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A case-control study of dietary salt intake in pediatric-onset multiple sclerosis

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ABSTRACT

Background: High salt intake may be associated with pro-inflammatory changes in the immune response, and increased clinical and MRI activity in adults with relapsing-remitting multiple sclerosis.
Objective: We sought to determine if dietary salt intake is associated with pediatric-onset MS risk in a multicenter, case-control study.
Methods: Pediatric-onset CIS/MS cases within four years of onset and controls less than 22 years old recruited from 14 pediatric-MS centers were studied. Dietary sodium intake was assessed using the validated Block Kids Food Screener (NutritionQuest). Sodium intake, excess sodium, and sodium terciles were compared between cases and controls. Logistic regression models were adjusted for age, gender, ethnicity, body mass index, and socioeconomic status.
Results: Among 170 cases (mean age = 15.2 ± 3.5) and 331 controls (mean age = 14.0 ± 3.7), no significant difference in unadjusted mean sodium intake was found between cases (2044 mg/d) and controls (2030 mg/d, $p = 0.99$). The proportion of subjects consuming excess sodium, based on the adequate intake for age and gender, was similar between cases and controls (65% versus 69%, $p = 0.34$). There were no increased odds of higher sodium intake among cases as compared to controls (for each 100 mg/d increase in sodium, OR = 1.00, 95% CI 0.98, 1.02; $p = 0.93$, for excess sodium intake, OR = 1.05, 95% CI 0.67, 1.64; $p = 0.84$).

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Conclusions: Our results show no strong association between dietary salt intake and pediatric-onset MS risk, suggesting that salt intake may not play a prominent role in susceptibility to MS in children.

1. Introduction

Between 3.0% and 10.5% of multiple sclerosis (MS) patients have disease onset in childhood (Yeh et al., 2011; Simone et al., 2002). Compared to adults, pediatric patients tend to experience more frequent and severe exacerbations in the early stages of the disease (Gorman et al., 2009; Fay et al., 2012) and transition to secondary progressive (SP) MS after a longer disease duration but at a younger age (Simone et al., 2002; Renoux et al., 2007).

An association between obesity in childhood and the development of MS has been consistently reported (Munger et al., 2013; Langer-Gould et al., 2013). Epidemiologic studies have explored the role of dietary factors and MS susceptibility with conflicting results (Ascherio and Munger, 2007). Vitamin D deficiency is associated with higher MS risk in adults, and an increased relapse rate in both pediatric and adult MS patients (Munger et al., 2006; Mowry et al., 2010). No association was found between vitamins C, E and carotenoids and MS risk in women (Zhang et al., 2001). Studies of high-energy diet and saturated fat consumption have reported conflicting results (Zhang et al., 2000; Ghadirian et al., 1998).

There is limited, but suggestive, evidence for the role of dietary salt intake in MS susceptibility. An observational study of adult relapsing-remitting (RR) MS noted an increased rate of clinical exacerbations and MRI activity in subjects with high versus moderate or low salt intake (Farez et al., 2015). These findings support research in the animal model of MS, experimental allergic encephalomyelitis (EAE), for which a high salt diet was associated with earlier disease onset and progression (Wu et al., 2013; Kleinewietfeld et al., 2013). These studies also suggested that salt was associated with pro-inflammatory changes. Taken together, available data suggest that dietary salt intake might play a role in disease activity via its pro-inflammatory effect but additional research is needed to ascertain the role of dietary salt intake on MS susceptibility.

Pediatric-onset MS offers a unique opportunity to study such factors, due to temporal proximity at the time of diagnosis to exposure, thereby minimizing recall bias. In this multi-center project (R01NS071463, PI Waubant), data from a dietary screener for children (NutritionQuest) were collected to determine whether dietary salt intake was associated with pediatric-onset MS risk.

2. Methods

2.1. Participating sites

This case-control study was carried out as part of a larger investigation on pediatric MS conducted at 14 pediatric MS centers, including University of California San Francisco, State University of New York at Buffalo, Massachusetts General Hospital for Children, Mayo Clinic Rochester, Stony Brook University Medical Center, Texas Children's Hospital Baylor, Loma Linda University, Children's Hospital of Philadelphia, Ann & Robert H. Lurie Children's Hospital of Chicago, Children's Hospital of Colorado, University of Texas Southwestern/Children's Medical Center Dallas, Boston Children's Hospital, University of Alabama, and Washington University School of Medicine in St. Louis. Each center recruited study participants and collected data on pediatric-onset MS cases and controls. Data, including demographic, developmental, environmental exposure and medical history information, were then merged into a collaborative database. Participants were recruited between November 2011 and June 2014. Approval was obtained by the institutional review board at each participating institution. All participants and one of their parents signed assent and consent forms, as required by each center's institutional review board, prior to enrollment.

2.2. Study participants

Cases included children with clinically isolated syndromes (CIS) or RRMS with onset before 18 years of age and less than four years of disease duration (Polman et al., 2011). All cases were confirmed by a review committee (LK, TL, and EW). Eligibility for controls included age less than 22 years, absence of autoimmune disorders except for asthma or eczema, no history of treatment with immunosuppressive therapy nor history of severe health conditions. Parents of controls could not have MS. Eligible controls were invited to participate by recruitment in general or specialty pediatric clinics at the same participating institutions.

Race and ethnicity were self-reported according to NIH categories. Socioeconomic status (SES) was defined by self-report as the highest level of education attained by the participants' mother.

2.3. Sodium intake assessment using block kids food screener (BKFS)

Dietary sodium intake (mg/d) estimates were obtained using the 2007 BKFS, a 41-item diet screener that focuses on fruit and fruit juices, vegetables, processed foods such as potatoes (including French fries) and processed meats, as well as other meat/poultry/fish, whole grains, dairy, legumes and saturated fat (NutritionQuest., 2014). The questionnaire is designed for children aged 2–17 years old and available in English and Spanish and evaluates the frequency and portion of foods and beverages consumed during the past week. The subject or his/her caregiver completed the questionnaire after receiving instructions from a member of the research staff. The BKFS is a simple method of dietary assessment that has been validated against three, 24-hour dietary recalls in children aged 10–17 for servings of fruits, vegetables, meats, grains and other food groups (Hunsberger et al., 2015). Subjects were instructed to select the frequency (none last week, 1 day, 2 days, 3–4 days, 5–6 days, everyday) and then the food-specific portion size (e.g. 1 slice, 2 slices, 3+ slices) that most closely matched their intake in the preceding week.

Daily nutrient values, including sodium, were obtained by first quantifying the nutrient in each of the 41-items, the averages of which were then summed to provide the daily nutrient intake. The amount of nutrient in each item was determined by multiplying the frequency of consumption (as a decimal fraction from 0=never to 1=everyday) by the sex- and gender-specific portion size consumed (which is then divided by 100), and then multiplied by the amount of nutrient-per-100 g. Nutrient values are based on the Food and Nutrient Database for Dietary Surveys (FNDSS), a database developed by the United States Department of Agriculture. Six age-sex categories were used to provide dietary estimates based on differing caloric intake patterns by age and sex: males and females 2–3 years old, males and females 4–8 years old,