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Diet quality, body weight, and postmenopausal hot flashes: a secondary analysis of a randomized clinical trial

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Abstract

Background A low-fat vegan diet, supplemented with soybeans, has been shown effective in reducing postmenopausal hot flashes. This secondary analysis assessed the association of a plant-based index (PDI), healthful (hPDI), and unhealthful (uPDI), with changes in hot flashes in postmenopausal women.

Methods Participants ($n = 84$) were randomly assigned to a low-fat vegan diet supplemented with soybeans ($n = 42$) or a control group ($n = 42$) for 12 weeks. Three-day dietary records were analyzed and PDI indices were calculated. A repeated measures analysis of variance (ANOVA) was used for statistical analysis.

Results All three scores increased in the vegan group, compared with no change in the control group; the effect sizes were: PDI + 9.8 (95% CI + 5.8 to + 13.8; $p < 0.001$); hPDI + 10.9 (95% CI + 6.4 to + 15.3; $p < 0.001$); and uPDI + 3.6 (95% CI + 0.5 to + 6.6; $p = 0.02$). The change in all three scores negatively correlated with change in body weight (PDI: r=-0.48; $p < 0.001$; hPDI: r=-0.38; $p = 0.002$; and uPDI: r=-0.31; $p = 0.01$). The changes in PDI and uPDI were negatively associated with changes in severe hot flashes (r=-0.34; $p = 0.009$; and r=-0.43; $p < 0.001$, respectively), and associations remained significant after adjustment for changes in body mass index (r=-0.31; $p = 0.02$; and r=-0.41; $p = 0.001$, respectively).

Conclusions These findings suggest that minimizing the consumption of animal products and oil may be an effective strategy to reduce hot flashes in postmenopausal women, and that categorization of plant foods as "healthful" or "unhealthful" may be unwarranted.

Trial registration ClinicalTrials.gov, NCT04587154, registered on Oct 14, 2020.

Keywords Diet quality, Hot flashes, Nutrition, Plant-based, Vegan

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Introduction

A low-fat vegan diet, supplemented with soybeans, has been shown to be effective in reducing body weight and postmenopausal hot flashes [1]. In another randomized clinical trial, the Women's Health Initiative, a dietary intervention increasing whole grains, fruits, and vegetables and decreasing dietary fat reduced hot flashes, particularly in those participants who lost at least 10% of body weight [9]. The positive effects of a plant-based diet on body weight and hot flashes may be partly explained by a reduction in dietary advanced glycation end-products [2] and changes in the gut microbiome [3]. Furthermore, changes in body weight, fat intake, and fiber consumption are known to modulate estrogen activity, including sex hormone binding globulin concentrations [4–7].

Based on observational studies, some have proposed quantifying the healthfulness of plant-food dietary patterns, creating plant-based (PDI), healthful plant-based (hPDI), and unhealthful (uPDI) plant-based dietary indices [8]. However, the association of such categorization with postmenopausal hot flashes has not been assessed in randomized trials. Therefore, this secondary analysis of previously published data [1] assessed the association of PDI, hPDI, and uPDI in the context of a vegan diet, with hot flashes in postmenopausal women. It was hypothesized that the increase in all three indices would be associated with weight loss and a reduction in hot flashes.

Methods

The methods have been described in detail previously [1]. Briefly, postmenopausal women (cessation of menstruation of more than 1 and less than 10 years), aged 40–65 years, reporting at least 2 moderate-to-severe hot flashes per day were recruited through social media and screened by telephone in two cohorts (fall and spring) for a parallel-design, 12-week study beginning in September 2020 and February 2021 in Washington, DC. Exclusion criteria were any.

cause of vasomotor symptoms other than natural menopause; current use of a low-fat, vegan diet; soy allergy; use of hormonal medications in the preceding 2 months; smoking; substance abuse; eating disorder history; use of weight-reducing medication during the last 6 months; a current effort at weight loss; and body mass index < 18.5 kg/m^2. Data on demographics and lifestyle factors, including race and ethnicity, marital status, education, medication use, and physical activity, were collected.

The study was performed in accordance with the Declaration of Helsinki. The Advarra Institutional Review Board approved the study on September 2, 2020 (Pro00045315). All participants provided written informed consent. This study follows the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines.

Simple random sampling has been used. Volunteers who met the participation criteria were assigned to a vegan group or control group using a computer-generated sequence. Assignment was done simultaneously, so allocation concealment was unnecessary. The main outcome was the number and intensity of hot flashes, which were tracked with a mobile application for 12 weeks. The vegan group was asked to follow a low-fat vegan diet including ½ cup (86 g) of cooked soybeans per day, which would be expected to include approximately 30 g fat/day, while the control participants maintained their usual diets. Dietary adherence was assessed weekly, and a detailed dietary assessment was based on analysis of 3-day dietary records. Participants in both groups were provided with a vitamin B12 supplement (100 μg) and were asked to keep their medications and physical activity constant. Alcoholic beverages were limited to one per day.

Measurements were performed at baseline and week 12. The frequency and intensity of hot flashes were recorded, using the My Luna mobile application (Blue Trail Software Holding, San Francisco, CA). Body weight was measured, using a self-calibrating digital scale (Renpho Model ES-CS20M, Anaheim, CA), accurate to 0.05 kg.

Each participant completed a 3-day dietary record (two weekdays and one weekend day) at baseline and week 12. Dietary intake data were collected and analyzed by a staff member certified in the Nutrition Data System for Research which was developed by the Nutrition Coordinating Center at the University of Minnesota, Minneapolis, MN [9]. No instructions on diet quality were given to either group.

PDI scores were calculated, using the method of Satija et al. (2016): [8]"Healthy" plant-based foods include fruits, vegetables, whole grains, nuts, legumes, oils, coffee and tea, and "unhealthy" plant-based foods include fruit juice, sugar-sweetened beverages, refined grains, potatoes, and sweets [8]. For the PDI, plant-based food groups were awarded positive scores, while animal-based food groups were assigned reverse scores. The hPDI allocated positive scores to "healthy" plant-based food groups, with "unhealthy" plant-based and all animal-based food groups receiving reverse scores. Conversely, the uPDI assigned positive scores to "unhealthy" plant-based food groups, with reverse scores applied to "healthy" plant-based and animal-based food groups. This method has been previously applied in a study with 244 overweight adults, randomly assigned to a low-fat vegan diet, or a control group that was asked not to make any dietary changes [10]. The summed scores across the 17 distinct food groups were used to compute the respective indices for each participant. Physical activity was assessed by the International Physical Activity Questionnaire (IPAQ) [11].

Statistical analysis

Sample size and power calculation

Because no prior study had examined the effects of a vegan diet with cooked soybeans on vasomotor symptoms, there was no sound basis for a power analysis. The investigators therefore aimed to enroll up to 40 participants evenly divided between study groups as an initial cohort, with one more cohort to compensate for seasonality.

Statistical methods

A repeated measures analysis of variance (ANOVA) was used by a statistician blinded to dietary interventions. This has been shown to be a suitable method for studies where each group has multiple dependent variable observations collected at several time points [12]. Results are presented as means with 95% confidence intervals. Pearson correlation was used to evaluate the magnitude and significance of the association between the changes in hot flashes and body weight and changes in all three indices and their individual food components, first unadjusted and then and then Pearson partial correlations controlling for the changes in body mass index.

Results

Of 1,662 women inquiring about the study, 361 were screened by telephone, and 84 participants were randomly assigned to the 2 study groups, with 71 participants completing the whole study (Supplemental Fig. 1). The detailed baseline demographics are given in Supplemental Table 1. There were no significant between-group differences, except for the vegan group being slightly younger.

Hot flashes and body weight

Severe hot flashes were reduced by 92% (from 1.3/day to 0.1/day) in the vegan group ($p<0.001$) and did not change significantly in the control group (from 0.7/day to 0.4/day; $p=0.13$; between-group $p=0.02$). Mean body weight decreased by 3.6 kg in the vegan group and 0.2 kg in the control group (effect size: -3.4 kg [-4.5 to -2.3]; $p<0.001$).

PDI, hPDI, uPDI

All three scores increased in the vegan group, compared with no change in the control group; the effect sizes were: PDI+9.8 (95% CI+5.8 to +13.8; $p<0.001$); hPDI+10.9 (95% CI+6.4 to +15.3; $p<0.001$); and uPDI+3.6 (95% CI+0.5 to +6.6; $p=0.02$). The scores for the individual food components are listed in Table 1. The changes in all three scores negatively correlated with changes in body weight, with PDI (r=-0.48; $p<0.001$), hPDI (r=-0.38; $p=0.002$), and uPDI (r=-0.31; $p=0.01$). The changes in PDI and uPDI were negatively associated with changes in severe hot flashes (r=-0.34; $p=0.009$; and r=-0.43; $p<0.001$, respectively), and remained significant after adjustment for changes in body mass index (BMI; r=-0.31; $p=0.02$; and r=-0.41; $p=0.001$, respectively).

Discussion

In contrast with a 2023 review that suggested that higher PDI and hPDI levels were associated with favorable health outcomes, while higher uPDI scores were mostly found unfavorable [13], the present analysis demonstrated that both "healthy" and "unhealthy" plant-based indices—hPDI and uPDI—were inversely associated with weight changes and with changes in vasomotor symptoms in the context of a low-fat vegan diet with daily soybean consumption. This finding resonates with findings of a previous report on weight loss in overweight adults [14].

The PDI and its subscales were developed solely on epidemiological associations with type 2 diabetes, cardiovascular disease, and certain cancers, along with mediating conditions, such as obesity, and not on clinical trial data or other evidence of true health effects. The foods used to create the "unhealthy" index include fruit juices, sweetened beverages, refined grains, potatoes, and sweets/desserts. The current results suggest that at least some of these foods may, in fact, lend themselves to healthful weight loss when they replace animal-derived products. The first four in this list are higher in carbohydrate (which has 4 kcal/g) and lower in fat (which has 9 kcal/g), compared with meat, dairy products, and eggs, and so are naturally lower in energy density. For example, potatoes are included among the "unhealthy" plant foods, yet evidence of an association between potato intake and type 2 diabetes risk is weak and inconsistent, and is a subject to potential confounders, such as the use of fat during the preparation, and the combination with meat and other animal foods with which potatoes are usually consumed. In a previous study in overweight adults with insulin resistance, potatoes were comparable to beans in weight loss and improvements in insulin resistance [15]. An explanation for the beneficial effects on vasomotor symptoms is more challenging because the mechanism by which a plant-based diet ameliorates these symptoms remains unclear. The PDI itself may have fundamental issues, given that it rates oils as "healthy," despite their high energy density.

In the Women's Health Initiative, a randomized clinical trial that included more than 17,000 women, increasing whole grains, fruits, and vegetables and reducing dietary fat increased the chances of becoming free of hot flashes at 1 year by 14% in women who followed the

Table 1 Plant-based dietary index (PDI), healthful (hPDI), and unhealthful plant-based dietary index (uPDI), and the individual PDI food components at baseline and 12 weeks. The listed food component scores reflect points for the PDI, where plant-based food groups were awarded positive scores, while animal-based food groups were assigned reverse scores. Data are presented as means with 95% confidence intervals. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

	Vegan group			Control group			Effect size	*P*-value
	Week 0	Week 12	Change	Week 0	Week 12	Change		
PDI	53.8 (50.3–57.2)	61.2 (59.3–63.2)	+ 7.4 (+ 4.5 to + 10.4)***	56.3 (53.0-59.6)	53.9 (50.8–57.1)	-2.3 (-5.1 to + 0.5)	+ 9.8 (+ 5.8 to + 13.8)	$p < 0.001$
hPDI	57.4 (53.7–61.1)	67.0 (65.0-69.1)	+ 9.6 (+ 5.8 to + 13.4)***	59.0 (55.4–62.6)	57.7 (54.4–61.1)	-1.3 (-3.7 to + 1.2)	+ 10.9 (+ 6.4 to + 15.3)	$p < 0.001$
uPDI	54.7 (52.9–56.5)	58.7 (56.9–60.5)	+ 4.0 (+ 1.9 to + 6.0)***	56.3 (53.8–58.9)	56.7 (54.7–58.8)	+ 0.4 (-2.0 to + 2.8)	+ 3.6 (+ 0.5 to + 6.6)	$P = 0.02$
"Healthy" Plant Foods								
Fruits	2.9 (2.4–3.4)	3.4 (3.0-3.9)	+ 0.6 (+ 0.1 to + 1.1)*	3.1 (2.6–3.6)	2.7 (2.2–3.1)	-0.4 (-0.9 to + 0.1)	+ 1.0 (+ 0.3 to + 1.7)	0.004
Vegetables	2.9 (2.4–3.4)	3.6 (3.2-4.0)	+ 0.7 (+ 0.2 to + 1.3)*	3.0 (2.5–3.6)	2.7 (2.2–3.1)	-0.4 (-0.8 to + 0.1)	+ 1.1 (+ 0.4 to + 1.8)	0.004
Whole Grains	2.8 (2.4–3.3)	3.4 (2.9–3.9)	+ 0.6 (+ 0.0 to + 1.1)*	3.1 (2.6–3.7)	3.2 (2.6–3.7)	+ 0.0 (-0.6 to + 0.7)	+ 0.5 (-0.3 to + 1.3)	0.1899
Nuts	2.8 (2.3–3.3)	1.9 (1.5–2.2)	-1.0 (-1.5 to -0.5)***	3.1 (2.5–3.7)	2.9 (2.3–3.4)	-0.2 (-0.7 to + 0.3)	-0.7 (-1.4 to -0.0)	0.0402
Legumes	3.0 (2.5–3.5)	4.8 (4.7-5.0)	1.8 (1.3 to 2.4)***	2.9 (2.3–3.4)	2.6 (2.0-3.1)	-0.3 (-0.9 to + 0.3)	+ 2.1 (+ 1.3 to + 2.9)	$p < 0.0001$
Vegetable Oils	3.0 (2.5–3.5)	2.2 (1.8–2.6)	-0.8 (-1.4 to -0.2)*	3.0 (2.4–3.5)	2.9 (2.3–3.5)	-0.1 (-0.7 to + 0.5)	-0.7 (-1.5 to + 0.1)	0.0974
Coffee and Tea	3.2 (2.7–3.6)	2.9 (2.4–3.5)	-0.2 (-0.8 to + 0.3)	2.8 (2.2–3.3)	2.8 (2.2–3.3)	+ 0.0 (-0.4 to + 0.4)	-0.2 (-0.9 to + 0.4)	0.5285
"Unhealthy" Plant Foods								
Fruit Juice	2.9 (2.3–3.4)	2.4 (1.9-3.0)	-0.5 (-1.2 to + 0.3)	2.7 (2.1–3.3)	2.7 (2.0-3.3)	+ 0.0 (-0.9 to + 0.9)	-0.5 (-1.6 to + 0.7)	0.4103
Sugar Sweetened Beverages	2.1 (1.5–2.7)	1.6 (1.1-2.0)	-0.5 (-1.1 to + 0.1)	2.1 (1.4–2.7)	1.7 (1.2–2.3)	-0.3 (-0.9 to + 0.2)	-0.2 (-0.9 to + 0.6)	0.6715
Refined Grains	2.7 (2.2–3.3)	2.6 (2.1-3.0)	-0.2 (-0.6 to + 0.3)	3.2 (2.7–3.7)	3.0 (2.5–3.5)	-0.2 (-0.8 to + 0.4)	-0.0 (-0.7 to + 0.8)	0.9492
Potatoes	2.4 (1.8–2.9)	2.8 (2.1–3.4)	+ 0.4 (-0.3 to + 1.1)	2.9 (2.2–3.5)	2.6 (2.0-3.3)	-0.3 (-1.1 to + 0.6)	+ 0.6 (-0.4 to + 1.7)	0.2190
Sweets	3.1 (2.6–3.6)	2.8 (2.2–3.4)	-0.3 (-1.0 to + 0.3)	2.8 (2.3–3.4)	3.1 (2.5–3.7)	+ 0.3 (-0.6 to + 1.1)	-0.6 (-1.6 to + 0.4)	0.2537
Animal Foods								
Animal Fats	3.2 (2.6–3.8)	4.5 (4.1–4.9)	+ 1.3 (+ 0.6 to + 2.1)**	3.8 (3.2–4.4)	3.3 (2.7-4.0)	-0.4 (-1.0 to + 0.2)	+ 1.8 (+ 0.8 to + 2.7)	$p < 0.0005$
Dairy	3.1 (2.6–3.6)	4.7 (4.4-5.0)	+ 1.6 (+ 1.0 to + 2.2)***	3.3 (2.7–3.9)	2.8 (2.2–3.4)	-0.5 (-1.0 to -0.1)*	+ 2.1 (+ 1.3 to + 2.9)	$p < 0.0001$
Eggs	3.5 (2.9–4.1)	4.8 (4.6–5.1)	+ 1.4 (+ 0.8 to + 2.0)***	3.8 (3.2–4.5)	4.0 (3.4–4.5)	+ 0.1 (-0.5 to + 0.8)	+ 1.2 (+ 0.3 to + 2.1)	0.0068
Meat	3.4 (2.8-4.0)	4.9 (4.8–5.1)	+ 1.6 (+ 0.9 to + 2.2)***	3.5 (2.9–4.1)	3.6 (3.0-4.3)	+ 0.1 (-0.4 to + 0.6)	+ 1.5 (+ 0.7 to + 2.2)	$p < 0.0004$
Seafood	3.9 (3.3–4.5)	4.9 (4.7–5.1)	+ 1.0 (+ 0.4 to + 1.6)**	4.2 (3.7–4.8)	4.5 (4.1-5.0)	+ 0.3 (-0.2 to + 0.8)	+ 0.7 (-0.1 to + 1.5)	0.0737

dietary recommendations, regardless of changes in body weight, and by 23% among those who lost at least 10% of body weight [16]. The main mechanisms responsible for the reduction in hot flashes in our study may include a high fiber and a low fat content of the vegan diet, weight loss, a reduction in markers of inflammation [17], and an increased consumption of soy isoflavones [18].

The strengths of the current trial include a randomized, parallel design, which accounted for seasonal variation in diet and other lifestyle factors. The study also has limitations. The PDI scores were based on self-reported diet records. The participants were volunteers and may not represent the general population.

In conclusion, all three scores increased in the vegan group and correlated negatively with changes in body weight. The changes in PDI and uPDI were negatively associated with changes in severe hot flashes and remained significant even after adjustment for changes in BMI. These findings suggest that minimizing the consumption of animal products and vegetable oil is an effective strategy for reducing postmenopausal hot flashes and body weight, and that categorization of plant foods as "healthful" or "unhealthful" in this context, as done by the PDI, is unwarranted.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12905-024-03467-4.

Supplementary Material 1

Acknowledgements

Human Ethics and Consent to Participate The study was performed in accordance with the Declaration of Helsinki. The Advarra Institutional Review Board approved the study on September 2, 2020 (Pro00045315). All participants provided written informed consent. This study follows the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines.

Author contributions

HK and NDB designed and executed the study; HB, TZ-M, and MS prepared the data for analysis; RH performed the statistical analysis. All authors had full access to the data, contributed to the manuscript, and approved its final version.

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Data availability

De-identified data will be made available upon reasonable request at hkahleova@pcrm.org.

Declarations

Human Ethics and Consent to participate

The study was performed in accordance with the Declaration of Helsinki. The Advarra Institutional Review Board approved the study on September 2, 2020 (Pro00045315). All participants provided written informed consent. This study follows the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines.

Consent for publication

Not Applicable.

Competing interests

Dr. Kahleova, Ms. Brennan, Ms. Znayenko-Miller, Ms. Sutton, and Dr. Holubkov received compensation from the Physicians Committee for Responsible Medicine for their work on this study. Dr. Barnard is an Adjunct Professor of Medicine at the George Washington University School of Medicine. He serves without compensation as president of the Physicians Committee for Responsible Medicine and Barnard Medical Center in Washington, DC, nonprofit organizations providing educational, research, and medical services related to nutrition. He writes books and articles and gives lectures related to nutrition and health and has received royalties and honoraria from these sources.

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References

1. Barnard ND, Kahleova H, Holtz DN, et al. A dietary intervention for vasomotor symptoms of menopause: a randomized, controlled trial. Menopause. 2023;30(1):80–7.
2. Kahleova H, Znayenko-Miller T, Uribarri J, et al. Dietary advanced glycation end-products and postmenopausal hot flashes: a post-hoc analysis of a 12-week randomized clinical trial. Maturitas. 2023;172:32–8.
3. Kahleova H, Holtz DN, Strom N, et al. A dietary intervention for postmenopausal hot flashes: a potential role of gut microbiome. An exploratory analysis. Complement Ther Med. 2023;79:103002.
4. Rose DP, Goldman M, Connolly JM, Strong LE. High-fiber diet reduces serum estrogen concentrations in premenopausal women. Am J Clin Nutr. 1991;54(3):520–5.
5. Goldin BR, Woods MN, Spiegelman DL, et al. The effect of dietary fat and fiber on serum estrogen concentrations in premenopausal women under controlled dietary conditions. Cancer. 1994;74(3 Suppl):1125–31.
6. Bagga D, Ashley JM, Geffrey SP, et al. Effects of a very low fat, high fiber diet on serum hormones and menstrual function. Implications for breast cancer prevention. Cancer. 1995;76(12):2491–6.
7. Barnard ND, Scialli AR, Hurlock D, Bertron P. Diet and sex-hormone binding globulin, dysmenorrhea, and premenstrual symptoms. Obstet Gynecol. 2000;95(2):245–50.
8. Satija A, Bhupathiraju SN, Rimm EB, et al. Plant-based dietary patterns and incidence of type 2 diabetes in US men and women: results from three prospective cohort studies. PLoS Med. 2016;13(6):e1002039.
9. Schakel SF, Sievert YA, Buzzard IM. Sources of data for developing and maintaining a nutrient database. J Am Diet Assoc. 1988;88(10):1268–71.
10. Kahleova H, Brennan H, Znayenko-Miller T, Holubkov R, Barnard ND. Does diet quality matter? A secondary analysis of a randomized clinical trial. Eur J Clin Nutr. 2024;78(3):270–3.
11. Hagströmer M, Oja P, Sjöström M. The International Physical Activity Questionnaire (IPAQ): a study of concurrent and construct validity. Public Health Nutr. 2006;9(6):755–62.
12. Muhammad LN. Guidelines for repeated measures statistical analysis approaches with basic science research considerations. J Clin Investig. 2023;133(11):e171058.
13. Rosenfeld RM, Juszczak HM, Wong MA. Scoping review of the association of plant-based diet quality with health outcomes. Front Nutr. 2023;10:1211535.
14. Kahleova H, Brennan H, Znayenko-Miller T, Holubkov R, Barnard ND. Does diet quality matter? A secondary analysis of a randomized clinical trial. Eur J Clin Nutr 2023.
15. Rebello CJ, Beyl RA, Greenway FL, Atteberry KC, Hoddy KK, Kirwan JP. Low-energy dense potato- and Bean-based diets reduce body weight and insulin resistance: a Randomized, Feeding, Equivalence Trial. J Med Food. 2022;25(12):1155–63.
16. Kroenke CH, Caan BJ, Stefanick ML, et al. Effects of a dietary intervention and weight change on vasomotor symptoms in the women's Health Initiative. Menopause. 2012;19(9):980–8.
17. Arabzadegan N, Daneshzad E, Fatahi S, Moosavian SP, Surkan PJ, Azadbakht L. Effects of dietary whole grain, fruit, and vegetables on weight and inflammatory biomarkers in overweight and obese women. Eat Weight Disord. 2020;25(5):1243–51.

18. Taku K, Melby MK, Kronenberg F, Kurzer MS, Messina M. Extracted or synthesized soybean isoflavones reduce menopausal hot flash frequency and severity: systematic review and meta-analysis of randomized controlled trials. Menopause. 2012;19(7):776–90.

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