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Does bicarbonated mineral water rich in sodium change insulin sensitivity of postmenopausal women?

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Abstract

Aim: **To study the effects of drinking 0.5 L of two sodium-rich bicarbonated mineral waters (BMW-1 and 2), with a standard meal, on postprandial insulin and glucose changes. And to determine, if the effects vary depending on insulin resistance, measured by homeostasis model assessment (HOMA).**

Methods: **In a 3-way randomized crossover study, 18 healthy postmenopausal women consumed two sodium-rich BMWs and a low-mineral water (LMW) with a standard fat-rich meal. Fasting and postprandial blood samples were taken at 30, 60 and 120 min. Serum glucose, insulin, cholesterol and triacylglycerols were determined. Insulin resistance was estimated by HOMA and insulin sensitivity was calculated by quantitative insulin sensitivity check index (QUICKY).**

Results: **Glucose levels did not change. HOMA and QUICKY values were highly inversely correlated ($r = –1,000$; $p < 0.0001$). Insulin concentrations showed a significant time effect ($p < 0.0001$) and a significant water x time interaction ($p < 0.021$). At 120 min insulin levels with BMW-1 were significantly lower than with LMW ($p = 0.022$). Postprandial insulin concentrations showed significantly different patterns of mineral water intake depending on HOMA n-tiles ($p = 0.016$).**

Conclusion: Results suggests an increase in insulin sensitivity after BMWs consumption. This effect is more marked in the women, who have higher HOMA values. These waters should be considered part of a healthy diet in order to prevent insulin resistance and cardiovascular disease.

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Key words: *Bicarbonated mineral water. Insulin. Glucose. Sodium. Fluoride.*

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¿MODIFICA EL AGUA MINERAL BICARBONATADA RICA EN SODIO LA SENSIBILIDAD A LA INSULINA DE LAS MUJERES POSTMENOPÁUSICAS?

Resumen

Objetivo: **Estudiar los efectos de la ingesta de 0.5L de dos aguas minerales bicarbonatadas ricas en sodio (BMW-1 y 2), junto con una comida estándar, sobre los cambios en la insulina y la glucosa postprandial; y determinar si los posibles efectos varían en función de la resistencia a la insulina evaluada a través del modelo homeostático (HOMA).**

Métodos: **18 mujeres postmenopáusicas sanas participaron en un estudio triple cruzado aleatorizado, en el que bebieron 2 aguas minerales bicarbonatadas ricas en sodio (BMW-1 y 2) y un agua mineral débil (LMW) junto con una comida estándar rica en grasa. Se tomaron muestras de sangre en ayunas y postprandiales a los 30, 60 y 120 min. Se determinó glucosa, insulina, colesterol y triglicéridos en suero. La resistencia a la insulina fue estimada a través del HOMA y la sensibilidad a la insulina se calculó mediante el índice de sensibilidad cuantitativa a la insulina (QUICKY).**

Resultados: **Los niveles de glucosa no presentaron cambios. Los valores de HOMA y QUICKY presentaron una fuerte correlación inversa ($r = –1,000$; $p < 0,0001$). Las concentraciones de insulina mostraron un efecto significativo en el tiempo ($p < 0,0001$) y una interacción agua x tiempo significativa ($p < 0,021$). A los 120 min los niveles de insulina fueron significativamente inferiores con BMW1 respecto a LMW ($p = 0,022$). Las concentraciones postprandiales de insulina mostraron patrones significativamente distintos según el tipo de agua que se bebía dependiendo de los n-tiles del HOMA ($p = 0,016$).**

Conclusión: **Los resultados sugieren un aumento de la sensibilidad a la insulina tras el consumo de las dos aguas minerales bicarbonatadas ricas en sodio. Este efecto es más marcado en las mujeres que tienen unos valores de HOMA más altos. Este tipo de aguas deberían ser consideradas como parte de una dieta saludable con objeto de prevenir la resistencia a la insulina y las enfermedades cardiovasculares.**

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Palabras clave: *Agua mineral bicarbonatada. Insulina. Glucosa. Sodio. Flúor.*

Introduction

Natural mineral water intake has only been recently considered from a perspective of nutrition and health. Over the last decade several clinical studies have been directed to investigate the health benefits of mineral water and its relation to chronic diseases. Several studies have demonstrated a connection between drinking water and ischemic and cardiovascular diseases.[1,2] Other studies demonstrated that salt rich mineral waters are able to reduce serum total cholesterol[3,4] and postprandial triacylglycerol (TAG) – lipaemia.[5] High fasting TAGs are associated to coronary heart disease risk and are one of the main characteristics of insulin resistance (IR),[6] that is associated to diabetes and a number of other diseases, including obesity, hypertension, dyslipidemia, and coronary artery disease.[7,8] There is some evidence suggesting that postprandial TAG increase may also be related to insulin resistance.[9]

The metabolic syndrome (MBS) is a cluster of interrelated common clinical disorders, including obesity, insulin resistance, glucose intolerance, hypertension and dyslipemia. The risk of cardiovascular disease (CVD), attributed to MBS, appears to be especially high in postmenopausal women,[10] as a result of the reduction of the positive effects of estrogens on lipid metabolism. 17-β-estradiol modulates the concentration of lipids in plasma by regulating lipid metabolism in adipocytes and hepatocytes.[11] This protective effect disappears after menopause.

The mechanism through which body fat contributes to IR is unclear, but previous studies have shown a correlation of body mass index (BMI) with insulin in postmenopausal women.[12]

In a previous study it was found that the consumption of this highly mineralised bicarbonated water, with a high sodium content, reduces CVD risk, fasting glucose and postprandial TAG lipemia in postmenopausal women.[4,5] Thus this work aims to study: the effects of drinking 0.5 L of two sodium rich bicarbonated mineral waters with a standard fat rich meal, compared to a low mineral water, on postprandial insulin and glucose changes. Moreover determine if the effects vary depending on insulin sensitivity measured with the homeostasis model assessment (HOMA and QUICKY).

Subjects and methods

Subjects

Eighteen postmenopausal women from the Menopause Program of the Madrid City Council Food and Health Department were recruited for the study. Postmenopause was defined as ammeorrheia status for at least one year. Subjects were 51 to 59 years old. Women in this prevention program periodically undergo clinical evaluation by means of anthropometric measurements, blood tests, bone mineral density determination and mammography. The women gave written informed consent to a protocol approved by the Ethics Committee of the Spanish Council for Scientific Research. No women suffered from any digestive or metabolic disease, as verified by medical history and fasting blood indices. Volunteers selected for the study could not be obese (BMI < 30 kg/m^2), could not be receiving oestrogen replacement therapy or any other medication known to affect bone and lipid metabolism, or be taking vitamin, mineral or phytoestrogen supplements. None of the women smoked. Study participants were instructed not to deviate from their regular habits, and to maintain their normal diet and body weight, alcohol consumption and exercise levels.

Postprandial study

The subjects visited the laboratory facilities 3 times at 2-wk intervals. On each occasion the subjects fasted overnight for ≥ 12 h. In order to unify food intake, the women followed written instructions with regard to dinner composition (lettuce and tomato with olive oil, vinegar and salt; grilled chicken filet; bread and fruit) the evening before the study. On the morning of each intervention blood pressure, weight, height, and waist-to-hip ratio were measured and compliance with dinner instructions was verified with a questionnaire. After a can-

Table I
Composition of the 3 mineral waters used in the study in mg/L (mmol/L)

Component	*Bicarbonated mineral water 1*	*Bicarbonated mineral water 2*	*Control water*
HCO_{3}^{-}	2,094.4 (34.34)	2,013 (32.99)	71.1 (1.17)
Cl^{-}	583.0 (16.44)	592 (16.7)	5.7 (0.16)
SO_{4}^{2-}	49.9 (0.52)	42.9 (0.45)	15.7 (0.18)
F^{-}	7.9 (0.42)	1.4 (0.07)	0.2 (0.01)
Ca^{2+}	43.6 (1.09)	52.1 (1.30)	25.2 (0.63)
Mg^{2+}	5.7 (0.24)	9.7 (0.40)	2.7 (0.11)
Na^{+}	1,116.5 (48.6)	948 (41.3)	9.0 (0.39)
K^{+}	54.7 (1.39)	47.7 (1.22)	1.4 (0.04)

Table II
Anthropometric and biochemical baseline values of the volunteers participating in the study

Parameter (n = 18)	
Age (years)	55.5 ± 2.28
Weight (kg)	64.23 ± 6.69
BMI (kg/m²)	26.88 ± 3.04
Waist circumference (cm)	83.07 ± 9.16
Hip circumference (cm)	103.19 ± 5.84
Waist/Hip-Ratio	0.80 ± 0.06
Glucose (mg/dL)[a]	80.89 ± 5.24
Insulin (µU/ml)[a]	7.65 ± 2.52
HOMA[a]	1.53 ± 0.52
QUICKY[a]	0.36 ± 0.21
S-chol (mmol/L)[a]	5.58 ± 0.79
S-triacylglycerol (mmol/L)[a]	1.08 ± 0.23

[a] Mean ± SD of the 3 baseline values of the whole study.

nula (ABOCATH 20G, Abbott Laboratories, Abbott Park, Illinois, USA) was inserted into a vein for blood sampling, baseline samples were obtained and the volunteers received the standard meal and 0.5 L of one of the study mineral waters. Three different mineral waters were used in the study: bicarbonated mineral water 1 (BMW 1), bicarbonated mineral water 2 (BMW 2), and low mineral water (LMW). The three waters were provided in 0.5 L bottles (Vichy Catalán, S.A.).

In a triple crossover design, volunteers were randomly assigned to an individual sequence of drinking the three mineral waters, until every woman had completed the postprandial study with all three waters. The two BMWs were both rich in bicarbonate, sodium and chloride, while the LMW was low in minerals (table I). BMW 1 contained 5.7 times more fluoride than BMW 2, and 37.5 times more than the LMW. The study meal provided 4,552 kJ, and contained 75.3 g of fat, 21.5 g of protein, 86.5 g of carbohydrates, and 289 mg of cholesterol. The energy profile was: protein 7.9% energy, lipids 62.3% energy and carbohydrates 29.8% energy, and the lipid profile was: SFA 11.8% energy, MUFA 39.7% energy, and PUFA 6.6% energy.

Postprandial blood samples were taken 30, 60 and 120 min after finishing the study meal. On the average, the meal was eaten in 31 min. To maintain hydration throughout the postprandial time, women drank 100 ml of demineralised water after 240 min and 390 min.

Blood samples were collected in Venoject tubes with Gel + Clot Activator for the serum separation.

Analytical methods

Blood samples were chilled, and centrifuged immediately for 15 min at 1,500 x *g* and 4 ºC, and subsequently stored at -80 ºC.

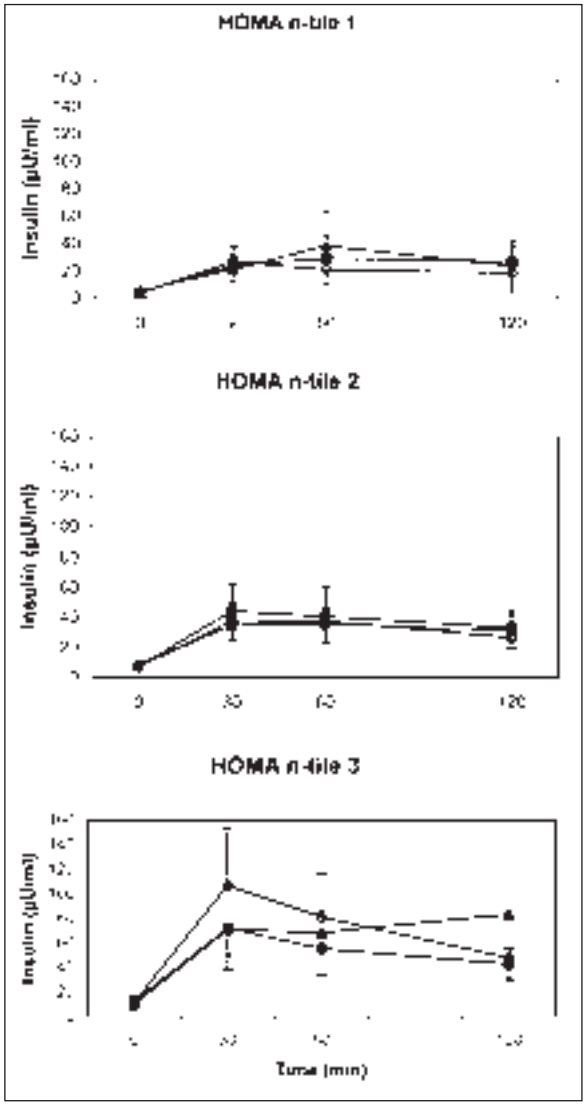

Fig. 1.—Mean (± SD) concentration of fasting and postprandial insulin values over 120 min, in 18 healthy postmenopausal women according to HOMA n-tiles 1, 2 and 3, before and after drinking: bicarbonated mineral water 1 (BMW 1, o), bicarbonated mineral water 2 (BMW 2, ■) and low mineral water (LMW) (▲). Postprandial insulin concentrations showed significantly different patterns of mineral water intake depending on HOMA n-tiles (p = 0.016). There were also significantly different time patterns (p < 0.0001) for all three waters and water x time interaction (p = 0.002) depending on HOMA n-tiles. Insulin concentrations showed nearly significant different postprandial responses in between HOMA n-tile 1 and 3 (Bonferroni test, p = 0.056).

Glucose was measured by an automatic analyzer (RA-XT Technicon, Tarrytown, NY). Insulin was determined in serum by means of an immunometric assay (Immulite® 2000 Insulin, Diagnostic Products Corporation (DPC), CA, USA) with an IMMULITE 2000 autoanalyzer.

Serum cholesterol and TAGs (S-chol, S-TAG) were determined utilising automated enzymatic methods (CHOD-PAP and GPO-PAP; Boehringer Mannheim, Germany; RA-XT Technicon, Tarrytown, NY).

Table III
Differences in baseline values depending on HOMA index n-tiles

*HOMA n-tiles**	*1 (< P25)*	*2 (> P25 and < P75)*	*3 (> P75)*	*p*
	N = 4	*N = 10*	*N = 4*	
Age (years)	57.25 ± 1.24	54.9 ± 2.18	55.25 ± 2.87	NS
Weight (kg)	55.12 ± 4.13	67.11 ± 4.93	66.13 ± 4.49	0.002
BMI (kg/m^2)	23.02 ± 1.4	27.63 ± 2.37	28.89 ± 2.51	0.004
Waist circumference (cm)	74.8 ± 4.50	87.1 ± 6.18	81.38 ± 13.89	NS
Hip circumference (cm)	96.13 ± 3.47	105.5 ± 5.0	104.5 ± 4.49	0.012
Waist/Hip-Ratio	0.78 ± 0.03	0.82 ± 0.04	0.78 ± 0.11	NS
S-cholesterol (mmol/L)[a]	5.40 ± 0.68	5.46 ± 0.58	5.58 ± 0.79	NS
S-TAG (mmol/L)[a]	0.80 ± 0.13	1.03 ± 0.26	1.08 ± 0.23	NS

[a] Mean ± SD of the 3 baseline values of the whole study.
* < P25: HOMA values < 1.18), > P25 and < P75: HOMA values > 1.18 and < 1.89 and > P75: HOMA values > 1.89.

Assessment of insulin status and classification in HOMA and QUICKY n-tiles

No areas under the curve for glucose and insulin were calculated because adjusting four time points only does not result in valuable affirmations.

Insulin resistance was estimated using the homeostasis model assessment (HOMA; fasting insulin [µU/ml] x fasting glucose [mmol/L] / 22.5).[13] Insulin sensitivity was estimated using the quantitative insulin sensitivity check index (QUICKY; 1/[log(fasting insulin mU/ml) + log(fasting glucose mg/dL)].[14] HOMA values were classified in three n-tiles, one central n-tile (P25 to P75), and two n-tiles for both extreme ends (< P25 and > P75). HOMA n-tile 1 was defined as all HOMA values < 1.18 (< P25), n-tile 2 was defined as all HOMA values > 1.18 and < 1.89 (> P25 and < P75), and n-tile 3 was defined as all HOMA values > 1.89 (> P75).

Statistical analyses

Statistical analyses of the results were performed using SPSS 13.0 for Windows XP. Data are presented as mean and standard deviation. TAG data were log normalised for statistical analysis.

A two-factor repeated measures analysis of variance (ANOVA) was carried out for serum glucose and insulin for water, time and water × time interaction effects for all three waters. When significant time x water interactions were found, post hoc analysis using the Bonferroni test was performed to study the effects of water and time separately.

A two factor (water and time) repeated measures ANOVA with one between factor (HOMA n-tiles) was carried out to determine influence of HOMA n-tiles on insulin concentrations.

A one-factor repeated measures ANOVA followed by Bonferroni test was performed to study peak concentrations of serum glucose and insulin concentrations, and to determine the influence of HOMA and QUICKY n-tiles on baseline lipoprotein and anthropometric parameters.

The water effect on time to peak was calculated and analysed by the Friedman non parametric test.

Relation between HOMA and QUICKY values was analysed by Spearman correlation.

P values < 0.05 were considered statistically significant.

Results

All the 18 volunteers completed the study, having drunk the three waters. Attending to the three baseline values, mean values were calculated for the three HOMA

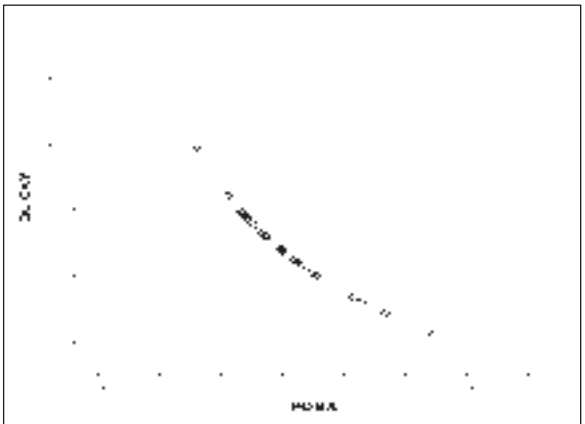

Fig. 2.—Correlation between HOMA and QUICKY indexes.

Table IV
Baseline and postprandial glucose (mmol/L) and insulin (µU/ml) concentrations in the three mineral waters tested

	Baseline	*30 min*	*60 min*	*120 min*
Glucose				
BMW 1	4.42 ± 0.35	4.96 ± 0.91	4.94 ± 0.76	4.65 ± 0.75
BMW 2	4.51 ± 0.30	4.91 ± 0.99	4.71 ± 0.84	4.88 ± 0.67
LMW	4.53 ± 0.45	4.94 ± 0.93	4.59 ± 0.71	4.99 ± 0.56
Insulin				
BMW 1	7.42 ± 2.99[a]	50.89 ± 38.69[bc]	43.62 ± 28.69[c]	31.22 ± 11.95[d]*
BMW 2	7.91 ± 3.27[a]	45.99 ± 25.95[b]	41.30 ± 20.41[bc]	34.01 ± 13.15[c]
LMW	7.63 ± 1.95[a]	39.88 ± 23.19[b]	43.55 ± 19.57[b]	42.86 ± 29.25[b]

Different letters in the same row indicate significant differences between time points, $p < 0.05$.
* At 120 min BMW1 insulin levels were significantly lower than with LMW ($p = 0.022$), while there was no differences between BMW1 and 2 at this point.

n-tiles. Likewise, mean values were calculated for weight, BMI, waist and hip circumferences, W/H-Ratio, serum cholesterol and TAG. Table II shows the baseline characteristics of the study women. Baseline weight, BMI, and hip circumference presented significantly different values depending on the HOMA n-tiles (table III).

Figure 1 shows postprandial insulin levels depending on HOMA n-tiles and figure 2 presents the correlation between HOMA and QUICKY indexes.

Glucose levels did not change along the 2h postprandial period for any of the three waters tested (table IV). Insulin concentrations showed a significant time effect ($p < 0.000$) and a significant water x time interaction ($p < 0.021$) (table IV).

No significant differences of insulin and glucose peak concentration, and time to peak were observed for all three waters (data not shown).

Discussion

Worldwide obesity epidemia is driving an increasing burden of preventable CVD and the perspective of hyperinsulinemia and IR grows. Postprandial triglyceridemia is considered an independent risk factor for coronary heart disease, but its relationship with IR has not yet been clearly established. The studied BMWs have been shown to be hypolipemic, lowering postprandial serum and quilomicron triacylglycerols.[4,5] The present results indicate that postprandial insulinemia varies depending on water composition and insulin HOMA.

The fact that after 120 min insulin concentration with BMW 1 was lower than that corresponding to LMW may be due to increased insulin secretion and sensitivity after the consumption of BMW 1. Polushina et al.[15] described significantly improved insulin sensitivity in patients with impaired carbohydrate tolerance and diabetes-2 patients after ingestion of a mineral water rich in sodium and bicarbonate. According to Krashenitsa and Botvineva,[16] the insulinotropic effect varies with the mineralization of the water and the concentration of bicarbonate and sodium, which is in agreement to the results obtained considering the sodium (aprox. 1 g/L) bicarbonated (aprox. 2 g/L) mineral water in the present study.

Mean fasting insulin values of the study subjects were half the values considered cut-off point for IR (15 µU/ml) according to Ten and Mclaren.[17] Only one woman presented an insulin value > 15 µU/ml. Thus, insulin data suggest, that in general terms, the volunteers were at very low risk for IR, and hence for MBS. According to ATPIII they were also at very low risk for CVD[4]. Results show that HOMA and QUICKY indexes are significantly correlated (fig. 2), and thus equally valid to assess differences in glucose and insulin metabolism. Therefore, all results are expressed for HOMA n-tiles. This correlation is higher than that reported by Katz et al.[14]

HOMA data suggest that all women presented an adequate insulin metabolism. Kuwana et al.[18] calculated the reference values to be 1.77 ± 0.44 in healthy non obese individuals. Mean HOMA levels were lower (table II) than the risk cut-off point (2.67) suggested by Nasution et al.[19] for elderly women. Ascaso et al.[20] using HOMA index P90 suggested the cut-off point of 3.8.

It is known that IR is strongly related to BMI[21] and in the present study even in non-obese postmenopausal women we observed that BMI values were associated to HOMA and QUICKY levels (data not shown for QUICKY levels). Egan et al.[22] suggest that BMI and HOMA indexes may be interchangeable, which is in agreement with the low HOMA levels found in these women. A waist-to-hip ratio cut point for a high risk of MBS is 0.85 in women and 0.9 in men, together with a BMI of 30 kg/m^2. In all 3 HOMA n-tiles mean waist-to-hip ratios of all subjects were lower than this cut point. Our results confirm that body weight, BMI and hip circumference, but not waist circumference, were associated to HOMA n-tiles. This suggests a typical gynoid, and not a central fat distribution.

Serum TAG showed a slight non significant association with HOMA index, probably due to the fact that the women were healthy and presented a low CVD risk.

When the women were divided into 3 different groups according to HOMA n-tiles, different responses to mineral water intake were obtained. In the HOMA-3 group all insulin values at 30 min were higher than in the other two HOMA groups, especially when BMW 1 was consumed. Interestingly, when consuming BMW1 glucose levels of the HOMA-3 group were also slightly higher than with the other two waters (data not presented).

Recent changes in the pertinent European legislation have established that the fluoride content of mineral waters may not exceed 5.0 mg/l.[23] Consequently, BMW 2 substitutes for BMW 1 in the market. It has been reported that fluoride inhibits a variety of different enzymes such as esterases and phosphatases, but the influence of fluoride contained in water on insulin is very difficult to explain. Fluoride in this study seems to increase insulinemia mostly in the women with higher HOMA n-tiles (fig. 1), because insulin levels with BMW1 tend to be higher at 30 min than with BMW2. Other studies suggest that NaF shows an inhibition of insulin secretion in isolated Langerhans islets.[24] Nevertheless, both BMWs, which presented higher fluoride content than LMW, normalised insulinemia faster than LMW, suggesting that fluoride plays a role in insulin metabolism. De la Sota et al.[25] observed in subjects from a geographic area of endemic fluorosis that the area under the curve of insulin, corresponding to a standard glucose tolerance test, showed an inverse relationship with fluoremia. Differences between the later studies and the present one should be adscribed to fluoride concentration, being less than 50% of the water fluorosis level, and to the different study models used (rats and *in vitro).*

In addition, it has been reported that HCO_3^- participates in the secretory sequence at sites distal to the identification of secretagogues in both endocrine end exocrine cells.[26] In the current study BMW 1 had the highest bicarbonate content; this fact could have increased the insulin secretion. This effect of mineral waters rich in bicarbonate has been described in medical hydrology literature.[27] Nevertheless, insulin concentrations at 120 min with BMW 1 was as low as with BMW 2, indicating that insulin degradation was faster with the two BMWs compared to the LMW, and/or that the insulinothrophic effect was not sustained during the whole postprandial 2 h. This was also reflected in the fact that comparing the two BMWs there was no significant differences observed, while BMW1 compared to LMW showed a significant water × time interaction.

Natural mineral waters rich in sodium bicarbonate have been extensively used in traditional crenotherapy as an accompanying component of diabetes therapy.[27] Debray and de la Tour[28] reported that alkalizing organic mediums favours insulinic actions. It has been reported that these mineral waters present a hypoglucemiant action and neutralize the hyperglucemiant response to adrenalin, cortisol, and aloxan, apart from the reinforcement of the insulinic action as evidences the potentiation of the "Staub effect" after glucose administration.[27] In the present study there was no effect of subject's glucose response; this could be related to the composition of the test meal: low in carbohydrates (28.9%) and high in fat (62%). Carbohydrate content was mainly provided by a plain sponge cake, which presents a glycemic index of 46 ± 6.[29]

The possible mechanisms behind these effects are not completely understood, but probably lay on the interaction of the total ionic strength and its multiple implications in physiological and pathological processes like neurosecretion, contraction, membrane stability, or enzymatic activation. There are reports which indicate the influence of high salt rich mineral waters on endocrine metabolism, pointing out various effects of these types of waters.[30,31] Unfortunately, these data are not easily accessible and more clinical trials have to be done in order to understand the exact mechanisms.

Conclusion

In short, bicarbonated sodium rich mineral water consumed with a fat rich meal by healthy postmenopausal women produced an insulinotropic effect, being more distinct in the women with a higher HOMA index and for the bicarbonated mineral water 1. Future studies are needed to test the effect of these bicarbonated waters on the insulinemia, glucemia and HOMA index of different obese/non obese populations consuming meals with different glycemic indexes.

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All authors read and approved the final manuscript.

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