Hypotensive effects of solitary addition of conventional nonfat dairy products to the routine diet: a randomized controlled trial1–3

Daniel R Machin, Wonil Park, Mohammed Alkatan, Melissa Mouton, and Hirofumi Tanaka

ABSTRACT
Background: The high consumption of low-fat and nonfat dairy products is associated with reduced risk of high blood pressure.

Objective: We aimed to investigate whether the solitary addition of nonfat dairy products to the normal routine diet was capable of lowering blood pressure in middle-aged and older adults with elevated blood pressure.

Design: With the use of a randomized, crossover intervention-study design, 49 adults (56% women) with elevated blood pressure (mean ± SEM age: 53 ± 2 y; systolic blood pressure: 135 ± 1 mm Hg) underwent a high-dairy condition (+4 servings conventional nonfat dairy products/d) and isocaloric no-dairy condition (+4 servings fruit products/d) in which all dairy products were removed. Both dietary conditions lasted 4 wk with a 2-wk washout before crossing over into the alternate condition.

Results: The high-dairy condition produced reductions in systolic blood pressure (135 ± 1 to 127 ± 1 mm Hg) and pulse pressure (54 ± 1 to 48 ± 1 mm Hg) (both P < 0.05). The hypotensive effects were observed within 3 wk after the initiation of the dietary intervention and in both casual seated and ambulatory (24-h) measurements (P < 0.05). Pulse pressure was increased after the removal of all dairy products in the no-dairy condition (54 ± 1 to 56 ± 1 mm Hg; P < 0.05). There were no changes in diastolic blood pressure after either dietary condition.

Conclusion: We concluded that the solitary manipulation of conventional dairy products to the normal routine diet would modulate blood pressure in middle-aged and older adults with prehypertension and hypertension. This trial was registered at clinicaltrials.gov as NCT01577030. Am J Clin Nutr 2014;100:80–7.

INTRODUCTION
Diseases of the cardiovascular system increase with advancing age and are responsible for more annual deaths than any other causes (1). One of the most important and predictive risk factors for cardiovascular disease (CVD)2 is elevated blood pressure (BP), particularly systolic BP and pulse pressure in middle-aged and older adults (2). Although risk of coronary heart disease is greater in hypertensive than normotensive adults at any age, the magnitude of risk elevation associated with hypertension is much greater in older than young adults (3). From a societal standpoint, it is of paramount importance to reduce the incidence of systolic hypertension, particularly isolated hypertension, in middle-aged and older adults.

In most individuals with elevated BP, the initial treatment approach is the adoption of healthy lifestyle modifications, including dietary changes (4). The identification of dietary changes that lower BP comes from the observation that dietary calcium consumption, particularly from dairy products, was lower in individuals with hypertension (5). In a follow-up study, it was shown that dairy products, fruit, and vegetables were inversely related to BP (6). These findings were used to describe the Dietary Approaches to Stop Hypertension (DASH) diet, which is high in fruit, vegetables, and low- and nonfat dairy products but low in total fat and sodium and has been shown to lower BP in individuals with elevated BP (7, 8). The DASH diet has become a mainstay of dietary modifications to reduce BP. In the DASH-diet interventional study (8), subjects completed one of the following 3 dietary interventions: 1) a typical Western diet, 2) a diet high in fruit and vegetables, and 3) the DASH diet. Subjects who consumed the DASH diet had greatest reductions in BP. These reductions were even greater than in subjects who consumed the fruit and vegetable diet and were attributed to the addition of low- and nonfat dairy products in the DASH diet. However, note that the hypotensive effects of the DASH diet cannot be ascribed to dairy products alone because other dietary changes (eg, a reduction in total and saturated fats) were also incorporated. Several other interventional studies have shown reductions in BP after the consumption of a diet high in low-fat and nonfat dairy products (7, 9–11), although some studies have not shown these reductions (12, 13). However, most of these studies were controlled feeding studies or incorporated other dietary or lifestyle changes. It has not previously been known if the solitary addition of nonfat dairy products to the normal routine diet, without any other lifestyle or dietary changes, is capable of reducing BP. We reasoned that such a dietary approach would be more practical, adaptable, and generalizable for the secondary prevention of hypertension.

Accordingly, the primary aim of the current study was to determine effects of conventional nonfat dairy products added to...
the normal routine diet in middle-aged and older adults with elevated BP. Our working hypothesis was that the addition of nonfat dairy products would reduce BP. BP was measured in the casual resting state and ambulatory (24-h) condition. To maximally differentiate dietary dairy intake, all dairy products were removed from the routine diet in the control condition.

SUBJECTS AND METHODS

Subjects

A total of 49 adults (44% men and 56% women) with a mean (±SEM) age of 53 ± 2 y were studied (Figure 1). Subjects were recruited via advertisements on The University of Texas at Austin website, via fliers posted on the campus and the surrounding community, and from our database of subjects who participated in previous studies in the laboratory. Inclusion criteria were as follows: elevated systolic BP in the seated position between 120 and 159 mm Hg (prehypertension or stage 1 systolic hypertension) with diastolic BP <100 mm Hg, no overt signs of chronic diseases on physical examination and medical history, normal blood chemistry, ankle-brachial index ≥0.9, nonsmoker for previous 2 y, not lactose intolerant, dairy product consumption ≥3 servings/d, and strenuous physical activity ≤3 d/wk. Five subjects were taking antihypertensive medications, and medication dosages and routines were maintained throughout the entire study. Before entrance into the study, all subjects underwent a 2-wk run-in period that included 3 screening visits to ensure that all subjects had stable BP within the appropriate range. The University of Texas at Austin Institutional Review Board reviewed and approved the study. All volunteers gave their written informed consent before participation.

Experimental design

We used a controlled, randomized, crossover experimental design with two 4-wk dietary conditions and a washout period of ≥2 wk.
separating dietary conditions. The rationale for 4 wk of dietary intervention was based on 1) recommendations from health care organizations regarding the use of nonpharmacologic treatment strategies to improve cardiovascular risk factors and 2) because BP changes very rapidly to intervention stimuli as early as 2–4 wk; therefore, the 4-wk intervention would allow a sufficient period of time for the dietary product stimulus to produce the hypothesized effects. Measurements were taken at the beginning and end of each dietary condition at the same time of day to eliminate any diurnal effects and after subjects had abstained from food, alcohol, caffeine, and exercise for ≥12 h. In premenopausal women, measurements were performed during the early follicular phase of the menstrual cycle.

The 2 dietary conditions were a high-dairy condition and an isocaloric no-dairy condition. During the high-dairy condition, subjects added 4 servings/d of nonfat milk (HEB Grocery Company), nonfat fruit-juice–sweetened yogurt (Cascade Fresh), and/or nonfat cheese (Kraft Foods Group) on top of their baseline dietary dairy intake. One serving of dairy was 245 g milk, 170 g yogurt, or 57 g cheese. The research bionutritionist explained how much one serving of all dairy products was to each subject. Milk was provided to subjects by the gallon or one-half gallon with measuring cups. Yogurt and cheese products were in single-serve packaging. Subjects were free to consume required servings at any time of day as a single dose or all at once. During the no-dairy condition, all dairy products were removed from the diet, and 4 daily servings of fruit juice, applesauce, and/or fruit cups were added to the diet. Additional servings of fruit products were provided to subjects with regular dairy consumption at baseline to counterbalance calories lost because of the removal of dairy products during the no-dairy condition. Before the start of each dietary condition, subjects met with a research bionutritionist to have specific instructions about the dietary conditions explained to them. After the dietary consultation, subjects received 1 wk worth of food products and returned weekly for additional food-product refills. Throughout the entire experimental protocol, subjects were instructed to maintain their normal lifestyles aside from dietary changes prescribed by the laboratory research bionutritionist to reduce the overall caloric content when 4 servings of dairy or fruit products were added. Research staff enrolled participants on the study, generated the random allocation to the treatment sequence (by using a coin-flip simple randomization), and implemented the allocation sequence. Because of the nature of experimental dietary conditions, it was not possible to blind subjects to what dietary condition they were currently in. In addition, there was no true placebo condition because a lack of treatment provision was considered unethical for this high-risk population. The study was conducted from January 2012 to November 2013.

Seated brachial BP measurements

Seated brachial artery BP measurements were made with a semiautomated BP device (Omron HEM-907XL; Omron Healthcare Inc) in triplicate on the right arm after 5 min in the upright seated position with the arm at heart level and under quiet, comfortable, ambient (∼24°C) laboratory conditions (14). In addition, to determine the time course of BP changes with the dietary intervention, casual seated BP was measured during weekly visits to the laboratory to refill food products.

Ambulatory (24-h) BP measurements

Ambulatory BP recordings were made over a 24-h period of normal daily activity by using a noninvasive ambulatory BP monitor (Model 90217; SpaceLabs Medical) (15). The ambulatory system was programmed to inflate automatically every 15 min from 0600 to 2300 and every 20 min between 2300 and 0600.

Blood samples

A blood sample was collected by venipuncture after an overnight fast. Fasting whole blood concentrations of total cholesterol, HDL cholesterol, triglycerides, and glucose were determined enzymatically. LDL cholesterol was estimated by using measured concentrations of total cholesterol, HDL cholesterol, and triglycerides. The whole blood glycated hemoglobin concentration was measured by using a commercially available glycated hemoglobin reagent kit (DCA Systems; Siemens Healthcare Diagnostics).

Dietary analyses

Subjects were given detailed instructions on how to keep 3-d dietary records by the research bionutritionist. During weekly visits to the laboratory to refill food products, dietary records were collected before and at the end of each dietary condition and analyzed with Nutritionist Pro software (Axxya Systems). The software is based on the comprehensive food-knowledge database with >51,000 foods and ingredients. Study compliance during each dietary condition was assessed by having each subject complete daily dietary surveys that indicated the consumption of food products provided as well as any dairy products consumed as part of their normal diets.

Statistical analyses

Power calculations were performed with nQuery Adviser computer software (Statistical Solutions). The α level used for power analyses was set at 0.05. Sample-size calculations were based on the number of subjects needed to detect significant changes in primary dependent variables from baseline in response to lifestyle modifications (16–19). With 49 subjects/group, we had >80% power to detect changes. A per-protocol analysis was conducted to compare treatment groups that include subjects who completed both dietary conditions. That is, the intention-to-treat analysis was not used. A 2- and 3-factor mixed-model ANOVA with repeated measures was used to evaluate the effect of the condition × time interaction with SPSS software (version 21; IBM). When a significant condition × time interaction was showed, paired-samples t tests with Bonferroni correction were conducted to determine the difference between specific time points. Statistical significance was set at P < 0.05 for all analyses. Data are presented as means ± SEMs.

RESULTS

Subject compliance and adherence to the study protocol was 97% and 96% in the high-dairy and no-dairy conditions, respectively, on the basis of the daily dietary survey. Although no subjects blatantly consumed dairy products while in the no-dairy condition, a few subjects accidentally consumed dairy products (<1 serving/wk) in the beginning of the no-dairy intervention.
In addition, a few individuals did not consume all servings of study food products on a daily basis. When this occurred, we instructed subjects to consume missing servings on the following day. Because the noncompliance was fairly minor in nature, these subjects were included in the study sample. Selected subject characteristics are presented in Table 1. Body mass and metabolic profiles did not change with either dietary condition. There were no sex-related differences in responses to dietary conditions or in any response described as assessed by using a 3-factor mixed model ANOVA with repeated measures (sex \times condition \times time). Accordingly, sex was dropped from analyses. The elimination or addition of subjects with antihypertensive medications (n = 5) did not affect overall results.

As shown in Table 2, there were no significant differences in total caloric intake between or within dietary conditions. Dietary protein intake increased after the high-dairy condition but decreased after the no-dairy condition (P < 0.05). In the high-dairy condition, total dairy intake increased significantly from 1.2 ± 0.1 to 4.7 ± 0.1 servings/d (P < 0.05) with laboratory-provided nonfat dairy products accounting for 4.0 ± 0.1 servings/d with 2.0 ± 0.1, 1.9 ± 0.1, and 0.1 ± 0.0 servings/d coming from milk, yogurt, and cheese, respectively. Conversely, in the no-dairy condition, total dairy intake decreased from 1.4 ± 0.1 to 0.0 ± 0.0 servings/d (P < 0.05). Baseline dairy intake consisted of 0.4 ± 0.1 servings nonfat dairy products/d and 0.7 ± 0.1 servings full-fat dairy products/d. As expected, after the high-dairy condition, potassium, calcium, magnesium, and vitamin D intakes increased (P < 0.05); all of these intakes, except for potassium, decreased after the no-dairy condition (P < 0.05). Most importantly, dietary consumption of potassium, calcium, magnesium, vitamin D, and dairy products were significantly different between conditions after 4-wk interventions (P < 0.05 for all).

As depicted in Figure 2, systolic BP decreased significantly after the high-dairy condition (P < 0.05). No such changes were observed after the no-dairy condition. There were no changes in diastolic BP after either dietary condition. Pulse pressure was reduced by 6 ± 1 mm Hg (P < 0.05) after the high-dairy condition and had an increase of 2 ± 1 mm Hg (P < 0.05) after the no-dairy condition.

Analyses of weekly BP measurements revealed that both systolic BP and pulse pressure were significantly decreased as early as week 3 of the high-dairy condition (P < 0.05) (Figure 3). In addition, these values at weeks 3 and 4 in the high-dairy condition were significantly different from those measured during the same weeks in the no-dairy condition (P < 0.05). There were no significant changes in diastolic BP in either group.

A general trend of changes in ambulatory BP was similar to those observed during the casual seated BP measurement (Figure 4). Ambulatory (24-h) systolic BP decreased significantly after the high-dairy condition with most of the BP reduction coming from daytime periods (P < 0.05). There were no changes in ambulatory diastolic BP after either dietary condition. Ambulatory
Pulse pressure decreased \((P < 0.05)\) after the high-dairy condition during the 24-h and daytime periods.

**DISCUSSION**

Primary findings from the current randomized crossover study were as follows. The addition of 4 daily servings of conventional nonfat dairy products to the normal routine diet decreased systolic BP and pulse pressure in middle-aged and older adults with elevated BP. The reduction in casual seated BP was accompanied by a similar reduction in ambulatory (24-h) BP that was attributable mainly to the decrease in daytime BP. Conversely, when all dairy products were removed from the routine diet, pulse pressure increased significantly. These findings indicate that the solitary manipulation of nonfat dairy products can modulate BP in middle-aged and older adults with elevated BP.

With advancing age, systolic BP increases, and diastolic BP decreases, which result in a widening of pulse pressure (20). In middle-aged and older adults, pulse pressure is highly predictive of CVD risk, even more so than systolic or diastolic BP (21). In the current study, we observed significant reductions in systolic BP and pulse pressure after the high-dairy condition. The pulse pressure decreased \((P < 0.05)\) after the high-dairy condition during the 24-h and daytime periods.

**FIGURE 2.** Mean (±SEM) seated resting brachial systolic blood pressure (A), diastolic blood pressure (B), and pulse pressure (C) before and after each condition \((n = 49)\). All significant differences were preceded by a significant condition \(\times\) time interaction. \(*P < 0.05\) compared with before; \(\dagger P < 0.05\) compared with after in the no-dairy condition.

**FIGURE 3.** Time course of mean (±SEM) changes in casual seated brachial systolic blood pressure (A), diastolic blood pressure (B), and pulse pressure (C) measured weekly \((n = 49)\). All significant differences were preceded by a significant condition \(\times\) time interaction. \(*P < 0.05\) compared with week 0 within condition; \(\dagger P < 0.05\) compared with no dairy.
analyses of the time course indicated that the hypotensive effects of the nonfat dairy products were significant as early as 3 wk after the initiation of the high-dairy condition. These results indicate that the solitary addition of conventional dairy products to the normal routine diet could produce significant reductions in systolic BP and pulse pressure well within the time frame that lifestyle modifications including dietary changes are typically prescribed.

Results of the current study were generally consistent with those of previous studies that reported that increased low-fat and nonfat dairy product consumptions were associated with BP-lowering effects (7–11). However, a dietary intervention study with a similar research design to that in the current study showed no hypotensive benefit after 61 overweight or obese individuals increased the consumption of low-fat dairy products (+4 servings/d) for 6 mo (12). The conflicting results may have been due to differences in dietary calcium intakes. Dietary calcium consumption has been shown to be lower in individuals with hypertension and inversely related to BP (5, 6). There has been evidence of calcium-metabolism disturbances in individuals with hypertension (22), which may have been attributable to low dietary calcium consumption (5, 6) because dietary calcium supplementation has been shown to reduce BP in hypertensive individuals (23). When dairy product consumption is increased, dietary calcium consumption is increased accordingly. In the current study, baseline calcium consumption was lower (~750 compared with ~1100 mg/d), and the gradient in dietary calcium after the high-dairy condition was nearly 2-fold greater (~1350 compared with ~700 mg/d) than in the previous study (12). Thus, changes in BP may have been attributable to differences in dietary calcium consumption after dietary interventions.

Not only did we observe reductions in systolic BP and pulse pressure in the casual resting state, but we also observed significant reductions in the ambulatory state. However, the magnitude of reductions in systolic BP and pulse pressure after the high-dairy condition was less in the ambulatory measurements. Although guidelines of BP treatment typically refer to BP values measured in seated resting conditions, ambulatory BP measured in 24 h is more representative of normal life and may be a better indicator of CVD risk than is casual resting BP (24). Thus, reductions in BP we observed in ambulatory measurements after the high-dairy condition may have a greater prognostic benefits for middle-aged and older adults with elevated BP who seek to gain a benefit from dairy products.

A rather unanticipated finding of the current study was that pulse pressure increased significantly when the regular consumption of dairy products was removed from the routine diet. Compared with the high-dairy condition for which 4 servings nonfat dairy were added, a much-lower quantity of dairy products were removed from the diet (1.4 servings/d) in the no-dairy condition. These results implied that the subjects in the current study enjoyed the hypotensive benefits from relatively modest consumption of dairy products in their routine diet. It is possible to argue that the increase in pulse pressure might have been a result of the addition of fruit products provided in the no-dairy condition. However, fruit consumption is inversely related to BP and CVD (6, 25). In addition, national BP guidelines recommend an increased dietary consumption of fruit products as well as of low-fat and nonfat dairy products to reduce BP (4). We observed no changes in blood lipid profiles, glucose, or glycated hemoglobin in the no-dairy condition that were consistent with hypertensive effects. Although fruit products provided were isocaloric to nonfat dairy provided in the alternate condition, they contained minimal protein and were higher in carbohydrate content. The amount that
high compliance and adherence, dairy products can be easily incorporated into the daily routine of older adults to gain hypotensive benefits.

The authors’ responsibilities were as follows—DRM, MM, and HT: designed the research; DRM, WP, and MA: conducted the research; DRM and MM: analyzed data; DRM and HT: wrote the manuscript; HT had primary responsibility for the final content of the manuscript; and all authors: read and approved the final manuscript. None of the authors had a conflict of interest. The Dairy Research Institute played no role in the study design, implementation, analysis, or interpretation of data.

REFERENCES


