Effect of Dietary Fats and Carbohydrate on Blood Pressure of Mildly Hypertensive Patients

FRANK M. SACKS, IAN L. ROUSE, MEIR J. STAMPFER, LOUISE M. BISHOP, CORNELIA F. LENHERR, AND RAYMOND J. WALTHER

SUMMARY The effect on blood pressure (BP) of replacing dietary saturated fat with either polyunsaturated fat (linoleic acid) or carbohydrate was studied in 21 untreated mildly hypertensive patients. In a randomized, double-blind, crossover protocol, all subjects received dietary supplements of cream, safflower oil, and carbohydrate in random sequence, each prepared in flavored yogurt or milk. Each supplement was administered for 6 weeks and followed by a 4-week washout period of no supplementation. Dietary linoleic acid increased from 4.6 to 13% of energy intake when the safflower oil replaced cream, while saturated fat decreased from 16 to 10%. Total fat intake was 37 to 38% during the cream and safflower oil periods but was 28% during the carbohydrate period. Compliance with the diets was demonstrated by significant changes in fasting plasma fatty acid measurements. Mean clinic BP was 135 ± 9/93 ± 6 mm Hg at baseline. There were no significant differences in BP measured in the clinic or at home among the three dietary periods. The protocol had more than 80% power to detect a mean effect of diet of 3 mm Hg systolic or 2 mm Hg diastolic BP. Therefore, replacing dietary saturated fat with carbohydrate or with linoleic acid does not affect BP in subjects with mild hypertension. (Hypertension 10: 452-460, 1987)

KEY WORDS • dietary fats • hypertension • blood pressure • plasma fatty acids • linoleic acid • polyunsaturated fats • ambulatory blood pressure measurements

VEGETARIANS living in industrialized societies and eating a diet that is relatively low in total fat and saturated fat but high in polyunsaturated fat have low mean blood pressure (BP), and in contrast with omnivores, their BP rises only slightly with age.1-3 Within vegetarian groups, those eating comparatively more animal products have higher BP.1-4 However, the changes in BP have not been consistent when vegetarian diets were given to nonvegetarians or when animal products were added to vegetarian diets.1-4 Two groups of researchers found that increasing the proportion of dietary polyunsaturated to saturated fatty acids in nonvegetarian diets lowered BP in both normotensive and hypertensive subjects.8-13 However, another group studying similar diets in normotensive subjects could not replicate these results.14 Differences in the dietary protocols may have contributed to the conflicting results of studies of vegetarian diets and of modifications in dietary fat intake. In some studies, saturated and polyunsaturated fats were tested against each other, but in other studies, the fat replaced carbohydrate or protein. Moreover, the dietary interventions always affected nutrients in addition to the fats; these nutrients could have either lowered BP directly or perhaps blocked an effect of dietary fats on BP. Many of these studies did not use randomized controls and none were double-blind, leaving open the possibility of a biased result.

Dietary linoleic acid has been proposed to lower BP by its conversion to arachidonate, the substrate for cyclooxygenase and prostaglandin synthesis.9,10 Some studies have found that hypertensive patients have lower levels of vasodilating prostaglandins than do normal controls.13 Conceivably, a low intake of linole-
ic acid or slowed conversion of linoleate to arachidonate could cause low prostaglandin levels in hypertensive subjects and could be corrected by augmenting the dietary intake. Therefore, we conducted a double-blind dietary trial to test whether replacement of saturated fats either by linoleic acid or by carbohydrate lowers BP in hypertensive subjects.

Methods

Subjects

Subjects were recruited from the clinical practices of staff physicians at Harvard University Health Services (HUHS; Cambridge, MA, USA). Male or female patients at HUHS were eligible if they had mild hypertension (defined as a pretreatment diastolic BP between 90 and 104 mm Hg inclusive) and were being treated either nonpharmacologically or with no more than two antihypertensive drugs. Subjects were not eligible if they were obese (body weight >20% of ideal weight for height according to Metropolitan Insurance Company tables), or had diabetes mellitus, hyperlipidemia (defined by the 95% limits for cholesterol and triglyceride at the HUHS clinical laboratory), or end-organ damage (defined as overt cerebrovascular or coronary vascular disease), left ventricular hypertrophy, abnormal serum creatinine levels, or hypertensive retinal abnormalities. Each prospective subject had a detailed clinical and laboratory evaluation to determine eligibility and to exclude secondary forms of hypertension according to standard guidelines.

Thirty-one hypertensive subjects were referred to the study by physicians at HUHS. Of this group, three subjects declined to participate due to the time demands of the protocol and four subjects were excluded: one person, apparently misdiagnosed as hypertensive, whose diastolic BP was consistently below 90 mm Hg on repeated measurement; one with established hypertension, whose diastolic BP remained over 104 mm Hg after withdrawal from medication; and two with established hypertension, who had BP below 85 mm Hg during the initial withdrawal from medication. After the remaining 24 subjects commenced the study, three dropped out for varied personal reasons unrelated to the supplements or their BP levels. The final study group consisted of 21 subjects who completed all phases of the study. Of these subjects, 16 were men (age range, 26–63 years) and five were women (age range, 30–62 years).

Experimental Protocol

The baseline period consisted of 1 week of measurements of BP and other variables (described in a subsequent section). Prior to the baseline period, subjects who were receiving antihypertensive medication were withdrawn from drugs for 8 weeks during which time their BP was monitored. Subjects were entered into the study if their baseline mean diastolic BP was between 85 and 104 mm Hg inclusive.

Following the baseline period, the subjects were randomly allocated in blocks of six, using a random number table, into one of the six possible orders of administration of the three following dietary supplements: 1) polyunsaturated fat — 30 ml of safflower oil that was deodorized and decolorized by standard commercial processing techniques (California Fats and Oils, Richmond, CA, USA), 2) saturated fat — 81 ml of cream (Hood Dairy, Charlestown, MA, USA), 3) low fat, high carbohydrate — 68 g of powdered skim milk and 40 g of polysaccharide (Sumacal; Organon Nutritional Products, West Orange, NJ, USA). The supplements were mixed with an emulsifier of monoglycerides and diglycerides, 1.3 g (DUR-EM 117; Durkee Foods, Strongsville, OH, USA), in flavored nonfat yogurt or skim milk as a milk shake. Three flavors were used and rotated. The nutrient content of the supplements is shown in Table 1. Each subject was required to eat an 8-oz (224-ml) portion of yogurt or drink a 12-oz (336-ml) milk shake daily. Aside from the dietary supplements, the subjects were free to eat their usual diet, modified to allow incorporation of the dietary supplement. The team dietician (L.M.B.) counseled the subjects to make the necessary changes with a goal of minimizing increases in total calories or body weight. Generally, the supplements were taken at lunchtime. Each supplement was consumed for 6 weeks. The periods of dietary supplementation were each separated by a 4-week washout period in which the subjects consumed their usual diet.

Double-blind conditions were maintained throughout. No researcher who had any contact with the subjects knew of the treatment assignments. The supplements were prepared and distributed weekly, labeled only with patients’ identification numbers. No subject had the opportunity to compare directly the taste of the different supplements.

Dietary Assessment

To quantitate the diet at baseline and during the three periods of supplementation, a semiquantitative food frequency questionnaire was completed by each subject. This questionnaire contained 116 food-related

![Table 1. Nutrient Content of the Dietary Supplements](https://example.com/table1.png)
items, each with a specified portion size, and nine possible categories of frequency of ingestion. The subjects were questioned by a dietitian (L.M.B.) when clarification of responses was needed. This questionnaire has been extensively validated against diet records and biochemical indices of nutrition in population studies and in clinical trials. The questionnaire was optically scanned and the data analyzed at the Harvard University Computing Center using a nutrient data base complete for all listed nutrients.

In addition to the questionnaires, each subject completed a 7-day diet record at baseline and during each period of supplementation. A dietitian used these records to show each subject how to incorporate the supplements into the usual diet and to verify that the instructions were followed.

BP Measurements

Clinic Readings

BP was measured on one random zero sphygmomanometer by a single observer (L.M.B.) throughout the protocol. The observer was trained at the East Boston Neighborhood Health Center, a performance site of the Hypertension Detection and Follow-up Program, using that program’s protocol. BP was measured on each of 3 consecutive days during the baseline period, at the midpoint of the supplementation periods, and in the final week of supplementation and washout periods. Before each measurement, the subjects sat quietly in a chair for 5 minutes. Then three readings were taken in succession from the left arm. BP was measured at the same time of day in each subject throughout the protocol, either in the morning or in the early afternoon.

Home Readings

All subjects were instructed to measure their own BP for 7 days during the midpoint and last week of the dietary supplementation periods and during the last week of the two washout periods using a fully automated machine (Lumiscope, Edison, NJ, USA). Home BP readings were not obtained during the baseline period. On each day during these week-long assessment periods, subjects were requested to make duplicate determinations in the morning, late afternoon, and evening. One machine was allocated to each subject for the entire study and was used to obtain all of the readings in that subject. The machine weighs 28 oz (784 g). It automatically inflates the cuff to a level that is 20 mm Hg over the subject’s previous systolic BP reading, decreases the pressure by 2 mm/sec while displaying the pressure that is in the cuff, and provides a printed record of date, time, systolic and diastolic BPs, and heart rate. Each machine was validated in the following manner before it was allocated to a subject. First, the pressure transducer of each machine was tested by connecting a Y tube from an inflatable arm cuff to a mercury manometer and to the automated machine and observing pressure readings from 0 to 200 mm Hg. Then, BP measurements of each automated machine were compared with auscultatory measurements obtained with a standard mercury sphygmomanometer (W.A. Baum, Copiague, NY, USA) by taking three consecutive simultaneous readings with both devices from the left arm of four normal subjects. Each machine was restested at the different assessment periods against the mercury sphygmomanometer. The mean difference between measurements made with the automated machine and the mercury sphygmomanometer was 0.15 ± 3.53 (SD) mm Hg for systolic BP and −1.55 ± 3.45 mm Hg (p<0.001) for diastolic BP based on 198 simultaneous readings.

Urine Measurements

Two consecutive 24-hour urine collections were made at the end of each period of supplementation. Sodium, potassium, calcium, and creatinine were determined by autoanalyzer at the Core Laboratory of the Clinical Research Center, Brigham and Women’s Hospital. Results of the two collections were averaged for each subject.

Plasma Fatty Acid Measurements

A fasting sample of venous blood anticoagulated with 3 mM edetic acid was taken at baseline and on 1 day during the last week of each of the three periods of dietary supplementation. Plasma fatty acids were measured by extracting and transmethyllating the lipids with methanolic HCl. The solvent was evaporated, and the fatty acid methyl esters were redissolved in hexane and quantitated by gas-liquid chromatography as follows: fused silica capillary column, 30 m x 0.24 mm, SP 2330 liquid phase, 0.22-μm film thickness (Supelco, Bellefonte, PA, USA); split injection, 100:1; hydrogen carrier gas at 48 cm/sec; flame ionization detector; Hewlett-Packard Model 5880A gas chromatograph (Palo Alto, CA, USA) with peak area integration; temperature program of 140 to 170°C at 10°C/min, 170°C for 4 minutes, 170 to 190°C at 10°C/min, 190°C for 2 minutes, 190 to 240°C at 10°C/min. Peak retention times were identified by injecting known standards (NuCheck Prep, Elysium, MN, USA). Results are expressed as percentage of the total fatty acid methyl esters.

Body weight was measured in light clothing without shoes at baseline and at the midpoint and end of each supplement period using one portable scale.

Data Analysis

Standard methods for analysis of crossover trials were followed for the analysis of changes in all of the variables. Clinic BP for each period of measurement is defined as the mean of nine readings, three each of 3 days, whereas home BP is defined as the mean of 42 readings, two each of three times per day for 7 days, as described previously. The significance of effects of treatment (diet) and of period (nonspecific or seasonal effects unrelated to the specific treatment) was tested using repeated-measures analysis of variance (ANOVA). Where there was a significant effect of diet, differences between the effects of any two dietary supplements were examined with least-signifi-
cant-difference tests. To evaluate whether there were any carryover effects of one treatment onto the next treatment (order or interactive effects), we adopted the strategy of Armitage and Hills, which models the change in BP during the supplementation periods as a function of period, diet, and their interaction. To determine whether changes in BP were related to changes in other variables, multiple regression analysis was performed using the General Linear Models Procedures of the Statistical Analysis System. In all analyses, two-sided p values were used.

**Results**

**Diet**

During supplementation with safflower oil as compared with cream, intake of polyunsaturated fat increased from 5 to 14% of total energy, whereas saturated fat decreased from 16 to 10% and monounsaturated fat decreased from 13 to 11% (Table 2). There were no differences among these periods in intake of protein, total fat, carbohydrate, potassium, calcium, magnesium, vitamin C, or vitamin E.

During both high fat periods, total fat constituted 37 to 38% of total calories and carbohydrate 42 to 43%, as compared with 28 and 52%, respectively, during consumption of the low fat carbohydrate supplement (see Table 2). In comparison to the carbohydrate period, the higher dietary fat in the polyunsaturated phase was accounted for entirely by linoleic acid. Two thirds of the increase in fat intake during the saturated fat period was accounted for by saturated fat (myristic, palmitic, and stearic acids) and one third by monounsaturated fat (oleic acid). During ingestion of the carbohydrate supplement, there were small but statistically significant increases in intake of energy, protein, potassium, calcium, and magnesium as compared with the high fat supplements. Most of these increases resulted from the nonfat milk powder added to the low fat supplement to render it isocaloric to the high fat supplements.

**Plasma Fatty Acids**

To verify that the subjects ate the supplements, fasting plasma fatty acids were measured. Since in a previous study, dietary supplements of safflower oil increased linoleate in all of the plasma lipid classes, we measured fatty acids in unfraccionated plasma lipids. Compared with the saturated fat period or with the carbohydrate period, intake of safflower oil enriched plasma fatty acids were measured. Since in a previous study, dietary supplements of safflower oil increased linoleate in all of the plasma lipid classes, we measured fatty acids in unfraccionated plasma lipids. Compared with the saturated fat period or with the carbohydrate period, intake of safflower oil enriched plasma fatty acids were measured. Since in a previous study, dietary supplements of safflower oil increased linoleate in all of the plasma lipid classes, we measured fatty acids in unfraccionated plasma lipids.

**TABLE 2.** Daily Dietary Intakes and Body Weight at Baseline and During Dietary Supplementation in 21 Subjects

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Baseline</th>
<th>Supplement</th>
<th>Comparisons (p-value)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>P</td>
<td>S</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>2023±728</td>
<td>2482±585</td>
<td>2198±431</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>232±77</td>
<td>321±64</td>
<td>235±60</td>
</tr>
<tr>
<td>% of kcal</td>
<td>46</td>
<td>52</td>
<td>43</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>75±26</td>
<td>94±21</td>
<td>76±17</td>
</tr>
<tr>
<td>% of kcal</td>
<td>15</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Total fat (g)</td>
<td>74±34</td>
<td>78±28</td>
<td>92±17</td>
</tr>
<tr>
<td>% of kcal</td>
<td>33</td>
<td>28</td>
<td>37</td>
</tr>
<tr>
<td>Saturated fat (g)</td>
<td>27±13</td>
<td>30±12</td>
<td>25±8</td>
</tr>
<tr>
<td>% of kcal</td>
<td>12</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Polyunsaturated fat (g)</td>
<td>14±8</td>
<td>14±6</td>
<td>34±3</td>
</tr>
<tr>
<td>% of kcal</td>
<td>6.0</td>
<td>5.0</td>
<td>14</td>
</tr>
<tr>
<td>P/S ratio</td>
<td>0.55</td>
<td>0.49</td>
<td>1.42</td>
</tr>
<tr>
<td>Linoleate (g)</td>
<td>13±7</td>
<td>12±5</td>
<td>32±3</td>
</tr>
<tr>
<td>% of kcal</td>
<td>5.7</td>
<td>4.4</td>
<td>13</td>
</tr>
<tr>
<td>Monounsaturated fat (g)</td>
<td>27±13</td>
<td>28±12</td>
<td>27±7</td>
</tr>
<tr>
<td>% of kcal</td>
<td>12</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Cholesterol (mg)</td>
<td>312±118</td>
<td>338±144</td>
<td>268±115</td>
</tr>
<tr>
<td>Dietary fiber (g)</td>
<td>19±8</td>
<td>17±5</td>
<td>15±5</td>
</tr>
<tr>
<td>Potassium (mg)</td>
<td>3174±1105</td>
<td>3796±835</td>
<td>3297±726</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>849±367</td>
<td>1529±476</td>
<td>1112±380</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>217±73</td>
<td>305±72</td>
<td>258±79</td>
</tr>
<tr>
<td>Vitamin C (mg)</td>
<td>294±243</td>
<td>316±277</td>
<td>258±219</td>
</tr>
<tr>
<td>Vitamin E (mg)</td>
<td>39±95</td>
<td>32±86</td>
<td>23±10</td>
</tr>
</tbody>
</table>

Values are means ± SD. C = carbohydrate; P = polyunsaturated fat; S = saturated fat.

*Comparisons of different supplements were made by least-significant-difference testing when the significance level of the overall repeated-measures ANOVA was <0.10.
Table 3. Composition of Fasting Plasma Fatty Acids During Dietary Supplementation with Carbohydrate and Fat in 21 Subjects

<table>
<thead>
<tr>
<th>Fatty acid (% of total)</th>
<th>Baseline</th>
<th>C</th>
<th>P</th>
<th>S</th>
<th>Comparisons (p-value)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>C14:0</td>
<td>0.28 ± 0.43</td>
<td>0.27 ± 0.25</td>
<td>0.16 ± 0.14</td>
<td>0.26 ± 0.20</td>
<td>&gt;0.10 &gt;0.10 0.004</td>
</tr>
<tr>
<td>C15:0</td>
<td>0.18 ± 0.26</td>
<td>0.13 ± 0.06</td>
<td>0.10 ± 0.04</td>
<td>0.16 ± 0.12</td>
<td>&gt;0.10 &gt;0.10 0.013</td>
</tr>
<tr>
<td>C16:0</td>
<td>17.2 ± 2.8</td>
<td>17.4 ± 3.2</td>
<td>16.2 ± 2.2</td>
<td>17.8 ± 2.4</td>
<td>0.036 &gt;0.10 0.005</td>
</tr>
<tr>
<td>C18:0</td>
<td>7.6 ± 0.9</td>
<td>7.9 ± 1.0</td>
<td>8.0 ± 0.8</td>
<td>7.8 ± 0.8</td>
<td>&gt;0.10 &gt;0.10</td>
</tr>
<tr>
<td>C18:1(c9)</td>
<td>17.7 ± 2.1</td>
<td>18.9 ± 2.7</td>
<td>15.8 ± 2.2</td>
<td>18.5 ± 2.2</td>
<td>&lt;0.001 &gt;0.10 &lt;0.001</td>
</tr>
<tr>
<td>C18:2(c6)</td>
<td>33.5 ± 4.1</td>
<td>31.3 ± 4.5</td>
<td>38.2 ± 4.3</td>
<td>31.5 ± 3.9</td>
<td>&lt;0.001 &gt;0.10 &lt;0.001</td>
</tr>
<tr>
<td>C18:3(c6)</td>
<td>0.53 ± 0.15</td>
<td>0.63 ± 0.17</td>
<td>0.57 ± 0.19</td>
<td>0.53 ± 0.20</td>
<td>&gt;0.10 0.011 &gt;0.10</td>
</tr>
<tr>
<td>C18:3(c3)</td>
<td>0.45 ± 0.12</td>
<td>0.46 ± 0.13</td>
<td>0.38 ± 0.08</td>
<td>0.43 ± 0.12</td>
<td>0.012 &gt;0.10</td>
</tr>
<tr>
<td>C20:2(c6)</td>
<td>0.27 ± 0.10</td>
<td>0.28 ± 0.10</td>
<td>0.29 ± 0.09</td>
<td>0.23 ± 0.06</td>
<td>&gt;0.10 0.034 0.013</td>
</tr>
<tr>
<td>C20:3(c6)</td>
<td>1.56 ± 0.28</td>
<td>1.87 ± 0.36</td>
<td>1.51 ± 0.33</td>
<td>1.64 ± 0.28</td>
<td>&lt;0.001 0.004 0.081</td>
</tr>
<tr>
<td>C20:4(c6)</td>
<td>9.09 ± 1.77</td>
<td>8.80 ± 1.57</td>
<td>9.25 ± 1.78</td>
<td>8.81 ± 1.68</td>
<td>&gt;0.10 &gt;0.10</td>
</tr>
<tr>
<td>C20:5(c3)</td>
<td>0.88 ± 0.70</td>
<td>0.65 ± 0.25</td>
<td>0.42 ± 0.19</td>
<td>0.66 ± 0.27</td>
<td>&lt;0.001 &gt;0.10 &lt;0.001</td>
</tr>
</tbody>
</table>

Values are means ± SD. C = carbohydrate; P = polyunsaturated fat; S = saturated fat.

*Comparisons of different supplements were made by least-significant-difference testing when the significance level of the overall repeated-measures ANOVA was <0.10.

The increase in plasma linoleate during the safflower oil period over levels during the ingestion of cream or carbohydrate (Figure 1). Arachidonate (20:4), the precursor to prostaglandins of the 2 series, and other desaturation and elongation products of linoleate, such as 18:3 and 20:3, did not increase during ingestion of linoleate. Paradoxically, 20:3 decreased during ingestion of linoleic acid, as we had found previously in normotensive subjects. The dietary saturated fatty acids and oleic acid in cream did not raise the respective plasma fatty acid levels over levels present during the carbohydrate period. Unlike safflower oil, which is composed predominantly of linoleic acid, cream contains moderate amounts of 14:0, 16:0, 18:0, and 18:1, and the increments in these individual dietary fatty acids may not have been enough to raise the respective plasma levels. Alternatively, since humans can synthesize saturated fatty acids and oleic acid (but not linoleic acid, an essential nutrient), plasma levels of the nonessential fatty acids are likely to be less sensitive than essential fatty acids to increments in the diet.

Blood Pressure
At baseline, mean clinic BP was 134.9 ± 9.5/92.6 ± 5.7 mm Hg. There were no significant differences in clinic BP among the three periods of dietary supplementation (Table 4). In fact, BP was remarkably stable throughout the protocol, including baseline and washout periods (Figure 2), with no evidence of a downward drift in BP during the study, such as might be caused by regression to the mean or by subjects becoming accustomed to the procedure of measurement. The pooled intravidual standard deviation of clinic BP over the entire study was 4.2 mm Hg for systolic BP and 3.0 mm Hg for diastolic BP. Therefore, with the use of ANOVA, the study had over 80% power to detect a treatment effect of 3 mm Hg systolic and 2 mm Hg diastolic BP with a p value of less than 0.05.

The effect of replacing saturated fat with either polyunsaturated fat or carbohydrate on home BP, like clinic BP, was strikingly null (see Table 4 and Figure 2). Home BP was significantly lower than clinic BP throughout the study.

Body Weight
Irrespective of the type of supplement eaten, weight increased during the first supplement period and remained stable thereafter. Increments of body weight over baseline were 0.9 kg for the first supplement period, 1.1 kg for the second period, and 0.9 kg for the third period. Analysis of changes in body weight by
TABLE 4. BP at Clinic and Home During Dietary Supplementation in 21 Subjects

<table>
<thead>
<tr>
<th>BP (mm Hg)</th>
<th>Baseline</th>
<th>Carbohydrate</th>
<th>Polysaturated</th>
<th>Saturated</th>
<th>RANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinic</td>
<td>134.9±9.5</td>
<td>135.9±7.4</td>
<td>135.7±7.2</td>
<td>137.0±8.4</td>
<td>4.3</td>
</tr>
<tr>
<td>Home</td>
<td></td>
<td>133.6±9.6</td>
<td>134.8±8.0</td>
<td>133.7±12.6</td>
<td>5.1</td>
</tr>
<tr>
<td>Diastolic</td>
<td>92.6±5.7</td>
<td>92.3±6.5</td>
<td>91.8±6.4</td>
<td>93.6±6.3</td>
<td>2.9</td>
</tr>
<tr>
<td>Clinic</td>
<td></td>
<td>85.8±9.0</td>
<td>87.5±7.1</td>
<td>86.7±8.5</td>
<td>3.6</td>
</tr>
<tr>
<td>Home</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD*</td>
<td>4.3</td>
<td>5.1</td>
<td>2.9</td>
<td>3.6</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD. RANOVA = repeated-measures ANOVA.

*Within-person SD of differences in BP among the three dietary periods.

Figure 2. A. Changes in BP during consumption of dietary supplements of fat and carbohydrate in a crossover study. B. Changes in BP in temporal sequence during the crossover study.
type of supplement showed that weight was significantly higher by 1.1 kg during the polyunsaturated fat supplement than during the saturated fat supplement (see Table 2). There was no significant difference in weight between the carbohydrate period and either of the two fat periods.

Regression analysis showed no relationship between changes in body weight and BP, and including change in body weight as a covariate of the effect of dietary supplements on BP did not change the null result.

**Urinary Analyses**

The average urinary excretion of sodium, potassium, calcium, and creatinine in two 24-hour collections was not significantly different among the dietary periods (Table 5).

**Period and Order Effects**

The nutritional data, plasma fatty acids, BPs, and urinary analytes were analyzed by sequence of supplementation (as well as by type of supplement) to assess drift in these variables (period effects) over the course of the study. No such effect was found for any of the variables except body weight, as discussed previously.

In a crossover study, the possibility that one treatment may affect the results of the subsequent treatment (order or carryover effect) could seriously bias the overall estimate of the treatment effects. Generally, the results of crossover trials are not examined for carryover effects, but in this study we used the approach of Armitage and Hills and found no evidence for a carryover effect on BP from one supplement to the next (p > 0.10 for all analyses).

**Discussion**

The present study was conducted to resolve some of the inconsistencies in previous work on dietary fats and BP. The goal was a nutritional study patterned after the rigorous principles often used in contemporary drug trials. Thus, the study design was a double-blind, controlled, crossover trial with biochemical validation of self-reported dietary compliance. This design minimizes the possibility of observing an effect on BP attributable to variables other than the dietary fats.

The principal comparison in the present study is of BP during the ingestion of supplements of saturated fat and linoleic acid. Dietary data show that adding the dietary supplements produced substantial alterations in overall daily intake of saturated fat and of linoleic acid, covering the practical dietary range. The magnitude of the resulting change in fasting plasma linoleate is consistent with many previous studies. The total dietary intake during these two dietary periods was very similar in nutrients other than fatty acids. However, BP, whether measured at the clinic or at home, was virtually unchanged by intake of the supplements of saturated and polyunsaturated fatty acids. The multiplicity of individual readings of BP taken on each subject during each period dampened the inherent within-person variability in BP and provided sufficient power to detect very small changes in BP.

We studied a third dietary supplement that was low in fat and high in carbohydrate as an additional nutritional control to help distinguish the effects of each type of fat. Clinically, a low fat, high carbohydrate diet is relevant since it is widely recommended to lower blood cholesterol and risk of cardiovascular disease. The carbohydrate supplement caused major changes in overall intake of fat and carbohydrate and small but statistically significant increases in the calculated dietary potassium, calcium, magnesium, and protein. Whereas the calculated increase in dietary potassium was 12 to 13 mmol/day, urinary potassium excretion over 48 hours was only 4 to 5 mmol/day higher on carbohydrate than on either supplement of fat (p > 0.10), suggesting that a change in potassium intake, if it did occur, was very small. Taken together, the existing literature would predict at most a hypotensive effect of the added cations of 1 to 2 mm Hg. Dietary protein has not been found to affect blood pressure. Moreover, ingestion of these nutrients was unaffected during the exchange of saturated for polyunsaturated fat. Therefore, the stability of BP during all three dietary periods suggests that exchanging linoleic acid or carbohydrate for saturated fat does not affect BP in mildly hypertensive subjects during a 6-week period of study.

Over the past 10 years, many studies have reported that removing some saturated fat from the diet and replacing it with either polyunsaturated vegetable oil or carbohydrate lowers BP. Most of the experimental designs involved a baseline period of a usual high saturated fat diet, a test diet, and a final period of the usual diet. The diets of the three periods were either self-selected, with instruction for the purchase and use of the foods for the test diet, or completely controlled. Except for one study that will be discussed subsequently, the apparent hypotensive effects of diets low in saturated fat or high in polyunsaturated fat were based on comparing BP at the baseline and/or the final period with BP measured at the end of the test period. Comparisons of treatment period with baseline BP when there is no randomized control group are difficult to interpret since the changes in BP from baseline could be the result of many influences unrelated.

**Table 5. Urinary Excretion of Cations and Creatinine During Dietary Supplementation Determined from 48-Hour Collections**

<table>
<thead>
<tr>
<th>Urinary excretion</th>
<th>Supplement</th>
<th>Carbohydrate</th>
<th>Polyunsaturated</th>
<th>Saturated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine (mg/day)</td>
<td>1440 ± 339</td>
<td>1530 ± 471</td>
<td>1390 ± 410</td>
<td></td>
</tr>
<tr>
<td>Sodium (mmol/day)</td>
<td>125 ± 47</td>
<td>123 ± 43</td>
<td>116 ± 60</td>
<td></td>
</tr>
<tr>
<td>Potassium (mmol/day)</td>
<td>65 ± 19</td>
<td>60 ± 19</td>
<td>60 ± 24</td>
<td></td>
</tr>
<tr>
<td>Calcium (mg/day)</td>
<td>217 ± 108</td>
<td>223 ± 109</td>
<td>192 ± 81</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD of 21 subjects. Differences among the means were not significant by repeated-measures ANOVA.
ed to the specific treatment. None of these studies utilized double-blind conditions.

In two studies, a section of the protocol allowed a comparison of two controlled diets that differed in dietary fat composition (see References 10 and 13), but the negative findings were disregarded in the conclusions. For example, completely controlled diets of 35 and 25% fat distributed among the saturated and unsaturated classes of fatty acids, sequentially administered, produced no difference in BP (see Study 1 in Reference 10). A randomized study of two diets containing 25% fat, one high in linoleic acid and the other high in saturated fats, showed no change in BP. But when compared with baseline, all of these test diets lowered BP.

Only one study that used a randomized control group suggested that changes in dietary fat altered BP. Subjects were randomized to either a low fat diet or a low salt diet with high fat intake or asked to continue their usual diet that was high in fat and salt. Each diet was eaten for 6 weeks and followed by a return to their usual diets. Compared with pretreatment and posttreatment levels, BP decreased significantly only in the low fat group. Unfortunately, the analysis did not make use of the randomized study design to test whether the decrease in BP of 8/6 mm Hg on the low fat diet was significantly greater than the decrease of 2/2 mm Hg that occurred in the no intervention control group. Moreover, since the low fat diet was a complex dietary intervention that caused changes in intake of other nutrients, including vitamins and minerals, it is difficult to attribute the decrease in BP exclusively to the lowered intake of saturated fat.

Several studies that changed intake of fat using a complex dietary program of intervention did not find effects on BP. The multicenter National Diet Heart Study randomized about 1000 participants to one of two experimental diets that lowered saturated fat and increased linoleic acid or to a high saturated fat control diet. The BP responses after 1 year of the experimental diets were within 1% of those of the control group. At one of the centers that enrolled 211 patients, a fourth randomized group received a very high (22%) linoleic acid diet that also had no effect on BP. The British Medical Research Council randomized controlled trial of soybean oil in 377 patients with myocardial infarction found no tendency toward lower BP in the intervention group as compared with the control group over 5 years of observation. In a series of small, controlled dietary studies on cholesterol metabolism that used a variety of combinations of dietary saturated fat, polyunsaturated fat, and carbohydrate, Brussaard et al. found no significant changes in BP in any of the studies in spite of substantial changes in plasma lipids.

In addition to the present study, three double-blind studies have compared the effects on BP of ingestion of different fatty acids. These studies involved simple interventions that minimized changes in other nutrients. Neither substitution of saturated fats for linoleic acid (present study) nor substitution of oleic acid (monounsaturated fat) for linoleic acid produced significant differences in BP of normotensive subjects or of hypertensive subjects (present study).

To summarize the results of trials of dietary fats and BP, studies that used a randomized control group, blind or open, generally did not find significant effects on BP. Uncontrolled observational studies that used baseline and posttreatment follow-up values for comparison often found small decreases in BP when the diet was enriched with linoleic acid. Such study designs may suffice for certain biological variables, but BP is notoriously and variably subject to placebo effects, observer influences, diurnal variation, and seasonal drift. Substantial effort needs to be taken in studies of BP to eliminate these extraneous effects. We believe that the rigor required of drug treatment trials should, as much as possible, be applied to nutritional studies.

It is likely that when the overall diet is changed to modify the content of fat, ingestion of one or more nutrients other than fats sometimes may increase to lower BP. For example, studies of two types of vegetarian diets obtained divergent results on changes in BP. Although the dietary fat content was altered in both diets, the hypotensive result was obtained with the diet that concomitantly increased dietary fiber, potassium, calcium, magnesium, and several vitamins. These results, together with the consistent findings of low BP in vegetarians, suggest that dietary fats per se are not directly involved in the regulation of BP but that changes in their intake may be a marker for another nutrient or set of nutrients that are hypotensive. Since modified fat diets have in common the ability to lower blood cholesterol and are widely recommended, the identification of associated nutrients that may also reduce BP should be a high priority for future research.

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