Editorial Commentary

Go Nuts and Go Extra Virgin Olive Oil!
Mediterranean Diets Reduce Blood Pressure

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The high population burden of hypertension and elevated blood lipids and glucose, risk factors for cardiovascular disease (CVD), not only emphasize the need for available efficient treatment, but also underscore the need for effective prevention. Above all, effective lifestyle-based prevention is essential because population-wide strategies to shift the entire distribution of risk cannot solely rely on prescription medication. The most reliable form of scientific evidence on effective prevention is produced by randomized, controlled trials because spurious causality and biases are reduced with this type of study design. Thus, results from successful randomized, controlled trials involving dietary interventions are important because these have the greatest potential to influence dietary guidelines as well as healthcare policies and practices with the ultimate aim of maintaining or improving the public health.

Although highly desirable, dietary interventions trials are not without limitations. First, they cannot be tested in a double-blind, placebo-controlled manner. Although proper randomization of treatments minimizes allocation bias, balancing both known and unknown prognostic factors—a potential pitfall of observational studies—dietary interventions suffer from lack of blinding, crossover between studied diets, and nonadherence. Second, if the desired effect of a dietary intervention is meant to be explored independent of a potential weight loss, the different treatment regimens need to be isocaloric and the participants should maintain their body weight, sometimes a task difficult to accomplish. Third, because dietary interventions are both costly and require an extended period to produce results, they often suffer from high-risk populations, or are restricted to secondary prevention. Additional limitations may concern the fact that a change in consumption of one food often alters the consumption of other foods.

In this issue *Hypertension*, Doménech et al report results from an impressive dietary intervention with 3 arms, evaluating the intervention effect on 24-hour amibulatory blood pressure and blood lipids and glucose. The 1-year trial consisted of a Mediterranean diet supplemented with either extra virgin olive oil (EVOO) or mixed nuts and was compared with that of a control diet in which participants were advised to reduce dietary fat intake. EVOO is rich in bioactive compounds, such as polyphenols, and in monounsaturated fat (=75%); and nuts are rich in polyphenols, monounsaturated fat, and polyunsaturated fat, including α-linolenic acid. The participants were 235 women and men, aged 55 to 80 years, at high risk of CVD (eg, 85% had hypertension) but with no CVD diagnosis at enrollment. This study was a subanalysis of the larger complete Prevención con Dieta Mediterránea (PREDIMED) trial, performed in 2 centers in Spain involving >7000 subjects in a 5-year intervention with the composite end point of cardiovascular death, myocardial infarction, and stroke as the primary outcome. Previous results reported from the complete trial, which was terminated early, prompted by interim analyses, consisted of a remarkable ≈30% reduced incidence of major CVD end points for the 2 Mediterranean diet intervention groups as compared with the control diet group. After the publication of the primary results, several publications have come out based on this trial. Thus, the interpretation of the results of their present publication needs to be considered in the light of the fact that it is a subanalysis of PREDIMED trial not addressing the primary outcome of the intervention.

The Mediterranean diet is not a single dietary pattern that is consumed across the Mediterranean countries. Rather, the emphasis on vegetables, fruits, beans, nuts, seeds, unreined grains, and olive oil (but not necessarily EVOO) with the inclusion of fish and wine and a low intake of meats and full-fat dairy products signify a common feature. These diets are generally high in fat, but the fat quality may differ compared with Western diets, because the intake of monounsaturated and polyunsaturated fats is generally higher, whereas the intake of saturated fat is lower.

What did the authors find in this study? In the 2 Mediterranean diet groups with EVOO and nuts, the mean 24-hour systolic blood pressure decreased statistically significantly after 1 year by 2.3 and 2.6 mm Hg, respectively, whereas a nonsignificant increase of 1.7 mm Hg was observed in the control group. For the mean diastolic blood pressure, the respective differences were −1.2 (95% confidence interval, −2.2 to 0.2), −1.2 (95% confidence interval, −2.2 to −0.2), and 0.7 (95% confidence interval, −0.4 to 1.7). Noteworthy, these numbers are based on adjusted analyses, because the on-trial prescribed antihypertensive medications were not proportionally distributed among the 3 randomized groups. The dropout was higher in the control diet group. Compared with the control diet group, the EVOO and mixed nuts groups had 4 and 4.3 mm Hg lower mean systolic...
and 1.9 and 1.9 mm Hg lower mean diastolic 24-hour blood pressure. Mean changes in fasting blood glucose and total cholesterol were also statistically significant compared with the control group. The dietary interventions effects on office blood pressure from the PREDIMED trial have been published previously. After 3 months of the intervention, systolic (5.9–7.1 mm Hg) and diastolic (1.6–2.6 mm Hg) blood pressure were significantly reduced for the EVOO and mixed nuts groups compared with the control diet group. For the complete PREDIMED trial, all 3 dietary interventions (the 2 Mediterranean diet groups with EVOO and mixed nuts and the control diet group, advised to lower the fat intake) had beneficial effects on office systolic blood pressure, whereas lower values of diastolic blood pressure were observed in the 2 groups with EVOO and mixed nuts.

Strengths of this study are as follows: (1) the comparably long intervention period of 1 year; (2) adherence was reflected by a change in objective biomarkers (measured in 50% of the participants) of EVOO intake (urinary hydroxytyrosol) and nut consumption (plasma α-linolenic acid, %), suggesting only minor crossover; (3) the diets were isocaloric in the sense that no weight reduction occurred in the 2 intervention groups with EVOO or mixed nuts (only a slight weight loss of 0.8 kg) and a slight reduction in the physical activity occurred in the control diet group after 1 year, although not significantly different from the other 2 groups; and finally, (4) this trial had the ability to measure 24-hour ambulatory blood pressure levels, and not only office blood pressure measurements, before and after 1 year of intervention.

There is no doubt that important health benefits were achieved by the interventions with EVOO and mixed nuts. The question that arises is what components of the diets could be responsible for the improvements observed for all 3 studied CVD risk factors? The energy intake from fat was high in all 3 diets, 43% in the 2 diets supplemented with either EVOO or mixed nuts and 39% in the control diet. Only small changes, if any, within and between the intervention groups occurred during the intervention in the consumption of fish (including fatty fish), fruits, vegetables, and legumes. Sodium intake, energy from saturated fats, and meat consumption were equally reduced in all 3 groups. The consumption of olive oil was 51, 44, and 37 g/d in the EVOO, mixed nuts, and control diet groups, respectively (ie, 14 g/d difference between the EVOO group and the control diet in total olive oil consumption). However, EVOO was the only oil consumed by the EVOO group, whereas the control group consumed 23 g of EVOO of 37 total oil grams per day. Thus, based on an overall evaluation of the diets in this dietary intervention, the control group that was advised to reduce dietary fat seemed to consume a variant of the Mediterranean diet. Nevertheless, the energy intake from mono- and polyunsaturated fatty acids was higher in the EVOO and mixed nuts groups than in the control diet group. A recent large meta-analysis reported no major benefit with regard to coronary disease for these unsaturated fatty acids. However, the separate effects of fatty acids are inherently difficult to disentangle, and the results for monounsaturated fat may not apply to consumption of olive oil and nuts, but rather to meat and dairy. In any case, the supplemental foods in this trial seemed to produce the notable differences between the randomized groups observed in the PREDIMED trial.

Does this leave us with the other bioactive components present in EVOO and nuts explaining the effects, at least in part? The most truthful answer to this question is probably—we don’t know. Regardless, the generally impressive results based on a relatively simple intervention from a participant’s perspective, this trial confirms that changes in diet can have powerful beneficial effects. The next issue to be resolved concerns the generalizability of the findings and their potential policy implications.

Disclosures

None.

References

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Hypertension. 2014;64:26-27; originally published online May 5, 2014;
doi: 10.1161/HYPERTENSIONAHA.114.03506

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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World Wide Web at:
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