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Kahleova H, Petersen KF, Shulman GI, Alwarith J, Rembert E, Tura A, Hill M, Holubkov R, Barnard ND. Effect of a Low-Fat Vegan Diet on Body Weight, Insulin Sensitivity, Postprandial Metabolism, and Intramyocellular and Hepatocellular Lipid Levels in Overweight Adults: A Randomized Clinical Trial. JAMA Netw Open. 2020;3(11):e2025454.

What We Know, Think We Know, or Are Starting to Know

What is currently called the "whole-foods plant-based diet" [WFBP] is an extreme iteration of a vegan diet which specifically restricts dietary fat intake to a range of 7-15% total energy, usually falling in the range of ~10%. As a result of the restriction of dietary fat to this level, the foundation of the diet is carbohydrate foods, and thus the protein content is derived from plant-sourced foods. Thus, a typical macronutrient breakdown of the WFPB diet is 15%, 10%, 75% carbohydrate.

Enthusiasm for the WFPB diet as a therapeutic intervention is not new, with studies in the 1990's, and the more recent BROAD study, extolling the apparent benefits of the dietary approach for cardio-metabolic health [1–3]. However, the use of very high-fibre, high-carbohydrate diets as an intervention goes back to the late 1970's and the research of James Anderson [4,5]. Anderson's research suggested that in lean men with type-2 diabetes [T2D], the use of such high-fibre – often ~60g/d – diets could lead to reductions in daily insulin use, or even cessation of insulin therapy for T2D.

In a Deepdive long ago [December 2019], we covered the BROAD study, which investigated the effects of a WFBP diet on cardiovascular risk factors. The BROAD study is one of the most biased nutrition interventions one could ever happen to read, and ultimately the results were underwhelming, with minimal reductions in blood cholesterol levels compared to the control group.

Nevertheless, the WFPB diet remains a potentially interesting intervention, particularly for certain aspects of metabolic health. For example, dietary fat and simple sugars are both major contributors to liver fat [6,7]. A WFPB diet effectively removes both fat and sugar from the diet, and may have potential to lower liver fat levels, although this has not been specifically tested. The present study investigated the effects of a WFPB diet on body weight, thermic effect of feeding, insulin sensitivity, and liver fat.

The Study

The study compared a WFPB diet to a control habitual diet in adults with overweight/obesity [BMI 28-40]. Participants were randomised to either the intervention [75% carbohydrate, 10% fat, 15% protein] or to the control, which was asked to make no changes to their normal diet.

The WFPB diet consisted of legumes, grains, vegetables, and fruits, with no added fats or animal-sourced foods. The WFPB group attended weekly classes for instruction, cooking demonstration, and printed supporting materials.

The primary outcomes of the study were bodyweight, insulin resistance, thermic effect of feeding [TEF]. In a subgroup of the overall study, participants also underwent measurements for liver fat and intramuscular fat, which were also outcomes. The study lasted 16-weeks; the primary outcomes were compared between start and end of the intervention, and differences between groups.

Results: 222 participants completed the study; 117 in the WFPB group and 107 in the control group. The average age was 53 and 57 in the intervention and control groups, respectively.

- ***Energy Intake*:** In the WFPB group energy intake decreased by 490kcal, and in the control group by 135kcal; there was a difference between groups of 354kcal.
- ***Bodyweight*:** In the WFPB group bodyweight decreased by 6.4kg compared to 0.5kg in the control group; there was a between-group difference of 5.9kg.
- ***Insulin Resistance*:** Fasting insulin levels decreased by 21.6pmol/L in the WFPB group; the difference between groups was 23.6pmol/L in favour of the WFPB group compared to the control group. HOMA-IR, a marker of insulin resistance calculated from fasting glucose and fasting insulin, decreased by 1.3 points in the intervention group. The predicted insulin sensitivity index [PREDIM] increased by 0.9 points. The improvement in PREDIM correlated with the loss of bodyweight.
- ***TEF*:** TEF increased by 18.7% in the WFPB group; the between group difference was 14.1%. The improvement in TEF in the WFPB group correlated with loss of fat mass and improved insulin sensitivity.

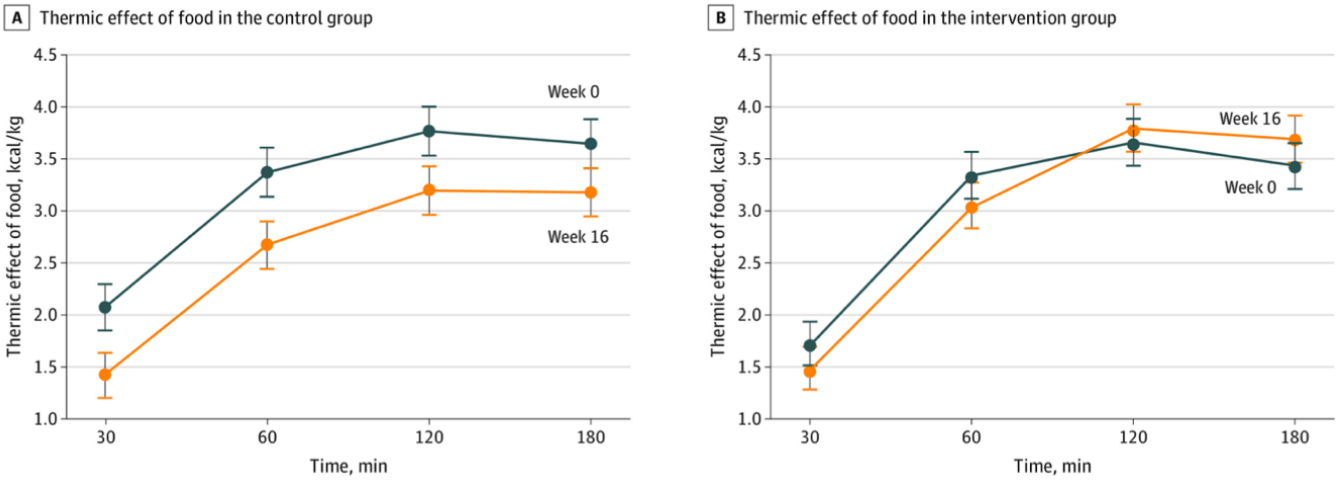

Figure *from the paper illustrating the change in TEF in the control group [**left graph**] and WFPB group [**right graph**]; the blue line is the baseline measure, and the orange line is the end of the intervention at 16-weeks. If you look at the left Y-axis, you'll see TEF is expressed in calories per kilogram of bodyweight; this appears from the supplementary data to mean kcal/kg per day. However, they only measured TEF over 2-hours, thus this finding is over-extrapolated; we would expect these miniscule differences to washout over the course of the whole day.*

- ***Liver Fat*:** In the subgroup of 44 participants, liver fat decreased from 3.2% to 2.4% in the WFPB group and increased from 3.3% to 3.6% in the control group. This change was correlated with the loss of bodyweight in the WPFB group.

The Critical Breakdown

Pros: Randomisation was appropriate [computer-generated, 1:1 ratio; researchers could not access randomisation protocol]; the outcome assessors [i.e., those doing the statistical analysis] were blinded to the allocation of participants. Apart from the difference in age, participants were overall well-matched for other characteristics. Participants were also excluded if they currently followed a vegan diet, which is a positive for determining effects of the diet independent of any carryover or habitual effects of diet.

Cons: The presentation of data and results leaves a lot to be desired [more under ***Key Characteristic***, below]. To an unsuspecting reader it would not be clear which findings are within-group differences [i.e., difference between baseline and end in either treatment or control group] and differences between intervention and control group. Some findings are presented as only within-group, or between group, and the authors appear to have picked and choose as it suited them. The extra attention – cooking classes, supporting materials – given to the WFPB group may have introduced a bias in their favour. Ultimately, participants all had relevant outcomes, i.e., fasting insulin, liver fat levels, within normal ranges, thus the findings reflect changes within healthy ranges for these outcomes.

Key Characteristic

There is something I think is worth mentioning here. Often, I get asked a question about funding sources and nutrition research, e.g., if the dairy industry sponsors a study, does that make the study immediately unreliable? My answer is always *'no'*, insofar as funding source doesn't immediately render a study unreliable. Rather, what matters is the methodological quality of the study; if factors like randomisation, blinding, participant characteristics, statistical analysis, reporting, etc., are all to standard, then there is little reason to question the merits of a study's findings just because it received funding from BigCow.

A similar consideration arises with the present study. The study was funded by the Physicians Committee for Responsible Medicine [PCRM], which despite its lofty title is in fact a highly biased activism group promoting vegan and strict vegetarian diets. Hana Kahleova and Neal Bernard, the first and last authors of the paper, respectively, are also respectively both the director and founder of the PCRM. It is also difficult to come across two more biased researchers in nutrition, the vegan equivalents of David Ludwig for the low-carb cartel.

In the present study, randomisation was appropriate and neither the first and last authors appeared to have been involved in the outcome assessment. Where things get fishy is with presentation of the effects of the diets, i.e., the reporting of results. Their presentation of the data does not include raw data, i.e., before-after data. It only includes results from their regression analyses, e.g., regression coefficients, which require a high level of statistical literacy to interpret. This suggests some hiding behind the data.

For example, the TEF findings are presented as a percentage change, with no raw data. If we squint at the figure in the paper, it appears that despite stating that TEF increased by 18.7% in the WFPB group, the actual magnitude was a difference of half a calorie per kilogram bodyweight. The control group appear to have had a change in TEF of <1kcal, also. The results are also presented by leading with *within-group* differences rather than *between-group* differences, the latter of which is the whole purpose of having a *control group* in an intervention. For example, with the HOMA-IR and PREDIM findings, it appears the within-group differences only are reported. All of which brings to mind a quote about the PCRM from the American Council on Science and Health:

"...by emphasizing only data that support their agenda, and by exaggerating the reliability and importance of such data, they obfuscate rather than clarify what can be a confusing body of information."

This certainly seems to be the case here; exaggerated reporting and obfuscation of the data to support what we know the authors believe to be true one way or the other.

Interesting Finding

Fasting insulin levels decreased from 91.2pmol/L to 69.6pmol/L in the WFPB group, a total reduction of 21.6pmol/L. The between-group difference was 23.6pmol/L lower compared to the control group. Unfortunately, we don't have data presented in the study on actual changes in food intake, only changes in certain macronutrients. This is unfortunate because previous research has demonstrated that whole-grain enriched diets improve insulin sensitivity, including reductions in fasting insulin of ~15pmol/L without any energy deficit, i.e., during weight-maintaining diets [8–10]. However, it is also important to note that normal range for fasting insulin using pmol/L as the unit is <174pmol/L; so all participants were already in normal range at baseline.

One would assume that the WFPB diet in the present study comprised of wholegrains, but it would have been informative to have data on actual food consumption. The data on macronutrient changes indicates that the WFPB diet group increased fibre by 10g [from 24g to 34g/d], lowered saturated fat to 5g, and decreased total energy intake by 490kcal/d; bodyweight also decreased by 6.4kg. Each of these variables would be expected to influence insulin sensitivity. In the regression analysis in the present study, the increase in insulin sensitivity correlated with the change in body weight. But no such analysis was conducted for fasting insulin. It would be interesting to investigate the effects of very low-fat, high-carbohydrate diets on insulin parameters independent of weight loss.

Relevance

As the medical phrase goes, "when you hear hoofbeats, think horses, not zebras." There is no evidence in this study of an independent effect of diet; weight loss is the primary driver of the results, and at least this is acknowledged in the discussion.

But let's also think about the magnitude of the findings. For example, the change in liver fat may be interesting, but baseline liver fat levels in both groups was already within normal ranges. Similarly fasting insulin levels were within normal ranges, although the decrease in the WFPB group and associated improvements in HOMA-IR and PREDIM are all encouraging findings, they appear to have primarily been driven by weight loss.

The finding for TEF also does not appear to be an independent effect of diet; the findings indicated that the slight increase in TEF correlated with loss of fat mass and improved insulin sensitivity. This is an established relationship in energy expenditure research, i.e., both higher adiposity levels and insulin resistance are associated with lower postprandial TEF [11]. It is important to bear in mind that the test meal after which TEF was measured was 720kcal, and postprandial energy expenditure was only measured for 2-hours; the energy content of the test meal and the duration of postprandial measures almost certainly means that the full TEF response was not captured [12].

Findings like the reduction in fasting insulin and increased insulin sensitivity from a diet comprised of ~75% carbohydrates drive a nail in the coffin of the "carbs = insulin = fat" rhetoric, even with an energy deficit. Nevertheless, we are left to draw conclusions in relation to the total WFPB dietary pattern, in the absence of any further analysis in the present study to tease out the respective contributions of specific foods.

Application to Practice

The WFPB diet still remains to have evidence match enthusiasm. I think that there are certain characteristics of the diet, such as the specifically low-fat level, which could have some useful application for metabolic disease. However, yet again another intervention study fails to match the hype offered in review papers.

While every practitioner could agree that encouraging an increase in fibre, vegetables and fruit, and food groups like legumes and wholegrains, is to be encouraged, the evidential justification for restricting dietary fat intake to ~10% of total energy is currently weak. Whether the early 1990' s research, the BROAD study, or this latest study, it is difficult to justify a diet of no-added fat on the basis of the evidence for the WFPB, for which most of the results have been confounded by added medications [3], other lifestyle variables and weight loss[2], and characterised by small effect sizes [1].

References

1. Wright N, Wilson L, Smith M, Duncan B, McHugh P. The BROAD study: A randomised controlled trial using a whole food plant-based diet in the community for obesity, ischaemic heart disease or diabetes. Nutrition & Diabetes. 2017;7(3):e256–e256.
2. Ornish D. Intensive Lifestyle Changes for Reversal of Coronary Heart Disease. JAMA. 1998 Dec 16;280(23):2001.
3. Esselstyn CB, Ellis SG, Medendorp S v, Crowe TD. A strategy to arrest and reverse coronary artery disease: a 5-year longitudinal study of a single physician' s practice. The Journal of family practice. 1995;41(6):560–8.
4. Anderson JW. Dietary fiber prevents carbohydrate-induced hypertriglyceridemia. Current atherosclerosis reports. 2000;2(6):536–41.
5. Anderson JW, Ward K. High-carbohydrate, high-fiber diets for insulin-treated men with diabetes mellitus. The American Journal of Clinical Nutrition. 1979;32(11):2312–21.
6. Yki-Järvinen H. Nutritional modulation of non-alcoholic fatty liver disease and insulin resistance. Nutrients. 2015;7(11):9127–38.
7. Yki-Järvinen H, Luukkonen PK, Hodson L, Moore JB. Dietary carbohydrates and fats in nonalcoholic fatty liver disease. Nature Reviews Gastroenterology & Hepatology. 2021;18(11):770–786.
8. Ross AB, Bruce SJ, Blondel-Lubrano A, Oguey-Araymon S, Beaumont M, Bourgeois A, et al. Effect of whole grains on insulin sensitivity in overweight hyperinsulinemic adults. American Journal of Clinical Nutrition. 2014;142(1):186–94.
9. Malin SK, Kullman EL, Scelsi AR, Haus JM, Filion J, Pagadala MR, et al. A whole-grain diet reduces peripheral insulin resistance and improves glucose kinetics in obese adults: A randomized-controlled trial. Metabolism: Clinical and Experimental. 2018;82:111–7.
10. Malin SK, Kullman EL, Scelsi AR, Godin JP, Ross AB, Kirwan JP. A Whole-Grain Diet Increases Glucose-Stimulated Insulin Secretion Independent of Gut Hormones in Adults at Risk for Type 2 Diabetes. Molecular Nutrition and Food Research. 2019;63(7): e1800967.
11. Ravussin E, Bogardus C, Schwartz RS, Robbins DC, Wolfe RR, Horton ES, et al. Thermic effect of infused glucose and insulin in man. Decreased response with increased insulin resistance in obesity and noninsulin-dependent diabetes mellitus. Journal of Clinical Investigation. 1983;72(3):893–902.
12. Reed GW, Hill JO. Measuring the thermic effect of food. American Journal of Clinical Nutrition. 1996;63(2):164–9.