementia [11]. Cherbuin et al. [12] investigated the relationship of dietary mineral intake to MCI and other mild cognitive disorders. Although intake of iron, magnesium, and potassium were found to be associated with the risk of progression from normal aging to MCI and mild cognitive disorders, potassium was found to be negatively related to progression to MCI, so that these investigators surmised that it may be a protective factor earlier in the disease process, but becomes a risk factor closer to the time of clinical diagnosis. Although the relationship of potassium to cognitive decline is complex, there is evidence that dietary potassium may have a role in the development of MCI and AD. However, recent studies have not assessed ethnicity as a variable that may affect the relationship. The Mexican-American population is rapidly expanding and represents the fastest aging segment of the US Hispanic population. The literature on AD and dementia in Mexican-Americans shows that they tend to be diagnosed at a younger age, are diagnosed at a more advanced stage of progression and have a disproportionate burden of vascular and other modifiable risk factors [13, 14]. Research on the potassium intake among Mexican-American children has shown that the vast majority have higher sodium intake and lower potassium intake than children from other ethnic groups [15]. A study of Mexican-American women found that the intake of potassium was lower than established standards in 70% of the study population [16]. These studies suggest that Mexican-Americans may be at risk for low dietary potassium intake which may impact cognition and the development of MCI. Potassium comes primarily from fruit and vegetable intake [17]. There are reported differences in potassium intake between urban and rural Mexican-Americans [18] that may affect the potassium/MCI relationship. The current study investigates the association of potassium levels and the diagnosis of MCI in a sample of Mexican-Americans. Additionally, urban versus rural effects were analyzed in light of recent research that has shown multiple differences between these groups.

Methods

A total of 510 Mexican-American participants aged 50 and older were recruited from two independent cohorts (Project FRONTIER and the HABLE Study). Project FRONTIER [19] is a study of rural health designed to examine factors affecting cognition. The HABLE is a study examining factors affecting cognition in Hispanic elders in an urban setting. The recruitment and research protocols for both studies are similar. Both studies used a community-based participatory research approach. Participants were recruited through a variety of methods such as: brochures/flyers, presentations and events, in-person and/or door-to-door solicitation as well as snowball recruitment. Recruitment is generally completed by community recruiters. To be included in the study, a participant must be ≥50 years old.

Following completion of the consent process, the participants underwent an interview (participant and informant), standardized medical examination, clinical labs, and neuropsychological testing. Consensus diagnoses of medical, psychiatric, and cognitive conditions were assigned by a panel of clinical experts consisting of psychologists, geriatric psychiatrists, geriatricians, and neuropsychologists according to standard criteria. The following diagnoses were assigned to participants: normal cognition (no observed deficits on cognitive examination and no self- or informant report of cognitive dysfunction adapted from the Mayo criteria) [20], age-associated cognitive impairment [21], MCI [22], AD [23], vascular dementia [24], or dementia not otherwise specified (meets criteria for dementia but does not fit into one of the other categories). Participants who were classified as cognitively normal controls performed within normal limits on all psychometric assessments. All participants from the FRONTIER and HABLE cohorts that had been classified as cognitively normal or MCI by consensus review and had a complete fasting blood test including potassium were included in the sample.

Fasting blood test was conducted by a CLIA (Clinical Laboratory Improvement Amendments)-certified lab, and assays included a lipid panel, comprehensive metabolic panel, complete blood count, blood glucose, HbA_{1c}, vitamin B_{12}, and thyroid levels. Serum electrolytes included in this study were sodium and potassium. Potassium levels were measured using the ion-selective electrode method and were reported as millimoles per liter (mmol/L).

The appropriate institutional review boards approved the FRONTIER (n = 195) and HABLE (n = 315) studies, including the informed consent forms.

Statistical Analysis

Data were analyzed using logistic regression analyses. Analyses were conducted using SPSS version 22 software. Serum electrolytes were entered into the model along with age and education as covariates.

Results

Demographic characteristics of the two sample cohorts are provided in Table 1. Although the two samples differed in the setting (FRONTIER – rural; HABLE – urban), the two samples did not differ in measures of socioeconomic status or health status. The analyses were split by diagnosis, normal control and MCI.

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Table 1. Demographics and characteristics of the FRONTIER and the HABLE cohorts

	Control	MCI
FRONTIER		
Age (mean ± SD, range), years	53.9±9.1, 40–83	60.4±11.1, 40–82
Education (mean ± SD, range), years	7.8±3.9, 0–18	6.6±4.3, 0–15
Female, %	76	56
Potassium (mean ± SD, range), mmol/L	4.0±0.37, 2.8–5.3	4.2±0.46, 3.3–5.4
Sodium (mean ± SD, range), mmol/L	140±2.3, 134–146	140±2.6, 135–145
HABLE		
Age (mean ± SD, range), years	58.5±6.6, 50–81	65.9±8.3, 50–86
Education (mean ± SD, range), years	8.5±4.2, 0–18	6.2±4.0, 0–17
Female, %	73	62
Potassium (mean ± SD, range), mmol/L	4.3±0.40, 3.2–5.4	4.4±0.48, 3.5–5.5
Sodium (mean ± SD, range), mmol/L	139±2.6, 129–149	139±2.6, 133–145

MCI, mild cognitive impairment; SD, standard deviation.

Table 2. Logistic regression results: risk factor for MCI

	B	SE B	Sig	Odds ratio (95% CI)
FRONTIER				
Age	0.048	0.022	0.028	1.05 (1.00–1.09)
Education	–0.005	0.057	0.931	0.99 (0.88–1.11)
Potassium	1.151	0.486	0.018	3.16 (1.21–8.19)
Sodium	0.061	0.109	0.577	1.06 (0.85–1.31)
HABLE				
Age	0.118	0.019	0.000	1.12 (1.08–1.16)
Education	–0.102	0.035	0.003	0.90 (0.84–0.96)
Potassium	0.726	0.355	0.041	2.06 (1.03–4.14)
Sodium	–0.016	0.072	0.823	0.98 (0.85–1.13)

SE, standard error; Sig, significance; CI, confidence interval.

Project FRONTIER

The sample consisted of 195 participants (152 normal controls and 43 MCI). On average, MCI participants were older, with a mean age of 60.4 years (SD = 11.1) and had lower levels of education. Normal control participants had a mean age of 53.9 years (SD = 9.1) and had an average of 8 years of education. Approximately 76% (116 participants) of the normal control sample were female and 24% (36 participants) were male. For the MCI sample, 56% (24 participants) were female and 44% (19 participants) were male.

The results indicated that potassium successfully predicted MCI status (OR = 3.1; p = 0.01). No other electrolytes were significant. Age was also a significant predictor of MCI status, but that was not the case for education level (Table 2).

HABLE Cohort

A total of 315 participants were part of the HABLE cohort (219 normal controls and 96 MCI). MCI participants were older, with a mean age of 65.9 years (SD = 8.3) and had lower

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education levels. Normal control participants had a mean age of 58.5 years (SD = 6.6) and an average of 9 years of education. About 73% (160 participants) of the normal control sample were female and 27% (59 participants) were male. For the MCI group, 62% (60 participants) were female and 38% (36 participants) were male.

Potassium was the only significant electrolyte that successfully predicted MCI status (OR = 2.0; $p = 0.04$). For this group, age and education level were significant (Table 2).

Discussion

In the current study, we examined the relationship of potassium level to MCI status in Mexican-Americans. In both rural and urban groups, a higher potassium level in MCI participants was predictive of MCI status. These findings contradict our premise of lower potassium levels that are related to MCI status. A plausible explanation may be the different socioeconomic status and biological components in our population. Also, this can be a result of confounding caused by unadjusted factors. Similar findings were reported by Nowak et al. [25] in 2018. In 1,194 subjects from the Health Aging and Body Composition study, they found that higher sodium and potassium intake was associated with increased odds of cognitive decline. For FRONTIER participants, the potassium level and age were predictors of MCI status, while education did not demonstrate a significant relationship. For HABLE subjects, the potassium level, age, and education were all significant predictors of MCI. These findings are important in terms of potassium as a modifiable risk factor for Mexican-Americans.

In the present study, we did not find a significant relationship between sodium level and MCI. Our findings agreed with findings from the Women's Health Initiative Memory Study [26] that reported no association between sodium intake and MCI.

Analysis of data comparing urban to rural participants showed that potassium was a risk factor for both groups. The literature regarding urban and rural differences in subjects has been mixed, but most reports indicate that urban areas are associated with less cognitive decline, less obesity [25, 26], greater physical activity [27], and lower rates of mortality and morbidity from chronic health conditions [28]. The reported differences in cognitive functioning between rural and urban participants have been variously attributed to different factors, including acculturation [29, 30], stage of change [16], neighborhood linguistic isolation [31], and geographic location [18]. However, the findings of Satia-Abouta et al. [32] suggest that, while acculturation had an impact on the blood pressure of Mexican-American women, the dietary impact of sodium and potassium was not as important as the way the subjects metabolized these nutrients.

Research into ethnic variations in physiological functioning has shown genetic influence in wide-ranging areas (e.g., macular degeneration [33], lipoprotein subfractions [34], and type 2 diabetes susceptibility [35]) as well as ethnic differences in drug metabolism [36]. These many ethnic variations allow us to find physiological processes that can be altered to provide treatments specific to an ethnic group, which may lead to effective personalized medicine.

A strength of this study is that the measures used with both groups were very similar, facilitating comparisons. Limitations of this study include a small sample size and data that are cross-sectional in nature. Additionally, although many investigators stress the role of diet in regulating potassium levels, information was not available for these participants. Since this study focuses on Mexican-Americans, the generalizability of the findings is limited in other populations.

Further studies are needed to expand knowledge of the various factors involved in potassium levels, with an attempt to understand which of the influences described in the literature are most important in clinical settings. The HABLE study is ongoing, and we are collecting longitudinal data that will allow us to better understand this relationship in the future.

Exploration of ethnicities is important to the understanding of diverse patients, but, in this case, it is particularly pertinent as potassium levels are modifiable. Discovering ethnic differences can lead to novel treatments based on these differences that may be more beneficial than current standard care for diseases.

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Disclosure Statement

The authors have no conflicts of interest to declare.

Author Contributions

All authors have read the paper and have agreed to be listed as authors. Conceived and designed the study: R.M.V., S.E.L., A.G., G.D.R., J.R.O., J.R.H., S.E.O., and L.A.J. Acquisition of subjects/data: R.M.V., S.E.L., A.G., and G.D.R. Analysis and interpretation of data: A.G., J.R.O., J.R.H., S.E.O., and L.A.J. Preparation of the manuscript: R.M.V., A.G., J.R.O., J.R.H., S.E.O., and L.A.J. Agree with manuscript results and conclusions: R.M.V., S.E.L., A.G., G.D.R., J.R.O., J.R.H., S.E.O., and L.A.J.

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