Brain, Behavior, and Immunity xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Full-length Article

The Dietary Inflammatory Index is associated with elevated white blood cell counts in the National Health and Nutrition Examination Survey

Michael D. Wirth [a,b,c,*], Maria Sevoyan [b], Lorne Hofseth [d], Nitin Shivappa [a,b,c], Thomas G. Hurley [a,b], James R. Hébert [a,b,c]

[a] Cancer Prevention and Control Program, University of South Carolina, 915 Greene Street, Suite 200, Columbia, SC 29208, United States
[b] Department of Epidemiology and Biostatistics, University of South Carolina, 915 Greene Street, Suite 200, Columbia, SC 29208, United States
[c] Connecting Health Innovations, LLC, 915 Greene Street, Suite 200, Columbia, SC 29208, United States
[d] University of South Carolina, South Carolina College of Pharmacy, 715 Sumter Street, CLS 513B, Columbia, SC 29208, United States

ARTICLE INFO

Article history:
Received 14 August 2017
Received in revised form 28 November 2017
Accepted 2 December 2017
Available online xxxx

Keywords:
Dietary Inflammatory Index
Leukocytes
Diet
Nutrition
NHANES

ABSTRACT

White blood cells (WBCs) are considered a reliable biomarker of inflammation. Elevations in both WBCs and pro-inflammatory cytokines are associated with several chronic conditions. Diet is a strong moderator of inflammation and WBCs. The purpose of this study was to examine the association between the Dietary Inflammatory Index (DII®) and WBCs using data from the United States National Health and Nutrition Examination Survey (NHANES). NHANES is a cross-sectional study that occurs in two-year cycles. Respondents from five cycles ($n = 26,046$) with available data on diet (collected through a single 24-h dietary recall [24HR]) and WBCs (derived using the Coulter method) were included. The DII (theoretical range is about −8 to +8) was derived from the micro and macronutrients calculated from the 24HR. Linear regression models, using survey design procedures, were used to estimate adjusted mean WBC (i.e., total, lymphocytes, monocytes, and neutrophils) counts and percentages by DII quartiles. Among all participants no statistically significant difference in WBCs were observed when comparing DII quartile 4 (most pro-inflammatory) to quartile 1 (most anti-inflammatory). However, a one-unit increase in the DII was associated with a 0.028 (1000 per μL) increase in total WBCs ($p = .01$). Additionally, a 0.024 increase in neutrophils ($p < .01$) was observed for a one-unit increase in the DII. In the group of participants with normal body mass index (BMI, 18.5–24.9 kg/m^2), those in DII quartile 4 had higher levels of total WBCs compared to subjects with normal BMI in DII quartile 1 (7.12 vs. 6.88, $p = .01$). Similar comparisons were observed for monocytes and neutrophils. However, these relationships were not observed for participants who were overweight or obese, which are pro-inflammatory conditions. Normal-weight individuals consuming more pro-inflammatory diets were more likely to have elevated WBCs. Because of its cross-sectional design, NHANES cannot inform directly on temporal relations, thus limiting causal inference. Future research is needed to examine the impact of anti-inflammatory diet adoption on lowering levels of WBCs, in addition to other inflammatory mediators.

1. Introduction

White blood cells (WBCs), or leukocytes, are one of three types of blood cells (other two include platelets and erythrocytes) that make up about 45% of whole blood (55% is plasma), which accounts for about 7% of an average human adult's body weight (Cameron and Grant, 1999; Pritchett and Reddy, 2015). Important functions of certain WBCs include, but are not limited to, destruction of virus-infected cells, directing the immune response through cytokine secretion, secretion of antibodies for phagocytosis detection (lymphocytes), destruction of pathogens by phagocytosis (neutrophils), and transformation into macrophages (monocytes) (Pritchett and Reddy, 2015). The specific properties and functions of the innate and adaptive immune systems have been described in detail elsewhere (Labrecque and Cermakian, 2015). It is important to note that elevations in WBCs can represent a normal response to infection and wound healing (Labrecque and Cermakian, 2015).

An important component of the immune system is the inflammatory response to injuries or insults. Cytokines are a type of

* Corresponding author at: Cancer Prevention and Control Program, University of South Carolina, 915 Greene Street, Suite 200, Columbia, SC 29208, United States.
E-mail address: wirthm@mailbox.sc.edu (M.D. Wirth).

https://doi.org/10.1016/j.bbi.2017.12.003
0889-1591/

Please cite this article in press as: Wirth, M.D., et al. The Dietary Inflammatory Index is associated with elevated white blood cell counts in the National Health and Nutrition Examination Survey. Brain Behav. Immun. (2017), https://doi.org/10.1016/j.bbi.2017.12.003

chemoattractants synthesized by macrophages with the capacity to activate other WBCs. They can act as second messengers and induce the expression of adhesion molecules on endothelial cells that promote attachment and transmigration of leukocytes (Levy, 1996; Pober and Cotran, 1990). Again, this is a necessary mechanism for proper wound healing and for combatting infections. However, concern is warranted when insults or injuries that increase inflammatory levels or WBCs become chronic over time. Given the reciprocal relationship between inflammatory cytokines and WBCs, a chronic injury or insult to the human body could create a perpetual cycle increasing levels of inflammatory cytokines and WBCs (Libby, 2007). Chronic levels of inflammation have been associated with numerous chronic conditions including, but not limited to, type 2 diabetes mellitus (T2DM), cardiovascular diseases (CVD), gastrointestinal illnesses, and cancer (Libby, 2007). WBCs have been considered a reliable cellular biomarker of inflammation (Kounis et al., 2015). Chronic elevation of WBCs has been linked to several chronic conditions including T2DM, coronary artery disease, stroke, and leukemia (Costas et al., 2016; Danesh et al., 1998; Ford, 2002; Libby et al., 2016; Vozarova et al., 2002).

One of the strongest environmental influencers of chronic systemic inflammation is diet (Ahluwalia et al., 2013). In general, diet patterns characterized by high consumption of fruits and vegetables, whole grains, and fish (e.g., Mediterranean) are associated with lower levels of systemic inflammation; whereas diets characterized by high consumption of total and saturated fats, protein, and simple carbohydrates (e.g., Western diet) are associated with higher levels of inflammation (Ahluwalia et al., 2013). Previous research has linked dietary patterns or indices to WBC counts. For example, studies utilizing indices and patterns such as the Mediterranean Diet Score (MDS), the Italian Mediterranean Index, indices measuring adherence to the Swedish or Flemish dietary recommendations, and the Healthy Eating Index (HEI) have demonstrated that healthier scores are inversely associated with leukocyte counts (Ambring et al., 2006; Bonaccio et al., 2014; Chrysohoou et al., 2004; Dias et al., 2015; Hoebeeck et al., 2011; Loprinzi et al., 2016). However, none of these dietary indices or patterns was developed specifically with respect to dietary inflammatory potential.

The Dietary Inflammatory Index (DII®) was developed to characterize an individual's dietary inflammatory potential using a quantitative scale from pro- to anti-inflammatory (Shivappa et al., 2014a). The DII was construct validated against inflammatory biomarkers (e.g., c-reactive protein, tumor necrosis factor-alpha, interleukin-6) in numerous studies (Julia et al., 2017; Shivappa et al., 2014b; Shivappa et al., 2016b; Tabung et al., 2015; Wirth et al., 2014). Additionally, the DII has been associated with a range of other inflammatory-related conditions including obesity, various cancers, CVD, telomere length, depression, asthma, and mortality (Graffouillere et al., 2016; Harmon et al., 2017; Kesse-Guyot et al., 2016; Neufcourt et al., 2016; Ruiz-Canela et al., 2015a; Shivappa et al., 2016a; Shivappa et al., 2015a; Shivappa et al., 2017b; Shivappa et al., 2015b; Shivappa et al., 2016b; Wirth et al., 2016b; Wirth et al., 2015; Wood et al., 2015). However, the DII has yet to be examined with respect to WBC levels. Therefore, the purpose of this study was to examine the cross-sectional association between DII scores and WBCs using the National Health and Nutrition Examination Survey (NHANES). Specifically, it was hypothesized that individuals with more pro-inflammatory diets would have elevated levels of WBCs compared to those with more anti-inflammatory diets. Additionally, given that both WBC levels and DII values differ according to body mass index (BMI) (Gregor and Hotamisligil, 2011; Ruiz-Canela et al., 2015a), which is known to be associated with chronic systemic inflammation, BMI was examined as a potential effect modifier.

2. Methods

2.1. Study population

NHANES collects cross-sectional information on American adults and children in two-year cycles. NHANES uses complex, multistage, probability cross-sectional sampling to ensure selection of participants from various geographical locations and racial/ethnic groups. This provides a representative sample of the entire United States population. NHANES participants start with an in-home interview where questionnaire information is obtained. This information includes a wide range of topics including demographics, medical histories, socioeconomic metrics, and behavioral, diet, and lifestyle habits. Participants are then invited for further examination in their mobile examination clinic (MEC) where biological samples are run and clinical tests conducted. For a full list of data available in NHANES and precise detail on data collection, please refer to their website and documentation (http://www.cdc.gov/nchs/nhanes.htm) (Johnson et al., 2013). From five 2-year cross-sectional cycles (i.e., 2005–2014), there were a total of 30,295 individuals aged ≥18 years. Of these individuals, 2618 were missing information on WBCs. An additional 1624 were missing dietary information. Lastly, seven participants were removed due to a reported energy intake of <100 kcal. This left an analytic sample size of 26,046. Participants provided informed consent and NHANES is continually reviewed by the National Center for Health Statistics Research and Ethics Review Board.

2.2. Outcomes assessment

To obtain leukocyte counts, blood draws were performed by trained phlebotomists during the participant visit to the MEC. Specific details on venipuncture can be found in the NHANES Laboratory Procedures Manual. Complete blood counts were conducted using the Coulter method (Coulter® HMX, Beckman Coulter, Brea, California) (CDC, 2013). The leukocytes analyzed in this study included total WBC, monocyte, lymphocyte, and neutrophil counts expressed as 1000 per microliter. Additionally, percentages of monocytes, lymphocytes, and neutrophils were examined. Although information on basophils and eosinophils was available, about 95% of participants had values below 0.4 (1000 per μL) for eosinophils and 99% had values below 0.2 (1000 per μL) for basophils. Given the limited range in values for these two leukocyte types, they were excluded from the analyses. All outcomes were treated as continuous measures.

2.3. The dietary inflammatory index and potential covariates

NHANES used 24-h dietary recall interviews (24HRs) to obtain dietary information. NHANES processed the dietary data to obtain micro and macronutrients by using the USDA's Food and Nutrient Database for Dietary Studies (FNDDS). The primary exposure of interest was the DII, which included the following macro and micronutrients (termed food parameters throughout): carbohydrates; fat; protein; vitamins A, B1, B2, B6, B12, C, D, E; niacin; grams of alcohol; saturated, monounsaturated, and polyunsaturated fatty acids; omega3 and omega6 polyunsaturated fatty acids; fiber; cholesterol; iron; magnesium; zinc; selenium; folic acid; beta carotene; and caffeine. Research from nearly 2000 peer-reviewed publications formed the basis of the DII. 'Inflammatory effect scores' were created from these peer-reviewed publications for each of the DII food parameters based on their effect on inflammatory cytokines (Shivappa et al., 2014a). At the same time, DII calculation is standardized to a regionally representative world database. This world database included dietary consumption from