A Sodium-Rich Carbonated Mineral Water Reduces Cardiovascular Risk in Postmenopausal Women[1,2]

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ABSTRACT This study was designed to investigate the possible beneficial effects of consuming a sodium-rich carbonated mineral water on lipoprotein metabolism and to determine whether consumption of this water influences endothelial dysfunction (ED) in postmenopausal women. Women included in the study were amenorrheic (>1 y), healthy, and not obese (BMI < 30 kg/m^2). The subjects did not take estrogen replacement therapy; supplements of vitamins, minerals, and phytoestrogens; or other medications known to affect bone and lipid metabolism. The study consisted of 2 intervention periods of 2 mo each, during which women drank 1 L/d of a control mineral water (low mineral content) for 2 mo followed by the carbonated mineral water, rich in sodium, bicarbonate, and chloride, for 2 mo. Body weight, height, and blood pressure were measured, and BMI was calculated. Blood samples were taken from fasting subjects and serum was analyzed for total cholesterol, HDL-cholesterol, LDL-cholesterol, triacylglycerols, apolipoprotein AI, apolipoprotein B, soluble intercellular cell adhesion molecule-1 (sICAM-1), soluble vascular cell adhesion molecule-1 (sVCAM-1), and glucose. Blood pressure levels did not change throughout the study. Carbonated water intake decreased total cholesterol and LDL-cholesterol levels by 6.8% ($P = 0.001$) and 14.8% ($P < 0.0001$), respectively, whereas HDL-cholesterol concentration increased by 8.7% ($P = 0.018$), compared to the control period. Therefore, cardiovascular disease (CVD) risk indexes (total cholesterol/HDL-cholesterol and LDL-cholesterol/HDL-cholesterol) were markedly reduced (both $P < 0.0001$). Soluble ICAM-1 and sVCAM-1 levels decreased by 8.4% ($P = 0.007$) and 14.8% ($P = 0.015$), respectively. Fasting serum glucose concentration decreased by 6.7% ($P < 0.0001$). Triacylglycerol levels did not change. Consumption of this sodium rich carbonated water can play a beneficial role in the prevention of CVD and the metabolic syndrome. J. Nutr. 134: 1058–1063, 2004.

KEY WORDS: • *carbonated mineral water* • *cardiovascular risk* • *postmenopausal women* • *lipid metabolism* • *sodium bicarbonate*

Although knowledge of the salutary properties of certain waters dates back to Hippocrates, the first epidemiological data relating water consumption with health and digestion appeared in the 20th century. Some studies demonstrated a positive geographical correlation between stroke-associated mortality and river water acidity (1–4). The health benefits of mineral water were studied, particularly in Eastern European spas (5–7). Epidemiological studies carried out over the past 10 y (8–11) found relations between the mineral content of drinking water and the cardiovascular disease (CVD)[4] mortality rate in various countries. Although epidemiological studies report the effects of different waters on lipid metabolism, experimental findings on the possible role of drinking water in modifying the lipid and lipoprotein profiles of plasma are very scarce.

Water intake favors the digestive solubility of foodstuffs and improves intestinal physiology (12). However, results vary depending on the type of water mineralization. Most authors (12–14) have suggested that thermal waters are valid tools in the treatment of illnesses such as functional dyspepsia, irritable

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[4] Abreviations used: ABC, ATP-binding cassette; ABC1, ABC protein-1; ATP-III, Adult Treatment Panel III; CHD, coronary heart disease; CVD, cardiovascular disease; ED, endothelial dysfunction; sICAM-1, soluble intercellular cell adhesion molecule-1; sVCAM-1, soluble vascular cell adhesion molecule-1.

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bowel syndrome, and functional disorders of the biliary tract, because carbonated waters stimulate the secretion and motility of the digestive tract (12). Other authors have reported important effects of various mineral waters, mostly fizzy bicarbonated mineral waters, on lipoprotein levels in humans (14–16). Toussaint et al. (17) suggested that in rats, salt-rich mineral waters enhance the conversion of cholesterol into bile acids and their subsequent secretion.

The present study was designed to investigate the possible beneficial effects of consuming a carbonated mineral water, rich in sodium, bicarbonate, and chloride, on lipoprotein metabolism and to determine whether consumption of such water affects indicators of endothelial dysfunction (ED) such as levels of the adhesion molecules, soluble intercellular cell adhesion molecule-1 (sICAM-1), and soluble vascular adhesion molecule-1 (sVCAM-1). Endothelial dysfunction plays a central role in atherosclerosis. The experiment was conducted with postmenopausal women, who have a more atherogenic lipid profile, higher levels of adhesion molecules, and a greater risk of CVD compared to premenopausal women (18).

SUBJECTS AND METHODS

Subjects. Postmenopausal women ($n = 18$) from the Menopause Program of the Madrid City Council Food and Health Department participated in the present study. Women enrolled in this prevention program periodically undergo clinical evaluation by means of anthropometric measurement, blood analysis, bone mineral density measurement, and mammography.

After being informed of the study conditions by physicians, the women were interviewed regarding their dietary habits. Individuals selected for the study were amenorrheic (≥1 y) and healthy. In addition, study participants were not obese (BMI < 30 kg/m^2), were not receiving estrogen replacement therapy or any other medication known to affect bone and lipid metabolism, and were not taking vitamin, mineral, or phytoestrogen supplements. Participants had not consumed diets intended to cause weight loss within 1 y of selection. The study protocols were approved by the Ethics Committee of the Spanish Council for Scientific Research.

Study design. The study consisted of 2 consecutive 2-mo intervention periods during the cold season. Subjects consumed 1 L/d of a control mineral water during period 1 and 1 L/d of the carbonated mineral water during period 2. Both mineral waters were provided in 0.5-L bottles (Vichy Catalán, S.A.). The mineral waters differed in appearance, because one contained carbonic gas. In addition, it was not possible to carry out a blind study because the subjects were in contact with each other. Therefore, we applied a well-controlled sequential design, beginning the water treatment with all subjects simultaneously. Compliance and possible variations in dietary habits were monitored with specific questionnaires. The carbonated mineral water was rich in bicarbonate, sodium, and chloride, whereas the control water was low in minerals **(Table 1)**.

TABLE 1

Composition of the mineral waters used in the study

Component	Carbonated water	Control water	Carbonated/control
	mg/L (mmol/L)		
HCO_3^-	2094.4 (34.34)	71.1 (1.17)	29.5
Cl^-	583.0 (16.44)	5.7 (0.16)	102.3
SO_4^{2-}	49.9 (0.52)	15.7 (0.18)	3.2
F^-	7.9 (1.0)	0.2 (0.01)	39.5
Ca^{2+}	43.6 (1.09)	25.2 (0.63)	1.7
Mg^{2+}	5.7 (0.24)	2.7 (0.11)	2.1
Na^+	1116.5 (48.57)	9.0 (0.39)	124.1
K^+	54.7 (1.4)	1.4 (0.04)	39.1

Dietary control and compliance. Each subject's dietary intake was evaluated to control for possible changes in lipid metabolism associated with modifications in dietary intake. A trained dietitian recorded the dietary intake of each volunteer in an interview at the beginning of the control period, using a validated version of the dietary history. Each subject also later completed a 3-d record corresponding to the last 3 d of the carbonated water treatment period. Only 1 dietary history was obtained because repeated histories are not needed in short-term studies. Other researchers have reported agreement between the food intake data obtained by the dietary history and that obtained by the 3-d record (19,20). Therefore, a 3-d record at the beginning of the study was considered unnecessary.

The dietary history was obtained to assess the dietary habits of each volunteer. It consisted of an FFQ for the preceding month in which portion sizes were assessed precisely. Moreover, all subjects completed questionnaires concerning physical activity, sun exposure, lifestyle, and socioeconomic status. Dietary intake and dietary quality indexes, including indexes of the energy provided by macronutrients, alcohol, and fatty acids, and the (MUFA + PUFA):SFA and PUFA:SFA ratios were calculated (21). Compliance was controlled using a specific questionnaire and personal phone interviews.

Anthropometric and blood pressure measurements. At the beginning and completion of each intervention period, weight, height, waist and hip circumference, and systolic and diastolic blood pressure were measured by trained staff. The BMI was also calculated.

Blood sampling and biochemical assays. Blood samples were collected by venipuncture between 0800 and 0830 h, after a 12-h fasting period. Only 1 blood draw was used to assay plasma lipids; therefore, the day-to-day variability in plasma lipids was not accounted for. Serum was separated by low-speed centrifugation for 15 min. Serum total cholesterol, HDL-cholesterol, and triacylglycerol concentrations were measured by automated enzymatic methods (CHOD-PAP and GPO-PAP, Boehringer Mannheim; and RA-XT autoanalyzer, Technicon). Fasting serum glucose concentration was measured by an automatic analyzer (RA 2000, Technicon). Serum LDL-cholesterol concentration was calculated using the Friedewald formula (22).

Soluble ICAM-1 and sVCAM-1 concentrations of serum stored at −80°C were measured by the ELISA technique, using a commercially available kit (Parameter, R&D Systems).

Risk index calculation. The CVD risk indexes were calculated as the total cholesterol:HDL-cholesterol and LDL-cholesterol:HDL-cholesterol ratios. The coronary heart disease (CHD) risk index was calculated using a simplified coronary prediction model, the Adult Treatment Panel III (ATP-III) model from the National Cholesterol Education Program (23). The ATP-III model uses a scoring system taking into account age, LDL- or total cholesterol level, blood pressure, smoking habits, and diabetes status to estimate the risk of developing CHD within 10 y.

Statistics. Data are presented as means ± SD and percentage changes. Data were analyzed by ANOVA with repeated measures. Values of $P < 0.05$ were considered significant. The SPSS statistical package (version 11.0) was used to analyze the data.

RESULTS

Dietary assessment. The compliance rate was high (83%). Dietary energy intake of the subjects did not vary throughout the entire study. The protein, carbohydrate, fat, cholesterol, and fiber intakes and the lipid profile of the subjects did not differ between the 2 treatment periods **(Table 2)**.

Anthropometric and blood pressure data. The weight, BMI, and blood pressure of the subjects did not change during the study **(Table 3)**. Waist circumference measurements were appropriate for postmenopausal women and did not differ between the 2 treatment periods.

Serum glucose, lipid, lipoprotein, and cellular adhesion molecule concentrations. The total serum cholesterol concentration of the subjects was 6.8% lower at the end of the carbonated mineral water treatment period, compared to the

TABLE 2

Energy and nutrient intake data for 18 postmenopausal women who consumed 1 L/d of control and carbonated water for 2 mo each[1]

	Control water			Carbonated water		
	Mean ± SD	Minimum	Maximum	Mean ± SD	Minimum	Maximum
Energy, *kJ/d*	8699 ± 1866	6284	12,355	8526 ± 1318	6586	10,895
Protein, *g/d*	96 ± 28	60	176	97 ± 20	68	140
Lipid, *g/d*	86 ± 27	54	152	88 ± 18	66	121
SFA, *g/d*	25.8 ± 10	16.5	49.4	27.6 ± 7.8	15	42.4
MUFA, *g/d*	41.2 ± 12.1	25.3	68.8	40.9 ± 7.8	30.4	54.6
PUFA, *g/d*	10.8 ± 3.5	6	19	10.3 ± 3.5	1.7	17.7
Carbohydrate, *g/d*	222 ± 45	151	301	205 ± 43	149	275
Fiber, *g/d*	21.2 ± 6	12.9	32.3	19.7 ± 6	12.4	32.2
Protein, *% energy*	18.4 ± 3.4	13.6	26.7	19.3 ± 3.4	12.4	26.1
Carbohydrate, *% energy*	40.5 ± 6.3	29.2	51.3	37.5 ± 6.3	25	50.2
Lipid, *% energy*	36.9 ± 5	29.3	47.2	38.9 ± 3.3	32.4	43.9
SFA, *% energy*	11 ± 2.3	7.7	15.5	12.7 ± 2.5	9.5	20.1
MUFA, *% energy*	17.7 ± 2.4	13.7	22.2	18.1 ± 2.2	14.9	21.5
PUFA, *% energy*	4.7 ± 1	3.3	6.1	4.8 ± 1	2.8	6.1
Cholesterol, *mg/d*	328 ± 119	149	543	397 ± 149	91	724
PUFA:SFA	0.43 ± 0.1	0.3	0.7	0.41 ± 0.1	0.2	0.7
(PUFA + MUFA):SFA	2.1 ± 0.4	1.6	2.9	2 ± 0.5	1.4	3.4
Linoleic acid, *g/d*	8.6 ± 3.3	4.1	16.6	8.5 ± 2.6	5	15.4
Linolenic acid, *g/d*	0.9 ± 0.4	0.5	1.7	1.2 ± 1.1	0.6	5.6

[1] The variables did not differ between the control and carbonated water treatment periods.

control water period ($P = 0.001$) **(Table 4)**. Serum triacylglycerol levels did not differ at the end of the 2 periods. After the carbonated water period, serum LDL-cholesterol decreased markedly (14.8%; $P < 0.0001$), whereas HDL-cholesterol increased significantly (8.7%; $P = 0.018$), compared to the control water period. Both CVD risk indexes (total cholesterol:HDL-cholesterol and LDL-cholesterol:HDL-cholesterol) were significantly lower after the carbonated water period ($P < 0.0001$). Apolipoprotein A-1 and apolipoprotein B levels did not differ at the end of the 2 periods. Soluble ICAM-1 and sVCAM-1 levels were lower after the carbonated water period than after the control water period, with reductions of 8.4% ($P = 0.007$) and 14.8% ($P = 0.015$), respectively. The serum glucose concentration was 6.7% lower after the carbonated water period ($P < 0.0001$) than after the control water period.

National Cholesterol Education Program ATP-III score. After treatment with the carbonated mineral water, the subjects had a lower mean ATP-III 10-y risk ($P = 0.007$) **(Table 5)**. When the participants were stratified by age, the decrease was significant only for those aged 55–59 y ($P = 0.041$).

TABLE 3

Anthropometric and blood pressure data for 18 women who consumed 1 L/d of control and carbonated water for 2 mo each[1]

Variable	Control water	Carbonated water
Weight, *kg*	63.5 ± 8.0	63.4 ± 8.1
BMI, *kg/m*^{2}	24.4 ± 6.8	24.3 ± 6.8
Waist circumference, *cm*	0.81 ± 0.05	0.81 ± 0.05
Systolic blood pressure,[2] *mmHg*	132 ± 15	123 ± 16
Diastolic blood pressure, *mmHg*	79 ± 9	77 ± 9

[1] Values are means ± SD.
[2] 1 mmHg = 133.32 Pa.

DISCUSSION

The present study indicates that the consumption of 1 L/d of this sodium-rich carbonated mineral water over a 2-mo period reduces several CVD risk indexes.

Diet may delay the appearance of risk factors for chronic and cardiovascular diseases, especially in postmenopausal women (24–26). All subjects in this study were participants in the Menopause Program of the Madrid City Council, through which they received information and advice about health and diet. For this reason, the lifestyle and dietary habits of the subjects closely resembled those recommended to improve health and forestall some of the consequences of the physiological changes that occur during this stage of life. Their diet provided an adequate energy profile, with a lower fat intake than that reported for the Spanish population at large (27). Their low cholesterol and PUFA intake, and their high MUFA intake, characteristic of the Mediterranean diet, were particularly notable (28).

As an essential component of the diet, daily water intake must be considered. Water intake was only recently included in dietary recommendations for the elderly (29). Moreover, water is the base of all drinks, and it supplies essential minerals.

Investigation in this field has focused mainly on such ions as magnesium and calcium, and less information concerning the possible roles of bicarbonate, fluoride, and sodium in lipid metabolism is available (30,31). The calcium and magnesium concentrations of the mineral waters studied were too low to produce beneficial effects. However, the carbonated mineral water contained high levels of bicarbonate (2.094 g/L), sodium (1.116 g/L), and chloride (0.583 g/L), supplying 124, 102, and 30 times the control levels of these ions, respectively.

Although the consumption of 1 L/d of this carbonated water provided ~1 g/d of supplemental sodium supplementation to the diet (which was poor in sodium; unpublished data), blood pressure was not affected. One reason for this could be individual "salt sensibility," but it might also be due to the role

TABLE 4

Serum lipid, adhesion molecule, and glucose concentrations and CVD risk indexes of 18 postmenopausal women who consumed control and carbonated water for 2 mo each[1]

	Control water	Carbonated water	Difference[2]
Total cholesterol, *mmol/L*	6.05 ± 0.84	5.64 ± 0.67**	−0.41 ± 0.40
Triacylglycerols, *mmol/L*	0.83 ± 0.38	0.91 ± 0.38	0.08 ± 0.35
HDL-cholesterol, *mmol/L*	1.50 ± 0.35	1.63 ± 0.30*	0.14 ± 0.22
LDL-cholesterol, *mmol/L*	4.25 ± 0.56	3.62 ± 0.59**	−0.63 ± 0.53
LDL-:HDL-cholesterol	2.96 ± 0.67	2.29 ± 0.59**	−0.66 ± 0.53
Total-:HDL-cholesterol	4.22 ± 0.94	3.44 ± 0.7**	−0.78 ± 0.73
sICAM-1, *μg/L*	336.3 ± 49.7	307.9 ± 37.6†	−28.3 ± 39.5
sVCAM-1, *μg/L*	474.3 ± 228.1	403.9 ± 162.9*	−70.4 ± 106.7
Apolipoprotein A, *g/L*	1.76 ± 0.21	1.71 ± 0.23	−0.05 ± 0.12
Apolipoprotein B, *g/L*	1.12 ± 0.17	1.09 ± 0.14	−0.02 ± 0.1
Glucose, *mmol/L*	5.54 ± 0.41	5.17 ± 0.41**	−0.37 ± 0.35

[1] Values are means ± SD. Symbols indicate difference from the control water period: * $P < 0.05$, † $P < 0.01$, ** $P \leq 0.001$.
[2] Difference = carbonated water − control water.

of bicarbonate ions (32). Sodium bicarbonate and sodium chloride have different effects on lipid metabolism (33); bicarbonate tends to reduce some of the negative effects of sodium in the body. The carbonated water contained 39 times more potassium than the control water; potassium counteracts some of the negative effects of sodium and protects against CVD (34). However, dietary potassium intake was similar in the control and carbonated water periods, and the contribution to total potassium intake from drinking water was ≤1.5% for both mineral waters.

The findings of the present study concur with those of Capurso et al. (15), who studied the effects of an Italian salt-rich mineral water in moderately hypercholesterolemic subjects. A decrease in total cholesterol has also been reported in normocholesterolemic rats drinking sodium bicarbonated mineral water (35).

It is generally recommended that individuals reduce their salt intake to control hypertension. However, some data indicate that low salt intake increases cholesterol levels, implying increased cardiovascular risk. Sharma et al. (36) examined the effects of sodium intake on plasma lipids in healthy subjects. Over a 3 wk period, a low-salt diet (20 mmol Na/d) increased total cholesterol levels by 6% and LDL-levels by 9.8%, compared to those of subjects who consumed a high-salt diet (220 mmol Na/d). Weder et al. (37) suggested that more attention should be paid to a potential adverse effect of dietary salt restriction on cardiovascular risk. According to these data, a salt-restriction period may induce higher total cholesterol levels. Increasing salt intake could lower total cholesterol and LDL-cholesterol levels. In the present study, the majority of the participants consumed a low-salt diet (by their own initiative, as none of them presented with high blood pressure). According to 24-h urine analysis, sodium excretion was 1.2 g/d (data not shown), which indicates a low sodium intake. The reduction in total cholesterol and LDL-cholesterol levels after the 2-mo intervention period may partially be due to the additional 1 g/d of sodium supplied by the carbonated water to the habitual low-sodium diet of the participants.

TABLE 5

Estimated 10-y risk of CHD of 18 postmenopausal women who consumed control and carbonated water for 2 mo each, calculated according to the ATP-III model[1,2]

Age	*n*	Control water	Carbonated water
y		%	
45–49	4	1.5 ± 1	0.8 ± 0.5
50–54	6	1 ± 0	0.8 ± 0.4
55–59	8	2.4 ± 1.2	1.5 ± 0.5*
Total	18	1.7 ± 1.1	1.1 ± 0.6**

[1] Values are means ± SD. Symbols indicate difference from control water period: * $P < 0.05$, ** $P < 0.01$.
[2] National Cholesterol Education Program (23).

Serum levels of total cholesterol and LDL-cholesterol are regulated by the following factors: the intestinal absorption of cholesterol, the conversion rate of cholesterol into bile acids, and the bile acid pool. The high-mineral carbonated water used in the present study is alkaline and has an osmotic effect (12) that may affect the absorption and/or excretion of cholesterol. Increasing fecal bile acid loss and reducing the size of the bile acid pool stimulates the synthesis of bile acids from serum cholesterol via 7-α-hydroxylase, which consequently decreases the level of serum cholesterol. Ingestion of the carbonated mineral water probably enhances the transformation of cholesterol into bile acids and their secretion; this is consistent with the increased fecal bile acid excretion and reduced gallbladder volume reported in hypercholesterolemic subjects who consumed another salt-rich mineral water (15).

The liver x-receptor regulates intestinal cholesterol absorption through the ATP-binding cassette (ABC) gene family. It was recently shown that this membrane-associated protein, ABC protein-1 (ABC1), is involved in cholesterol efflux from the intestinal cells. However, it is not known whether the activity of ABC1 is regulated by the ionic strength in the duodenum. Consumption of the carbonated mineral water probably reversed cholesterol transport, because the HDL-cholesterol level was elevated (38). Cholesterol mobilized from tissues may be incorporated into HDLs, enhancing their concentration, and later be secreted into the intestinal lumen as a result of enhanced ABC1 activity. According to Robins & Fasulo (39) only HDLs provide a vehicle for unesterified cholesterol elimination in bile that is consistent with their putative function in reverse cholesterol transport. Moreover, our group recently reported that the consumption of this alkaline water enhances chylomicron postprandial metabolism

in postmenopausal women (40). This mechanism is related to higher HDL levels (41), which in turn explains the HDL-cholesterol levels in the women in the present study. However, data to support these hypotheses regarding the digestive tract are lacking, and further investigation is needed to ascertain the mechanism involved.

Endothelial dysfunction occurs in atherosclerosis, and the adhesion molecules sICAM-1 and sVCAM-1 are now used as biomarkers for ED in the early stages of atherogenesis. Despite many reports on the expression and function of adhesion molecules, the exact biological properties and functions of the circulating forms of these molecules remain unclear. Miles et al. (42) wrote that there is a significant linear correlation between age and sICAM-1 and sVCAM-1 plasma concentrations. Data on postmenopausal women indicate that sICAM-1 values fall within a range of 266 to 356 μg/L, whereas sVCAM-1 values vary between 548 and 818 μg/L (42–45). The values obtained for sVCAM-1 in the present study were at the low end of the range reported by others, probably because the women studied were healthy and at low risk for atherosclerosis.

After the carbonated water period, sVCAM-1 concentration was 14.8% lower than at the end of the control water period. At the same time, there was a marked increase in HDL-cholesterol levels (8.7%), in accordance with studies reporting a strong inverse correlation between the concentrations of plasma HDLs and sVCAM-1. High-density lipoproteins may have a direct inhibitory effect on one of the earliest events in atherogenesis. They are able to inhibit cytokine-induced cell surface expression of adhesion molecules (sVCAM-1 and sICAM-1) and may therefore inhibit atherogenesis at an early stage by preventing monocyte adhesion to the endothelium. On the contrary, LDLs, especially if minimally oxidized, increase monocyte adhesion to endothelial cells. Furthermore, lysiophosphatidylcholine, a major component of oxidized LDLs, induces expression of sVCAM-1 and sICAM-1 (46).

The results of the present study reflect an overall improvement in cardiovascular risk status. This less-atherogenic profile of the study subjects is also reflected in the ATP-III results (20). The prediction score sheets indicate that the women studied present optimal health conditions and have a lower risk of developing CHD over the next 10 y than the Framingham study women (47). Moreover, carbonated mineral water intake markedly reduces this risk.

In addition, the subjects presented a marked decrease in fasting serum glucose concentration. This reduction indicates the relation between lipid metabolism and glucose, suggesting that consumption of the carbonated sodium-rich water studied can play a beneficial role in preventing cardiovascular disease and the metabolic syndrome.

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