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Race differences in the relation of vitamins A, C, E, and β-carotene to metabolic and inflammatory biomarkers

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ABSTRACT

Using archival data, we conducted a secondary analysis to examine race differences in the relation of serum vitamins A, C, E and β-carotene to insulin resistance (IR), fasting insulin and glucose, high sensitivity C-reactive protein (hs-CRP), and leukocyte count in 176 non-smoking, healthy, white, and African American (AA) adults aged 18 to 65 years (48% women, 33% AA). We hypothesized that micronutrient concentrations would be associated with early risk markers of cardiometabolic diseases in a race-dependent manner. Fasting blood samples were analyzed for micronutrients, insulin, glucose, hs-CRP, and leukocyte count. Insulin resistance was estimated using the homeostatic model assessment. After adjusting for age, body mass index, gender, educational level, use of vitamin supplements, alcohol intake, leisure time physical activity, menopausal status, and total cholesterol, we observed that β-carotene was significantly associated with insulin resistance and fasting insulin in a race-dependent manner. Among AA, lower β-carotene levels were associated with higher estimates of insulin resistance and fasting insulin; whereas, these same associations were not significant for whites. Race also significantly moderated the relation of vitamin C to leukocyte count, with lower vitamin C being associated with higher leukocyte count only in AA but not whites. For all subjects, lower β-carotene was associated with higher hs-CRP. In AA, but not whites, lower levels of β-carotene and vitamin C were significantly associated with early risk markers implicated in cardiometabolic conditions and cancer. Whether or not lower levels of micronutrients contribute uniquely to racial health disparities is a worthwhile aim for future research.

1. Introduction

Despite improvements in the overall health of the population of the United States, racial health disparities continue to pose a major challenge [1]. When comparing African Americans (AA) to whites, it is overwhelmingly evident that AA have worse health outcomes and higher mortality rates from type 2 diabetes and cardiovascular disease (CVD) [2–4]. Similarly, AA have a lower rate of survival for a variety of cancers [5,6]. At this time, factors contributing to race-related differences are not well understood [7]. However, it has been postulated that racial health disparities may reflect race differences in the prevalence of obesity [8,9], hypertension [10–12], hyperinsulinemia [13,14], insulin resistance (IR) [15,16], and inflammation [15,17], which are factors implicated in heart disease, type 2 diabetes, and obesity-related cancers [18–22]. While the best

Abbreviations: AA, African American; HOMA, homeostatic model assessment; IR, insulin resistance; CVD, cardiovascular disease; hs-CRP, high sensitivity C-reactive protein.

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risk models are successful in predicting disease-related outcomes, they fall short of fully explaining the underlying causes of racial health disparities [23].

It has been reported that cardiometabolic conditions and various forms of cancers are closely linked to dietary intake and blood levels of micronutrients [24–27]. To date, the most consistent findings have been reported for carotenoids where both dietary intake and serum concentrations have been inversely related to occurrence of type 2 diabetes [28,29] and CVD mortality [30]. As suggested by a recent meta-analysis, lower levels of carotenoids are also associated with an increased risk of breast cancer [31], with recent evidence suggesting that this association is stronger when carotenoids are assessed in blood [32]. Low serum levels of β-carotene have also been associated with an increased risk of colon and colorectal cancers [33] and non-Hodgkin lymphoma [34]. In contrast, higher levels of β-carotene appear to be associated with an increased risk of prostate cancer [35]. For vitamins E and C; however, findings have been inconsistent, with some studies reporting inverse, albeit modest, associations with CVD [30,36–38], type 2 diabetes [39,40], and various forms of cancer [41,42]. In light of these prior findings, the greater prevalence of cardiometabolic conditions, and some forms of cancers in AA, we examined whether the relation of serum micronutrient concentrations to early risk biomarkers differed in AA and whites. For the most part, prior studies either adjusted for the effects of race or did not include sufficient numbers of AA participants to conduct analysis [29,43–45]. Interestingly, one study observed that the relation of serum β-carotene concentration to C-reactive protein (CRP) was moderated by race, although no additional details were provided [46]. More recently, one study suggested that the relation of a serum indicator of vitamin D mediates race-differences in the prevalence of insulin resistance in AA and whites [47].

Surprisingly, race differences in early risk factors of cardiometabolic conditions and some forms of cancer, such as hyperinsulinemia and insulin resistance, have not been associated with race differences in dietary intake [24], even when intake of fruits and vegetables has been reported to be higher for AA compared to whites [24,48]. Those findings may explain the results of one meta-analysis that suggested that blood concentrations of micronutrients, relative to dietary assessment of intake, were more strongly associated with breast cancer risk [32]. Given the lack of evidence for the relation of early risk markers to dietary intake and the relative strength of the relation of blood concentrations to disease, we determined whether blood concentrations of micronutrients are associated with early markers of disease risk and whether these associations are race-dependent. More specifically, we examined the cross-sectional relationship of β-carotene, vitamin A, vitamin C, and vitamin E to metabolic and inflammatory biomarkers in a sample of apparently healthy, non-smoking community volunteers who self-identified as either white or AA. The data were derived from a study that examined the relation of psychosocial factors to early risk biomarkers of CVD and type 2 diabetes [49–52]. The aim of this secondary analysis, however, was to examine the relation of micronutrients to early risk biomarkers and whether these associations differed by race. We hypothesized that the relationship between micronutrient concentrations and early risk markers of cardiometabolic conditions would be race-dependent. Analyses focused on determining whether or not race moderated the relation of vitamin A, C, E, and β-carotene to fasting insulin and glucose, estimation for insulin resistance, high-sensitivity (hs)-CRP and white blood cell count. Given the high prevalence of nutrition related cardiometabolic conditions among AA, we speculated that micronutrients would be more strongly associated with early risk markers in AA than in whites.

2. Methods and materials

2.1. *Participants and recruitment*

Subjects in these analyses were 176, apparently healthy, adults (age, 18-65 years) that were recruited between 1999 and 2004 and self-identified as being white or AA. The 176 subjects in these analyses represent a subsample of 210 adults who enrolled in the initial study [53]. The remaining 34 subjects self-identified as being of another race or ethnicity. The procedures described in this article are the same as those used in the original study [53]. Individuals were initially screened for health criteria using a self-report health questionnaire and in-person interview. Inclusion criteria included the following: negative history and no current diagnosis of psychiatric conditions; no current or previous use of anti-depressant medications; and no chronic medical conditions, such as asthma, allergies, arthritis, diabetes, cancer, and cardiovascular diseases. Subjects who had a history of smoking were excluded. We excluded women if they reported use of oral contraceptives or hormone replacement therapy within the previous 6 months. This study was approved by the institutional review board of Duke University and informed consent was obtained prior to the collection of data.

2.2. *Protocol*

Following an overnight fast, subjects reported to the laboratory. Subjects were instructed to not use prescription or over-the-counter medications, including low-dose aspirin, during the two-weeks prior to the study visit. On the day of the study visit, staff verified via interview that participants were free of acute infections, had not incurred any injuries, and had not undergone any medical/dental procedures two weeks prior, which are conditions known to increase C-reactive protein (hs-CRP) and other markers of inflammation. To minimize menstrual cycle effects, pre-menopausal women were studied during the follicular phase (days 4-9 of the menstrual cycle).

2.3. *Biomarkers*

Fasting blood samples were analyzed for vitamins A, C, E, β-carotene, lipids, and hs-CRP. Blood samples used to assess micronutrients were drawn in chilled serum separator tubes containing Na-heparin. Careful attention was placed on protecting samples from light. Samples were immediately centrifuged and serum was transferred to an amber plastic transport tube. Due to issues with stability, analyses were