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Low-fat, plant-based diet in multiple sclerosis: A randomized controlled trial

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ABSTRACT

Background: The role that dietary interventions can play in multiple sclerosis (MS) management is of huge interest amongst patients and researchers but data evaluating this is limited. Possible effects of a very-low-fat, plant-based dietary intervention on MS related progression and disease activity as measured by brain imaging and MS related symptoms have not been evaluated in a randomized-controlled trial. Despite use of disease modifying therapies (DMT), poor quality of life (QOL) in MS patients can be a significant problem with fatigue being one of the common disabling symptoms. Effective treatment options for fatigue remain limited. Emerging evidence suggests diet and vascular risk factors including obesity and hyperlipidemia may influence MS disease progression and improve QOL.

Objectives: To evaluate adherence, safety and effects of a very-low-fat, plant-based diet (Diet) on brain MRI, clinical [MS relapses and disability, body mass index (BMI)] and metabolic (blood lipids and insulin) outcomes, QOL [Short Form-36 (SF-36)], and fatigue [Fatigue Severity Scale (FSS) and Modified Fatigue Impact Scale (MFIS)], in relapsing-remitting MS (RRMS).

Methods: This was a randomized-controlled, assessor-blinded, one-year long study with 61 participants assigned to either Diet (N=32) or wait-listed (Control, N=29) group.

Results: The mean age (years) [Control -40.9 ± 8.48; Diet -40.8 ± 8.86] and the mean disease duration (years) [Control -5.3 ± 3.86; Diet -5.33 ± 3.63] were comparable between the two groups. There was a slight difference between the two study groups in the baseline mean expanded disability status scale (EDSS) score [Control -2.22 ± 0.90; Diet -2.72 ± 1.05]. Eight subjects withdrew (Diet, N=6; Control, N=2). Adherence to the study diet based on monthly Food Frequency Questionnaire (FFQ) was excellent with the diet group showing significant difference in the total fat caloric intake compared to the control group [total fat intake/total calories averaged ~15% (Diet) versus ~40% (Control)]. The two groups showed no differences in brain MRI outcomes, number of MS relapses or disability at 12 months. The diet group showed improvements at six months in low-density lipoprotein cholesterol ($\Delta = -11.99$ mg/dL; $p=0.031$), total cholesterol ($\Delta = -13.18$ mg/dL; $p=0.027$) and insulin ($\Delta = -2.82$ mg/dL; $p=0.0067$), mean monthly reductions in BMI (Rate $= -1.125$ kg/m2 per month; $p<0.001$) and fatigue [FSS (Rate $= -0.0639$ points/month; $p=0.0010$); MFIS (Rate $= -0.233$ points/month; $p=0.0011$)] during the 12-month period.

Conclusions: While a very-low fat, plant-based diet was well adhered to and tolerated, it resulted in no significant improvement on brain MRI, relapse rate or disability as assessed by EDSS scores in subjects with RRMS over one year. The diet group however showed significant improvements in measures of fatigue, BMI and metabolic biomarkers. The study was powered to detect only very large effects on MRI activity so smaller but clinically meaningful effects cannot be excluded. The diet intervention resulted in a beneficial effect on the self-reported outcome of fatigue but these results should be interpreted cautiously as a wait-list control group may not completely control for a placebo effect and there was a

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baseline imbalance on fatigue scores between the groups. If maintained, the improved lipid profile and BMI could yield long-term vascular health benefits. Longer studies with larger sample sizes are needed to better understand the long-term health benefits of this diet.

1. Introduction

The role of diet in ameliorating the severity of multiple sclerosis (MS) has been long debated, but there remains a paucity of relevant research. Observational studies by Dr. Roy Swank, published between 1953 and 2003, suggested significantly reduced MS disease activity and disability progression and longer survival in people following a diet low in total and saturated fat compared with those who did not (Swank, 1953; Swank and Goodwin, 2003; Swank, 1970). Swank's diet book, last published in 1987, remains popular among patients with MS. However, this approach to treating MS has never been subjected to a well-controlled clinical trial.

The supposed large clinical effect of the Swank low fat diet led to our hypothesis that a very-low-fat, plant-based diet might have a large effect on MRI activity. We conducted a pilot study to explore the tolerability and potential benefits of a very-low saturated fat, plant-based diet followed for 12 months by people with relapsing-remitting MS (RRMS) with the primary endpoint being brain MRI disease activity.

2. Methods

This study sought to determine whether people with MS can adhere to a very-low-fat, plant-based diet (Diet) and explore its effects on brain MRI and other MS disease-specific measures and metabolic measures. The outcomes of interest included 1) diet adherence, safety, and tolerability, 2) changes in brain MRI, MS clinical activity, fatigue and quality of life (QOL) and 3) blood lipids, insulin and high sensitivity C-reactive protein (hs-CRP) in those randomized to the Diet versus a wait-listed (Control) group. Oregon Health & Science University (OHSU) Institutional Review Board approved the study protocol. Written informed consent was obtained from all study participants. The study was registered at www.clinicaltrials.gov (NCT00852722).

2.1. Design

The study was a single-center, assessor-blinded clinical trial with subjects randomized to the Diet or Control group. After randomization, study participants, caring neurologists (VY, DB), study coordinators and the dietician knew group assignments. The blinded assessors in the study included the radiologists reviewing the MRI at the MS/MRI Research Group at the University of British Columbia, EDSS assessing neurologists and the statistician analyzing the primary and secondary outcomes. Randomization was stratified dependent upon DMT use, with random blocks of 2 and 4 generated using the Excel random number generator function. Subjects were considered to be “on treatment” if they were taking a Food and Drug Administration (FDA)-approved DMT (interferon beta-1a, interferon beta-1b, glatiramer acetate, or natalizumab) within 6 months of screening, or “off treatment” if they were on no DMT within 6 months of screening.

2.2. Participants

Subjects were recruited from the OHSU MS Center and through national advertisements by the National MS Society. Inclusion criteria were as follows: RRMS (McDonald criteria (McDonald et al., 2001; Polman et al., 2011)); abnormal brain MRI consistent with MS; MS duration < 15 years; EDSS ≤ 6.0 (Kurtzke, 1983); age 18–70 years; documented clinical relapse or active disease by MRI in the previous 2 years; baseline diet with over 30% of total daily caloric intake from fat as determined by the self-administered Nutrition Quest® Block 2005 Food Frequency Questionnaire (FFQ) (Block et al., 1994). Subjects were allowed to be on a DMT during the trial if they were on a stable dose for at least 6 months prior to screening and maintained stable treatment throughout the study. We excluded subjects who were pregnant or breastfeeding and those with any clinically significant MS exacerbation or systemic corticosteroid use within 30 days of screening.

2.3. Procedure

After enrollment, diet group subjects received residential diet training in Santa Rosa, California through the McDougall Program (Anonymous, 2014) and were then followed for 12 months. The control group received no diet training at study onset and continued their usual diet throughout the study. After study exit at 12 months, control group subjects were offered the 10-day residential diet training at no cost. The study required 6 clinic visits at OHSU. A telephone pre-screen was used to gauge interest and eligibility. Baseline visit included consent, blood draw [complete blood count (CBC), complete metabolic panel (CMP), vitamin B-12 (B12), thyroid-stimulating hormone (TSH); fasting lipid profile, serum insulin, and hs-CRP (Liposcience, Inc.®)], pregnancy test if indicated, vital signs, medical history, physical exam, EDSS, MS Functional Composite (MSFC) (Cutter et al., 1999), FFQ, Fatigue Severity Scale (FSS) (Krupp et al., 1989), MS QOL Inventory (MSQLI) (Cella et al., 1996), Beck Depression Inventory (BDI), Rapid Assessment of Physical Activity (RAPA) (Topolski et al., 2006), brain MRI, and concomitant medication check. After the baseline visit, subjects randomized to the diet group received the diet training and the control group received an exercise education seminar conducted by a licensed physical therapist within three weeks of the baseline visit. Subsequent visits occurred at months 1, 3, 6, 9, and 12 and included physical exams, MSFC, FFQ, FSS, MSQLI, BDI, RAPA, concomitant medications check, and adverse events (AEs) reporting. EDSS was completed at months 3, 6, 9 and 12. Fasting serum biomarkers including lipid profile were re-measured at months 6 and 12. The exit visit after 12 months included CBC, CMP, B12, TSH, brain MRI and blinding check.

2.4. The very-low-fat, plant-based study diet

The study diet was based on starchy plant foods (beans, breads, corn, pastas, potatoes, sweet potatoes, and rice with the addition of fruits and non-starchy vegetables). Approximately 10% of calories were derived from fat, 14% from protein and 76% from carbohydrate (Anonymous, 2014). Meat, fish, eggs, dairy products and vegetable oils (such as corn and olive oil) were prohibited.

We used monthly FFQ and telephone contact to assess diet adherence. Subjects were considered diet adherent if they consumed 20% or less of calories from fat at least 80% of the time during the study. Additional counseling in clinic or by telephone