

The DASH Diet and Insulin Sensitivity

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Published online: 9 November 2010
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Abstract Lifestyle modifications, including adoption of the Dietary Approaches to Stop Hypertension (DASH) dietary pattern, weight loss in individuals who are overweight or obese, and physical activity, are effective in the prevention and treatment of hypertension. A healthy lifestyle may also have beneficial effects on metabolic abnormalities, such as insulin resistance, that are associated with high blood pressure. This review examines the independent and combined effects of the DASH diet and weight loss plus exercise on blood pressure and insulin sensitivity, with a focus on recently published results from the ENCORE study. Our data suggest that the DASH eating plan alone lowers blood pressure in overweight individuals with higher than optimal blood pressure, but significant improvements in insulin sensitivity are observed only when the DASH diet is implemented as part of a more comprehensive lifestyle modification program that includes exercise and weight loss.

Keywords Hypertension · Blood pressure · Diabetes · Insulin sensitivity · DASH diet · Exercise · Physical activity · Weight loss · Lifestyle modification

Introduction

High blood pressure is a major risk factor for cardiovascular disease and contributes to the risk of adverse events in a continuous, graded, and independent fashion [1–4]. Patients with hypertension are also predisposed to the development of insulin resistance and diabetes, in part through an association with excess weight [5–7]. The combination of high blood pressure and diabetes—each a powerful atherogenic risk factor—places patients in “double jeopardy” for coronary heart disease, stroke, heart failure, and chronic kidney disease, greatly increasing the risk of these adverse consequences of hypertension [5, 8–11].

Although elevated blood pressure can be lowered pharmacologically, antihypertensive medications may be costly, often must be used in combination to achieve adequate blood pressure control, and can be associated with adverse effects that impair quality of life and reduce adherence [12, 13]. Moreover, metabolic abnormalities associated with hypertension, including insulin resistance, may be exacerbated by some medications [14]. For these reasons, lifestyle interventions are preferred as the initial approach to treating most patients with uncomplicated high blood pressure.

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) [15] recommends that lifestyle modifications, such as weight loss and regular aerobic exercise, be the initial strategy for lowering high blood

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pressure. It specifically recommends the Dietary Approaches to Stop Hypertension (DASH) diet, a diet rich in fiber, fruits, vegetables, and low-fat dairy products that is also low in fat. This review examines the independent and combined effects of the DASH eating plan and weight loss plus exercise on blood pressure and insulin sensitivity, with a focus on recently published data from the ENCORE study.

Effects of Weight-Loss Diets and Exercise on Insulin Sensitivity and the Development of Diabetes

Previous randomized trials of lifestyle interventions have demonstrated that increasing physical activity combined with a diet to encourage weight loss can decrease the incidence of type 2 diabetes in susceptible individuals. In the Diabetes Prevention Program, for example, nondiabetic persons with elevated fasting and post-load plasma glucose concentrations were randomized to a diet and exercise intervention (with a goal of at least 7% weight loss and a minimum of 150 min of physical activity weekly), metformin (850 mg twice daily), or placebo [16]. The lifestyle intervention was more effective than metformin in reducing the risk of diabetes over the 2.8 years of follow-up; the incidence rates of diabetes were 11.0, 7.8, and 4.8 cases per 100 person-years in the placebo, metformin, and lifestyle groups, respectively. The Finnish Diabetes Prevention Study compared an intensive lifestyle intervention (targeting a reduction in weight of at least 5% and moderate exercise for at least 30 min per day) to diet and exercise advice, and found that the intensive intervention reduced the incidence of diabetes by 58% over a mean of 3.2 years of follow-up [17]. A recent meta-analysis describes the results of these and other randomized trials that included exercise plus diet and standard recommendation arms [18••]. The exercise interventions varied from trial to trial, ranging from advice to promote physical activity to supervised exercise programs of differing intensities. Diet interventions generally focused on caloric restriction, reduced fat intake, and increased fiber consumption. Overall, the exercise plus diet interventions resulted in significant weight loss and reduced the risk of diabetes by 37%.

Three large trials of lifestyle interventions for the prevention of diabetes randomized patients to weight-loss diet only, exercise only, diet plus exercise, or control, thus allowing a comparison of the independent effects of diet and exercise on glucose metabolism. In the Da Qing Impaired Glucose Tolerance and Diabetes Study [19], subjects with impaired glucose tolerance randomized to the diet-only group were counseled to consume more vegetables, limit consumption of alcohol, and reduce intake of simple sugars; those with a body mass index (BMI)

greater than 25 kg/m² also reduced their calorie consumption. Participants in the exercise intervention group were taught and encouraged to increase their leisure-time physical activity. The dietary intervention resulted in a 31% reduction in the incidence of diabetes over 6 years. Fasting and 2-hour postprandial plasma glucose levels both increased less in the diet arm than in the control group. Of note, the incidence of diabetes was not changed by dietary modification in lean participants (who did not reduce caloric intake). The exercise intervention also lowered the cumulative incidence of diabetes (by 46%) and ameliorated the increase in glucose levels.

The Oslo Diet and Exercise Study enrolled sedentary, nondiabetic individuals with BMI greater than 24 kg/m² [20]. Dietary counseling was individualized for each person and encouraged reduction in caloric intake; increased consumption of fish, vegetables, and fiber-rich complex carbohydrates; and decreased intake of total and saturated fat and sugar. The exercise intervention included supervised workouts three times weekly at 60% to 80% of maximum heart rate. Weight at 12 months decreased by 6.8 kg in the diet group and increased by 1.1 kg in the control group. The weight loss in the diet intervention was associated with a decrease in fasting glucose and insulin levels and an improvement in insulin sensitivity as measured by the homeostasis model. Participants in the exercise-alone intervention had no significant weight loss and did not exhibit significant decreases in fasting glucose or insulin levels or improvement in insulin sensitivity.

In a third study conducted by Wing et al. [21], the effects of lifestyle interventions were examined in a US cohort of overweight individuals with a family history of diabetes. Subjects in the diet group received instruction in a low-fat, low-calorie diet from a multidisciplinary team of counsellors. Participants in the exercise intervention were encouraged to gradually increase their levels of physical activity to 1,500 calories per week. In both treatment arms, subjects attended weekly group sessions for the first 6 months, then biweekly meetings for 6 months, and then two 6-week refresher courses in the second year of the trial. Participants in the diet condition lost 9.1 kg in the first 6 months of the program and exhibited significant decreases in fasting glucose and insulin levels. At the end of 24 months, however, these individuals were only 2.1 kg lighter than at baseline, and the improvements in glucose and insulin levels were not maintained. Those in the exercise group had a more modest weight loss (2.1 kg) at 6 months and no significant change in biochemical measures of glucose tolerance and insulin sensitivity. Weight loss from baseline to 2 years was a strong independent predictor of absence of diabetes.

These and other studies demonstrate that intervention strategies that emphasize caloric restriction and achieve

weight loss lead to improved insulin sensitivity and decrease the risk of diabetes in vulnerable populations [22–24]. It is less clear whether limiting specific macronutrients such as fat and refined carbohydrates retards the development of diabetes independent of a reduction in calories [25–27]. Similarly, studies examining the effects of exercise on glucose metabolism have produced mixed results [28–34]. Physical activity may have a beneficial acute effect: studies of both healthy adults and patients with type 2 diabetes have shown that improved insulin sensitivity is maintained for at least 6 h after a single bout of exercise, but it may be diminished within 60 h after the final exercise training session [35–38]. In general, studies demonstrating improvements in glucose metabolism after longer-term exercise training have not established that these effects are attributable to exercise independent of weight loss.

Effects of the DASH Diet on Blood Pressure

Recent research examining dietary strategies to lower blood pressure has focused on the effects of healthful dietary patterns, rather than on the benefits of specific nutrients or single foods. The DASH diet and similar dietary patterns emphasize fruits, vegetables, and low-fat dairy products; include whole grains, poultry, fish, and nuts; and minimize red meat, sweets, and beverages containing sugar. Although no specific nutrient is identified as the key element in blood pressure reduction, these diets are rich in potassium, magnesium, calcium, and fiber, and have a low content of saturated fat.

The DASH eating plan has been shown to be effective in lowering blood pressure in a series of well-designed clinical trials. In a landmark study, the DASH Collaborative Group established the efficacy of the DASH diet in 459 adults with systolic blood pressure less than 160 mmHg and diastolic blood pressure 80–95 mmHg [39]. Importantly, weight was kept constant by manipulating calorie consumption in this controlled feeding study. The DASH diet reduced systolic blood pressure by 5.5 mmHg and diastolic blood pressure by 3.0 mmHg more than a control diet; the reductions were even greater (11.4 mmHg/5.5 mmHg) in those with hypertension. The dietary intervention lowered blood pressure regardless of the participants' age, gender, BMI, or physical activity levels, and was particularly effective in African Americans [40]. A subsequent trial demonstrated that the DASH diet lowered blood pressure at each of three levels of sodium intake and that reduction of dietary sodium and the DASH diet were more effective in combination than separately [41].

The DASH diet is also effective in lowering blood pressure when implemented as part of a more comprehensive lifestyle modification program in an outpatient setting. In the

PREMIER trial, 810 adults with higher-than-optimal blood pressure (systolic blood pressure 120–159 mmHg, diastolic blood pressure 85–90 mmHg) were randomized to one of three 6-month interventions: 1) advice only; 2) an established intervention, which included a behavioral intervention to achieve weight loss in those who were overweight, reduced sodium intake, increased physical activity, and limited alcohol intake in those who drank alcohol; and 3) an intervention that implemented the established lifestyle modifications plus the DASH diet [42]. Both active interventions resulted in significant weight loss (4.9 kg in the established-intervention group and 5.8 kg in the established-plus-DASH group, compared with a loss of 1.1 kg in the advice-only group), as well as improved fitness and lower dietary sodium intake; the established-plus-DASH intervention also increased fruit, vegetable, and dairy consumption. The net reduction in systolic blood pressure (relative to advice only) was 3.7 mmHg in the established group and 4.3 mmHg in the established-plus-DASH group ($P < 0.001$ for reductions with each intervention vs advice only; $P = 0.43$ for established vs established-plus-DASH).

More recently, our research group published results of the ENCORE study (Exercise and Nutritional Interventions for Cardiovascular Health), a trial that examined the independent and combined effects on blood pressure of the DASH diet and weight loss plus exercise [43]. In ENCORE, 144 overweight or obese patients with higher than optimal blood pressure (systolic blood pressure 130–159 mmHg or diastolic blood pressure 85–99 mmHg) were randomized for 4 months to a usual-diet control group, the DASH diet alone, or the DASH diet in combination with a weight management intervention (consisting of a cognitive behavioral weight loss program and supervised aerobic exercise). Participants in the DASH diet plus weight management group lost weight (8.7 kg) and exhibited a significant increase in aerobic capacity, whereas participants assigned to the DASH diet alone or usual care maintained their weight and had no improvement in fitness levels. Relative to the control group, the DASH diet resulted in a decrease in systolic blood pressure of 7.8 mmHg, and an even greater decrease (12.7 mmHg) when combined with exercise and weight loss.

Effects of the DASH Diet on Insulin Sensitivity

Although the efficacy of the DASH diet in reducing blood pressure is well established, less is known about the metabolic effects of this dietary pattern, including its influence on insulin sensitivity. Observational data from the Insulin Resistance Atherosclerosis Study suggest that the DASH diet may prevent the development of diabetes in

Table 1 Glucose and insulin values before and after treatment in the ENCORE study

Variable	Time	Treatment group, mean (95% CI)			P value from comparisons after treatment ^a		
		DASH+WM	DASH-A	UC	DASH +WM vs DASH-A	DASH +WM vs UC	DASH-A vs UC
Fasting glucose (mg/dL)	Before	89.4 (86.4–92.3)	90.4 (87.3–93.5)	91.3 (88.4–94.3)			
	After	87.2 (85.1–89.3)	89.4 (87.3–91.5)	91.9 (89.9–93.9)	0.324	0.006	0.214
Fasting insulin (μ U/mL)	Before	18.1 (15.7–20.4)	16.6 (14.2–19.0)	18.0 (15.7–20.3)			
	After	12.5 (10.8–14.3)	17.6 (15.9–19.4)	18.6 (16.9–20.2)	<0.001	<0.001	0.711
Glucose AUC (mg/dL·min)	Before	6,057 (5,221–6,893)	6,087 (5,224–6,951)	6,345 (5,508–7,181)			
	After	4,947 (4,340–5,554)	6,238 (5,637–6,838)	6,334 (5,756–6,912)	0.011	0.005	0.958

AUC area under the curve, DASH dietary approaches to stop hypertension, DASH+WM DASH plus weight management, DASH-A DASH alone, UC usual care

(Data from Blumenthal et al. [47].)

^a Values after treatment are adjusted for pretreatment levels of outcome variable, age, gender, and ethnicity. P values are adjusted using Tukey's Honestly Significant Difference procedure

some individuals [44]. Habitual dietary intake at baseline was assessed using a semiquantitative, 114-item food frequency interview, from which a DASH adherence score was derived. A significant inverse association of the DASH score with incident diabetes over 5 years of follow-up was observed in whites, but not in blacks or Hispanics and not in the study cohort as a whole.

In an ancillary study of PREMIER, insulin sensitivity was measured in a subset of 52 participants using the frequently sampled IV glucose tolerance test with minimal model analysis [45]. Over the course of the 6-month intervention, the insulin sensitivity index was unchanged in the advice-only group, improved from 2.32 to 2.97 with the established intervention ($P=0.146$ in comparison with advice only), and improved from 1.96 to 2.95 in the patients randomized to the established intervention plus DASH diet ($P=0.047$ for established plus DASH vs advice

only; $P=0.616$ for established plus DASH vs established). The results of this small study suggest that the DASH dietary pattern in combination with a comprehensive lifestyle modification program for hypertension may improve insulin sensitivity. Whether the DASH diet provides incremental benefit over exercise and weight loss is uncertain, however, as participants in the established-plus-DASH group tended to lose more weight than those receiving the established intervention, and the changes in insulin sensitivity index were not significantly different between these two groups. In another secondary analysis of PREMIER, the established and established-plus-DASH interventions both led to significant decreases in fasting insulin levels and in the homeostasis model index of insulin resistance [46]. However, there were no differences in the insulin resistance index between the active intervention arms.

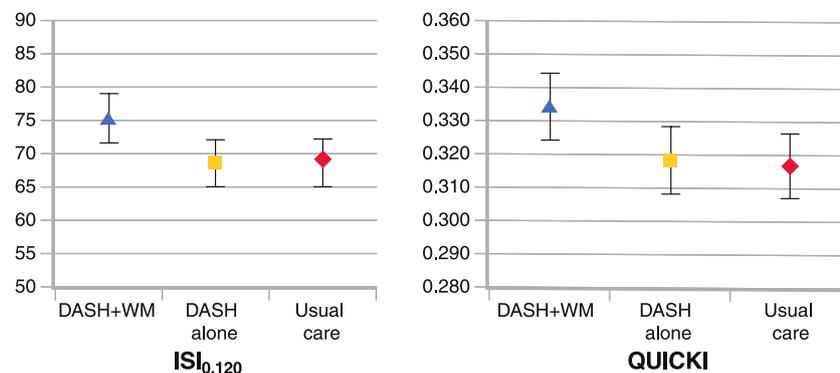


Fig. 1 Indices of insulin sensitivity, adjusted for age, sex, ethnicity, and pretreatment insulin sensitivity values: comparison of posttreatment means and 95% confidence intervals in the three arms of the ENCORE study. For the Insulin Sensitivity Index ($ISI_{0,120}$), contrasts were significant for DASH plus weight management (DASH+WM)

versus usual care ($P=0.026$) and for DASH+WM versus DASH alone ($P=0.031$). For the quantitative insulin sensitivity check index (QUICKI), contrasts were also significant for DASH+WM versus usual care ($P<0.001$) and for DASH+WM versus DASH alone ($P<0.001$). (Data from Blumenthal et al. [47].)

The design of the ENCORE study permitted an assessment of the effects on insulin sensitivity of the DASH diet alone and in combination with weight loss [47•]. Glucose tolerance tests using an oral glucose load of 75 g were performed at baseline and at the conclusion of the 4-month interventions. Glucose tolerance was assessed by calculating the area under the glucose concentration curve. Insulin sensitivity was estimated using the quantitative insulin sensitivity check index (QUICKI), as described by Katz et al. [48]; and also by using the Insulin Sensitivity Index (ISI_{0,120}), a method based on dynamic glucose and insulin levels [49]. Both of these surrogate measures provide estimates of insulin sensitivity that correlate closely with glucose clamp measurements and are predictive of the onset of type 2 diabetes [50].

Compared with usual-care participants, those who completed the DASH plus weight management intervention showed lower fasting glucose and insulin levels and lower values for area under the glucose concentration curve (Table 1). The DASH plus weight management participants also exhibited greater insulin sensitivity, as measured by both QUICKI and ISI_{0,120}, compared with either DASH-alone or usual-care participants (Fig. 1). The DASH-alone group did not differ from the usual-care group on any measure of glucose metabolism. Thus, although participants in the DASH plus weight management condition achieved significant improvements in glucose tolerance and insulin sensitivity, no change in these metabolic parameters was noted in response to the DASH diet alone.

Based upon their glucose levels 2 h following the oral glucose load, ENCORE participants were classified as diabetic (>199 mg/dL), prediabetic (141–199 mg/dl), or normal (<140 mg/dL). Overall, 72% ($n=13$) of the 18 participants in the DASH plus weight management group who were either prediabetic or diabetic at study entry improved by at least one category over the course of the trial, compared with 54% (7/13) randomized to DASH alone and 44% (8/18) in usual care. Among participants who were not diabetic or were prediabetic upon study entry, diabetic risk status worsened in only 2% (1/44) of participants in the DASH plus weight management intervention, versus 16% (7/43) in the DASH-alone group and 11% (5/46) in usual care.

Conclusions

Adoption of the DASH dietary pattern is effective in lowering blood pressure in individuals with higher than optimal blood pressures. Whether the DASH diet also improves metabolic abnormalities associated with hypertension, such as insulin resistance, is less clear. A number of trials have demonstrated that increasing exercise com-

bined with a diet to encourage weight loss can reduce the incidence of diabetes in susceptible individuals. The key element of these interventions is probably caloric restriction: though studies examining the influence of dietary composition or physical activity have yielded mixed results, weight loss consistently results in improved glucose metabolism. Data from the ENCORE study suggest that the DASH eating plan alone lowers blood pressure in overweight individuals with high blood pressure, but significant improvements in insulin sensitivity are observed only when the DASH diet is implemented as part of a more comprehensive lifestyle modification program that includes exercise and weight loss.

Acknowledgment Supported by grants from the National Heart, Lung, and Blood Institute (HL074103) and the General Clinical Research Center, National Institutes of Health (M01-RR-30).

Disclosure No potential conflicts of interest relevant to this article were reported.

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- Of major importance

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