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Hypolipidemic Activity of a Natural Mineral Water Rich in Calcium, Magnesium, and Bicarbonate in Hyperlipidemic Adults

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ABSTRACT

Purpose: This study compared the effects of a mineral water rich in calcium, magnesium, bicarbonate, and sulfate and a marketed mineral water with a composition similar to that of urban water on the lipid profile of dyslipidemic adults.
Methods: In a randomized controlled trial, 32 adults received one liter of "rich mineral water" daily for one month, and 37 adults drank the same amount of normal mineral water for the same period. Changes in lipid profiles were compared separately in each studied group at the end of one month.
Results: Results showed that mean cholesterol and low density lipoprotein LDL levels were significantly decreased in both studied groups after one month of drinking mineral water ($P<0.05$); however, no significant differences in high density lipoprotein (HDL) and triglyceride (TG) levels were seen in either group one month after drinking. There were no statistically significant differences between the "rich mineral water" and the normal mineral water groups in any of the above-mentioned lipid levels ($P>0.05$).
Conclusion: A one-month intake of mineral water rich in calcium, magnesium bicarbonate, and sulfate decreased cholesterol and LDL levels but not TG or HDL levels in dyslipidemic adults.

Introduction

Atherosclerosis, the principal contributor to the pathogenesis of myocardial and cerebral infarction, is known to be one of the leading causes of morbidity and mortality worldwide. An elevated plasma concentration of cholesterol, especially low density lipoprotein (LDL), is recognized as a primary cause in the development of atherosclerosis. Epidemiological studies have revealed an association between the increased consumption of antioxidant-rich vegetables and fruits and a decreased risk of coronary heart disease.[1,2]

Among dyslipidemias, an elevated level of low density lipoproteins (LDL) – cholesterol - has for many years been considered the major risk factor of atherosclerosis.[3,4] Today's studies in human endothelium have uncovered molecular mechanisms by which oxidized-LDL-cholesterol *via* the oxidized-LDL receptor (LOX-1) or other pathways induce the phenotype of endothelial dysfunction.[5] On the other hand, the role of triglycerides in atherosclerosis had been neglected for many years as it was a widely held view that elevated triglycerides do not represent a risk factor for this disease.[6] This notion was challenged by a number of important clinical studies,[7] and today, hypertriglyceridemia is considered an important risk factor of atherosclerosis.[8-11] Evidence is also increasing that prolonged hypertriglyceridemia induces typical features of endothelial dysfunction.[12,13] Furthermore, transient postprandial hypertriglyceridemia may also induce impairment of endothelial function that contributes to the risk of atherosclerosis development.[14-16] In keeping with data from humans, hypercholesterolemia in rabbits, mice, pigeons, monkeys, and other species leads to the development of atherosclerosis,[17-19] and many studies have confirmed its association with the phenotype of endothelial dysfunction. In contrast, rats fed a high-cholesterol diet were resistant to developing atherosclerosis.[20-22] Conversely, rats fed a high-fructose diet developed hypertriglyceridemia insulin resistance and a mild degree of hypertension – abnormalities that mimic metabolic syndrome in humans.[22,23] Importantly, the

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development of insulin-resistance in rats was suggested to be linked to the impairment of NO-dependent function.[24,25]

Hyperlipidemia has been implicated in atherosclerosis, which is the leading cause of death among the world's population. A high cholesterol diet increases serum LDL levels and oxidative stress which results in increased oxidized LDL levels and thereby increases atherosclerotic plaque formation.[2] Efforts to develop effective and better hypolipidemic drugs have led to the discovery of natural agents.

The aim of this study was to assess the hypolipidemic effects of a natural mineral water rich in calcium, magnesium, bicarbonate, and sulfate on humankind and compare its effects with those of a mineral water sample similar in composition to that of Tabriz's urban water.

Materials and Methods

Patients

In a case-control and descriptive-analytical study, the effects of mineral water and drinking water on lipid profiles were evaluated. Totally, 32 patients received mineral water rich in sodium, calcium, magnesium, bicarbonate, and sulfate as the case group, and 37 patients received mineral water with physicochemical properties similar to drinking water as the control group for one month. The patients were selected from among workers of an industrial company whose diets were similar (breakfast and lunch). Their ages ranged between 30-60 years, and their cholesterol and triglyceride levels were higher than 200 mg/dl, LDL>150 mg/dl and HDL< 40 mg/dl.

According to the prevalence of hyperlipidemia, a total of 69 patients with hyperlipidemia in the age range of 30 to 60 years were selected. Patients were randomly divided into two groups: the control group which consumed marketed mineral water, and the case group which consumed enriched mineral water. Time and amount intended for the consumption of mineral water was one month and one liter per day, respectively.

Water samples

Two types of water were used in this study. The first one was a mineral water available in the Iranian market with similar physicochemical characteristics to those of drinking water in Tabriz. The second one was a mineral water rich in calcium, magnesium, and bicarbonate. Table 1 shows their physicochemical compositions.

Table 1. The Physicochemical composition of water samples used in study

Physicochemical characteristics	Mineral water rich in minerals	Mineral water in market
Total Hardness (mg/l as $CaCO_3$)	805	54
HCO_3^-(mg/l)	1350	29
SO_4^{2-}(mg/l)	165	20
NO_3^-(mg/l)	3	3
PO_4^{3-}(mg/l)	0.15	0.4
pH	7.2	6.7
Na(ppm)	150	5
K(ppm)	9	2
Mg(ppm)	48	1.7
Conductivity(µs/cm)	2100	95
Ca^{2+}(mg/l)	250	7
As(mg/l)	0.01	< 0.01
Turbidity	0.3	0.03

Biochemical analysis

The equipment used in this study included an auto-analyzer device made in Switzerland used to measure the chemical factors by the enzymatic-photometry method, a centrifuge device made in Iran, and Pars Azmoon company kits. Blood samples taken from the patients were centrifuged for 5 minutes. Test tubes containing supernatant and cholesterol oxidase enzyme were placed in the analyzer device. Oxygen released from cholesterol in the presence of cholesterol oxidase enzyme, antipyridine, and phenol forms kinonimin. The amount of kinonimin was measured by the photometry method and was directly proportional to the cholesterol amount. The level of triglycerides was measured by a similar method. The direct method was used to measure HDL.

Statistical analysis

Data are presented as Means ± SE. The SPSS statistical package for Windows (version 15.0) was used to analyze the data. Student t-test was used for data comparison. $P<0.05$ was considered significant.

Results and Discussion

The results of this study showed that means of cholesterol and low density lipoprotein (LDL) significantly decreased in patients in both groups ($P<0.05$), but a group comparison showed that these differences were not statistically significant. This reduction for mineral rich water was clinically valuable. Neither water had a statistically significant effect on TG or high density lipoprotein (HDL) levels in plasma ($P>0.05$). The results are shown in Table 2.

Mineral-rich water could provide an important supplementary contribution to total calcium and magnesium intake according to the results of a French study.[26] The suggested mechanisms are related to the moderately alkaline nature of the study mineral water and an osmotic effect that may affect fat and cholesterol absorption and/or increase bile acid excretion. It is known that the rate of fatty acid and cholesterol absorption from the micellar solution formed in the small intestine desires a lower pH[27-29] and that the action of pancreatic enzymes and bile salts is increased by the addition of pH. Therefore, an increase in luminal pH induced by the mineral water may decrease the uptake of both cholesterol and fat. Various mineral waters are able to increase the excretion of bile consumed with or without a meal.[30]

Table 2. The results for consumption of drinking and mineral water consumption in patients with hyperlipidemia before (a) and after (b) treatment

Lipid profile	Case (mineral water)		Control (drinking water)	
	Mean±SE	P value	Mean±SE	P value
CHOL [a]	250.75±6.88	0.0001	236.24±6.42	0.0006
CHOL [b]	224.47±5.52		218.65±7.02	
TG [a]	197.75±17.49	0.5019	244.08±25.25	0.1006
TG [b]	207.72±23.23		217.32±20.86	
HDL [a]	37.50±1.81	0.148	38.68±1.54	0.1843
HDL[b]	39.44±1.7		37.38±1.17	
LDL [a]	174.35±6.29	0.0001	157.40±6.94	0.0047
LDL [b]	150.31±5.34		138.48±6.94	

CHOL: total cholesterol, TG: triglycerides, HDL: high density lipoprotein, LDL: low density lipoprotein, a: before treatment, b: after treatment

Other authors have also showed reductions in gallbladder volume with the consumption of mineral waters that are rich in sulfate and calcium,[31,32] bicarbonate and calcium,[33] and sulfate and bicarbonate.[34]

Fiorucci et al. approved the effects of increasing concentrations of NaCl solutions and found that a significant reduction in gallbladder volume was seen when hyperosmolar saline was delivered into the duodenum.[35] Evacuation was not produced when the solution was infused into the gastric antrum or the ileum.

Therefore, it is possible that mineral waters with very different ionic compositions all effect the stimulation of biliary flow into the duodenum due to their high osmolality. In fact, laxative waters generally contain a high ionic concentration.[36] The mechanisms by which mineral water lowers serum total and LDL cholesterol levels could simulate those of soluble fiber. Many published reports have presented the adjustment of cholesterol metabolism in response to dietary fiber consumption. Soluble fiber reduces cholesterol absorption, mainly due to viscosity, and also interacts with the enterohepatic circulation of bile acids; both are believed to change cholesterol homeostasis by two related mechanisms: a decrease in the delivery of dietary cholesterol to the liver through chylomicron remnants, resulting in a direct reduction in the hepatic cholesterol pool, and increased loss of bile acids in feces, which may stimulate the liver to produce more bile acids from cholesterol.[13,37-39] Consequently, hepatic receptors of LDL increase, and serum LDL cholesterol declines. Consumption of soluble fiber has been associated with increased hepatic LDL receptor expression, reduction in hepatic Apo B secretion, and decreased numbers of intermediate-density lipoproteins and LDL. Phytosterols, alone or in combination with soluble fiber, have similar effects.[40,41]

Another similarity comes from hypocholesterolemic drugs, such as cholestyramine, that are also typical bile acid sequestrants. They act as ionic exchange resins rich in ammonium groups that are considered basic because they interchange with the negatively charged hydroxide ions from bile acids.

Conclusion

This study shows that consuming 1 L/day mineral water reduces cholesterol and LDL. Further investigation is needed to establish the mechanisms involved. It is also recommended that the consumption of mineral water be continued for a longer period of time.

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Zou Y, Lu Y, Wei D. Hypocholesterolemic effects of a flavonoid-rich extract of Hypericum perforatum L. in rats fed a cholesterol-rich diet. *J Agric Food Chem* 2005;53(7):2462-6.
2. Warnholtz A, Mollnau H, Oelze M, Wendt M, Munzel T. Antioxidants and endothelial dysfunction in hyperlipidemia. *Curr Hypertens Rep* 2001;3(1):53-60.
3. Homma Y. Predictors of atherosclerosis. *J Atheroscler Thromb* 2004;11(5):265-70.
4. Mertens A, Holvoet P. Oxidized LDL and HDL: antagonists in atherothrombosis. *FASEB J* 2001;15(12):2073-84.
5. Mehta JL. The role of LOX-1, a novel lectin-like receptor for oxidized low density lipoprotein, in atherosclerosis. *Can J Cardiol* 2004;20 Suppl B:32B-6B.
6. Grundy SM, Denke MA. Dietary influences on serum lipids and lipoproteins. *J Lipid Res* 1990;31(7):1149-72.
7. Albrink MJ, Man EB. Serum triglycerides in coronary artery disease. *AMA Arch Intern Med* 1959;103(1):4-8.
8. Assmann G, Schulte H. Role of triglycerides in coronary artery disease: lessons from the Prospective Cardiovascular Munster Study. *Am J Cardiol* 1992;70(19):10H-3H.
9. Austin MA. Plasma triglyceride as a risk factor for cardiovascular disease. *Can J Cardiol* 1998;14(Suppl B):14B-7B.
10. Davignon J, Cohn JS. Triglycerides: a risk factor for coronary heart disease. *Atherosclerosis* 1996;124 Suppl:S57-64.
11. Gotto AM Jr. Triglyceride as a risk factor for coronary artery disease. *Am J Cardiol* 1998;82(9A):22Q-5Q.
12. Kusterer K, Pohl T, Fortmeyer HP, Marz W, Scharnagl H, Oldenburg A, et al. Chronic selective hypertriglyceridemia impairs endothelium-dependent vasodilatation in rats. *Cardiovasc Res* 1999;42(3):783-93.
13. Everson GT, Daggy BP, Mckinley C, Story JA. Effects of psyllium hydrophilic mucilloid on LDL-cholesterol and bile acid synthesis in hypercholesterolemic men. *J Lipid Res* 1992;33(8):1183-92.
14. Bae JH, Bassenge E, Kim KB, Kim YN, Kim KS, Lee HJ, et al. Postprandial hypertriglyceridemia impairs endothelial function by enhanced oxidant stress. *Atherosclerosis* 2001;155(2):517-23.
15. Bae JH, Schwemmer M, Lee IK, Lee HJ, Park KR, Kim KY, et al. Postprandial hypertriglyceridemia-induced endothelial dysfunction in healthy subjects is independent of lipid oxidation. *Int J Cardiol* 2003;87(2-3):259-67.
16. McCarty MF. Does postprandial storage of triglycerides in endothelial cells contribute to the endothelial dysfunction associated with insulin resistance and fatty diets? *Med Hypotheses* 2003;61(2):167-72.
17. Faggiotto A, Ross R. Studies of hypercholesterolemia in the nonhuman primate. II. Fatty streak conversion to fibrous plaque. *Arteriosclerosis* 1984;4(4):341-56.
18. Lewis JC, Taylor RG, Jerome WG. Foam cell characteristics in coronary arteries and aortas of White Carneau pigeons with moderate hypercholesterolemia. *Ann N Y Acad Sci* 1985;454:91-100.
19. Masuda J, Ross R. Atherogenesis during low level hypercholesterolemia in the nonhuman primate. I. Fatty streak formation. *Arteriosclerosis* 1990;10(2):164-77.
20. Kitagawa S, Sameshima E, Yamaguchi Y, Kwon Y, Shinozuka K, Kunitomo M. Comparison of the effects of hypercholesterolemia on relaxation responses in aortas of spontaneously hypertensive rats and Dahl salt-sensitive rats. *Clin Exp Pharmacol Physiol Suppl* 1995;22(1):S251-3.
21. O'Neal RM, Still WJ. Pathogenesis of atherosclerosis. *Fed Proc* 1962;21(4) Pt 2:12-4.
22. Boehm BO, Claudi-Boehm S. The metabolic syndrome. *Scand J Clin Lab Invest* 2005;65(s240):3-13
23. Cockey CD. Defining metabolic syndrome. AWHONN Lifelines 2005;9(3):208-9.
24. Jonkers IJ, van de Ree MA, Smelt AH, de Man FH, Jansen H, Meinders AE, et al. Insulin resistance but not hypertriglyceridemia per se is associated with endothelial dysfunction in chronic hypertriglyceridemia. *Cardiovasc Res* 2002;53(2):496-501.
25. Sasaki S, Yoneda Y, Fujita H, Uchida A, Takenaka K, Takesako T, et al. Association of blood pressure variability with induction of atherosclerosis in cholesterol-fed rats. *Am J Hypertens* 1994;7(5):453-9.
26. Mooradian AD. Dyslipidemia in type 2 diabetes mellitus. *Nat Clin Pract Endocrinol Metab* 2009;5(3):150-9.
27. Chijiiwa K, Linscheer WG. Effect of intraluminal pH on cholesterol and oleic acid absorption from micellar solutions in the rat. *Am J Physiol* 1984;246(5 Pt 1):G492-9.
28. Chijiiwa K, Linscheer WG. Mechanisms of pH effect on oleic acid and cholesterol absorption in the rat. *Am J Physiol* 1987;252(4 Pt 1):G506-10.
29. Linscheer WG, Vergroesen AJ. Lipids. In: Shils ME, Olson JA, Shike M, editors. Modern nutrition in health and disease. 8th ed. Philadelphia: Lea and Febiger; 1994. P. 47–88.
30. Albertini MC, Dachà M, Teodori L, Conti ME. Drinking mineral waters: biochemical effects and health implications - the state-of-the-art. *Int J Environ Health* 2007;1(1):153-69.
31. Coiro V, Volpi R, Vescovi PP. [Choleretic and cholagogic effect of sulphuric sulfate water from

the springs of Tobiano in cholestasis in alcohol related liver diseases]. *Clin Ter* 1997;148(1-2):15-22.
32. Cuomo R, Grasso R, Sarnelli G, Capuano G, Nicolai E, Nardone G, et al. Effects of carbonated water on functional dyspepsia and constipation. *Eur J Gastroenterol Hepatol* 2002;14(9):991-9.
33. Bellini M, Spataro M, Costa F, Tumino E, Ciapparrone G, Flandoli F, et al. [Gallbladder motility following intake of mineral bicarbonate-alkaline water. Ultrasonographic assessment]. *Minerva Med* 1995;86(3):75-80.
34. Grossi F, Fontana M, Conti R, Mastroianni S, Lazzari S, Messini F, et al. [Motility of the gastric antrum and the gallbladder following oral administration of sulfate-bicarbonate]. *Clin Ter* 1996;147(6):321-6.
35. Fiorucci S, Bosso R, Morelli A. Duodenal osmolality drives gallbladder emptying in humans. *Dig Dis Sci* 1990;35(6):698-704.
36. Capurso A, Solfrizzi V, Panza F, Mastroianni F, Torres F, Del Parigi A, et al. Increased bile acid excretion and reduction of serum cholesterol after crenotherapy with salt-rich mineral water. *Aging (Milano)* 1999;11(4):273-6.
37. Ganji V, Kies CV. Psyllium husk fiber supplementation to soybean and coconut oil diets of humans: effect on fat digestibility and faecal fatty acid excretion. *Eur J Clin Nutr* 1994;48(8):595-7.
38. Matheson HB, Colon IS, Story JA. Cholesterol 7 alpha-hydroxylase activity is increased by dietary modification with psyllium hydrocolloid, pectin, cholesterol and cholestyramine in rats. *J Nutr* 1995;125(3):454-8.
39. Rideout TC, Harding SV, Jones PJ, Fan MZ. Guar gum and similar soluble fibers in the regulation of cholesterol metabolism: current understandings and future research priorities. *Vasc Health Risk Manag* 2008;4(5):1023-33.
40. Shrestha S, Freake HC, Mcgrane MM, Volek JS, Fernandez ML. A combination of psyllium and plant sterols alters lipoprotein metabolism in hypercholesterolemic subjects by modifying the intravascular processing of lipoproteins and increasing LDL uptake. *J Nutr* 2007;137(5):1165-70.
41. Sánchez-Muniz FJ. Metabolic and physiological effects of phytosterol consumption. In: Vaquero MP, García Arias T, Carbajal A, editors. Bioavailability of micronutrients and minor dietary compounds: Metabolic and technological aspects. India: Research Signpost; 2003. P. 83-94.