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BRIEF ARTICLE

Chronic cola drinking induces metabolic and cardiac alterations in rats

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Abstract

AIM: To investigate the effects of chronic drinking of cola beverages on metabolic and echocardiographic parameters in rats.

METHODS: Forty-eight male Wistar rats were divided in 3 groups and allowed to drink regular cola (C), diet cola (L), or tap water (W) *ad libitum* during 6 mo. After this period, 50% of the animals in each group were euthanized. The remaining rats drank tap water *ad libitum* for an additional 6 mo and were then sacrificed. Rat weight, food, and beverage consumption were measured regularly. Biochemical, echocardiographic and systolic blood pressure data were obtained at baseline, and at 6 mo (treatment) and 12 mo (washout). A complete histopathology study was performed after sacrifice.

RESULTS: After 6 mo, C rats had increased body weight (+7%, $P < 0.01$), increased liquid consumption (+69%, $P < 0.001$), and decreased food intake (-31%, $P < 0.001$). C rats showed mild hyperglycemia and hypertriglyceridemia. Normoglycemia (+69%, $P < 0.01$) and sustained hypertriglyceridemia (+69%, $P < 0.01$) were observed in C after washout. Both cola beverages induced an increase in left ventricular diastolic diameter (C: +9%, L: +7%, $P < 0.05$ *vs* W) and volumes (diastolic C: +26%, L: +22%, $P < 0.01$ *vs* W; systolic C: +24%, L: +24%, $P < 0.05$ *vs* W) and reduction of relative posterior wall thickness (C: -8%, L: -10%, $P < 0.05$ *vs* W). Cardiac output tended to increase (C: +25%, $P < 0.05$ *vs* W; L: +17%, not significant *vs* W). Heart rate was not affected. Pathology findings were scarce, related to aging rather than treatment.

CONCLUSION: This experimental model may prove useful to investigate the consequences of high consumption of soft drinks.

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Key words: Cola beverages; Echocardiography; Metabolic syndrome; Soft drinks

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INTRODUCTION

Metabolic syndrome has been linked to an increased risk of type 2 diabetes, cardiovascular disease, stroke and premature death[1]. Soft drinks are the leading source of added sugar worldwide, and their consumption has been linked to obesity, diabetes, and metabolic syndrome[2-4]. Epidemiological and experimental evidence indicate that a greater consumption of sweet carbonated beverages is associated with overweight and obesity by virtue of the high sugar content, low satiety, and incomplete compensation for total energy in subsequent meals[5]. The health impact of soft drink consumption is becoming alarming, particularly among adolescents. A recent survey on the dietary habits and nutritional status of 4 to 18 years olds in Great Britain showed that on average 56% of total fluid intake was in the form of soft drinks[2].

Recently, we have demonstrated that most features of metabolic syndrome can be replicated in an experimental model of soft drink consumption. Body weight gain, hypertension, decreased food intake, hyperglycemia, hypertriglyceridemia, and a tendency to hypercholesterolemia were found after chronic consumption of regular (sucrose-sweetened) cola beverage in rats[6].

As a logical extension to that earlier report, the present paper aimed to investigate possible biochemical, echocardiographic and pathological alterations associated with chronic consumption of cola beverage in rats. This experimental model has the advantage of being able to dissect out potentially confounding factors usually associated with soft drinks consumption in human subjects, such as increased smoking, increased junk food consumption, and sedentary lifestyle, which might all indirectly contribute to development of metabolic syndrome. Furthermore, compared with previous animal models of metabolic syndrome[7], this approach has the potential advantage that it lends itself well to a direct comparison with the situation commonly found in real life.

MATERIALS AND METHODS

Experimental protocol

Forty-eight male Wistar rats were randomly assigned to 3 groups, receiving 3 different beverages *ad libitum* as the only liquid source for 6 mo: water (W), regular cola (C) (commercially available sucrose-sweetened carbonated drink, Coca-Cola™, Argentina), and Light Cola™ (L) (commercially available low calorie -aspartame-sweetened carbonated drink, Coca-Cola light™, Argentina). The soft drinks had carbon dioxide content largely removed by vigorous stirring using a stirring plate and placing a magnetic bar in a container filled with the liquid prior to being offered to the animals at room temperature.

After 6 mo, 50% of the animals in each group (C, L and W) were randomly chosen to be euthanized. The remaining C and L rats were switched to tap water *ad libitum,* while the W group continued to drink tap water as usual for another 6 mo (washout period; end of study: 12 mo after the start). Rats were weighed weekly, while food and drink consumption were assessed twice a week. Biochemical, echocardiographic and systolic blood pressure (SBP) measurements were obtained at baseline, and at 6 mo (treatment) and 12 mo (washout); histopathological data were obtained at the time of sacrifice.

According to company specifications, Coca Cola™ is a carbonated water solution containing (for each 100 mL): carbohydrate 10.6 g, sodium 7 mg, caffeine 11.5 mg, caramel, phosphoric acid, citric acid, vanilla extract, natural flavorings (orange, lemon, nutmeg, cinnamon, coriander, *etc.*), lime juice and fluid extract of coca (*Erythroxylon novogranatense*). As far as nutritional information is concerned, the only difference between regular and light cola is the replacement of carbohydrates with non-nutritive sweeteners (aspartame + acesulfame K) in the latter.

Animals were housed at the ININCA facilities under controlled temperature (21 ± 2℃) and 12-h light-dark cycles (7 am to 7 pm). Rats were fed a commercial chow (16%-18% protein, 0.2 g% sodium (Cooperación, Buenos Aires, Argentina) *ad libitum*.

Animal handling, maintenance and euthanasia procedures were performed according with international recommendations[8]. This study was approved by the Ethics Committee for Scientific Research of the ININCA.

Biochemical determinations

Plasma levels of glucose, triglycerides and uric acid were determined by enzymatic conventional assays in blood samples collected from the tail vein after 4-h fasting[9]. Plasma concentrations of coenzyme Q_{10} and α-tocopherol were determined by HPLC-RP with UV detection using Waters 1500 Series, HPLC binary pump, Waters 717 plus Autosampler, Symmetry C_{18} 4.6 mm × 150 mm and 5 μm particle size column, guard column 4 mm × 4 mm (5 μm), Waters 2487 Dual λ Absorbance Detector, and Waters 2465 Electrochemical Detector. Waters Breeze™ Chromatography Data System software version for Windows NT was used for data acquisition and storage[6].

Blood pressure determination

SBP was measured by tail cuff plethysmography in unanesthetized rats restrained in a plastic chamber. The average of at least 3 readings per session was recorded. A pneumatic pulse transducer positioned on the ventral surface of the tail, distal to the occlusion cuff, detected the return of the pulse following a slow deflation of the cuff. Cuff pressure was determined by a pneumatic pulse transducer, using a programmed electro-sphygmomanometer PE-300 (Narco Bio-Systems, Austin, Texas). Pulses were recorded on a Physiograph MK-IIIS (Narco Bio-Systems, Austin, Texas).

Echocardiographic evaluation

Transthoracic echocardiograms were obtained in unanesthetized, gently restrained rats using an ATL 3000 HDI (Bethold, WA, USA) echocardiographic system equipped with a 10.5 MHz transducer. M-mode and 2-dimensional echocardiography images were acquired in short axis views at the level of the papillary muscle. Interventricular

septal end diastolic dimension (IVSd) and left ventricular end diastolic posterior wall dimension (LVPWd) were determined at the parasternal long axis at the midchordal level. Left ventricular diastolic dimension (LVDD) and left ventricular end-systolic posterior wall dimension (LVPWs) were measured perpendicularly to the long axis of the ventricle also at the midchordal level. Shortening fraction (Sf) was calculated by the following formula: 100 × (LVPWd - LVPWs)/LVDD. LV mass (LVM) was determined using the standard cube method[10] according to LVM = (LVDD + RWTh + LVPWd)^3 - (LVDD)^3 × 1.04. Other parameters were calculated as follows:

Relative posterior wall thickness (RWTh) = (LVPWd + IVSd)/LVDD; end diastolic volume (EDV) = 0.85 × (LVDD)^3; end systolic volume (ESV) = 0.85 × (LV systolic dimension)^3; cardiac output = (EDV - ESV) × heart rate (HR); systolic volume (SV) = EDV - ESV. Echocardiographic images and HR were simultaneously recorded.

Histopathological study

At the above indicated times euthanasia was performed by subtotal exsanguination under anesthesia (sodium thiopental 40 mg/kg, ip) of 50% of the animals (all 3 groups). The abdominal aorta was cannulated to perfuse with isotonic saline solution until the blood was washed out and the liver parenchyma presented a pale appearance. Complete autopsies were performed. Heart, liver, thoracic and abdominal aorta, kidneys, pancreas and muscle were excised and harvested for light microscopy. Tissues were immersed in 10% formalin at pH 7.4. After 48 h fixation, tissues were dehydrated in alcohol, cleared in xylene, and embedded in paraffin. Sections (3-5 μm thick) were cut and stained with hematoxylin and eosin, Masson's trichrome, or periodic acid-Schiff. Two independent evaluators (blinded to group assignment) examined the slices under a light microscope (Leitz Laborlux S) for histopathological changes.

Statistical analysis

Data were analyzed by two-way analysis of variance followed by *post hoc* tests (Bonferroni multiple comparison *t*-test) in order to evaluate selected pairs of groups. $P < 0.05$ was considered significant. SPSS™ version 15.0 software was used to analyze data.

RESULTS

Nutritional aspects

At baseline, experimental groups were comparable to each other with respect to all variables measured (Table 1). Table 2 shows the effects of regular cola and diet cola drinking on body weight and daily intake of food, liquid, sodium and calories, after treatment and following washout (6 and 12 mo, respectively, from the beginning of the study). Liquid and caloric consumption increased (by 70%, $P < 0.001$ and 11%, $P < 0.05$ respectively) and food intake decreased (31%, $P < 0.001$) after 6 mo of regular cola drinking (C_6). After washout, liquid intake normalized only partially (59% increase, $P < 0.05$ *vs* W_{12}; 11% reduction, $P < 0.05$ *vs* C_6). A sustained reduction in food intake was observed (by 38%, $P < 0.05$ *vs* W_{12}); caloric and sodium intake were accordingly reduced to a similar extent (31%, $P < 0.05$ *vs* W_{12}) in group C. Drinking diet cola did not affect food intake but a decrease in food intake was observed during washout (by 11%, $P < 0.05$).

Table 1 Body weight, systolic blood pressure, biochemical and echocardiographic data of rats at baseline (n = 16) (mean ± SD)

	W	C	L
Body weight (g)	390 ± 6	393 ± 6	395 ± 5
SBP (mmHg)	127 ± 7	127 ± 10	120 ± 11
Glucose (mg/dL)	110 ± 3	112 ± 3	111 ± 3
Triglycerides (mg/dL)	72 ± 9	70 ± 10	72 ± 8
LVDD (mm)	6.2 ± 0.5	6.3 ± 0.6	6.8 ± 0.5
RWTh	0.34 ± 0.06	0.37 ± 0.03	0.34 ± 0.06
ESD (mm)	2.7 ± 0.5	2.7 ± 0.5	3.3 ± 0.5
IVSd (mm)	0.84 ± 0.15	0.93 ± 0.09	0.91 ± 0.12
LVPWd (mm)	1.2 ± 0.2	1.4 ± 0.1	1.4 ± 0.3
LVPWs (mm)	2.6 ± 0.4	2.6 ± 0.4	2.6 ± 0.3
HR (bpm)	447 ± 45	421 ± 69	425 ± 49
Aorta (mm)	2.7 ± 0.1	2.9 ± 0.3	2.8 ± 0.4
LA (mm)	2.5 ± 0.3	2.7 ± 0.6	2.8 ± 0.4
Sf (%)	55.6 ± 6.9	56.8 ± 8.8	51.7 ± 4.9
EDV (mL)	0.21 ± 0.05	0.22 ± 0.06	0.27 ± 0.06
ESV (mL)	0.02 ± 0.01	0.02 ± 0.01	0.03 ± 0.01
Ef (%)	90.7 ± 3.7	91.0 ± 5.5	88.4 ± 3.5
SV (mL)	0.19 ± 0.05	0.20 ± 0.06	0.24 ± 0.05
CO (mL/min)	83.2 ± 20.1	85.5 ± 32.22	88.6 ± 23.8

SBP: Systolic blood pressure; LVDD: Left ventricular diastolic dimension; RWTh: Relative wall thickness; ESD: End-systolic dimension; IVSd: Interventricular septal end-diastolic dimension; LVPWd: Left ventricular end-diastolic posterior wall dimension; LVPWs: Left ventricular end-systolic posterior wall dimension; HR: Heart rate; Aorta: Aorta diameter; LA: Left atrial dimension; Sf: Shortening fraction; EDV: End diastolic volume; ESV: End systolic volume; Ef: Ejection fraction; CO: Cardiac output; SV: Systolic volume.

Plasma biochemistry

Regular cola drinking led to mild hyperglycemia (15% increase, $F_{2,18} = 3.611$, $P < 0.05$), and hypertriglyceridemia (3-fold, $F_{2,18} = 5.998$, $P < 0.01$) (Table 2). Normoglycemia and sustained hypertriglyceridemia were observed in group C after washout. Diet cola drinking caused only a trend to hypertriglyceridemia (2-fold, NS) (Table 3).

At the end of 6 mo, plasma levels of CoQ_{10} were reduced by 52% in the C group compared with the levels in W rats ($F_{2,18} = 3.576$, $P < 0.05$). No differences in plasma CoQ_{10} concentration were found across groups after washout ($F_{2,16} = 2.379$, NS), though W rats had 46% lower levels compared with those at baseline ($F_{1,34} = 5.197$, $P < 0.03$)[6].

Treatment did not modify plasma levels of α-tocopherol at any time ($F_{1,34} = 2.018$, NS) although, similar to that observed for CoQ_{10}, plasma levels of α-tocopherol decreased by 48% ($F_{1,34} = 4.532$, $P < 0.04$) in the W group at the end of the washout period compared with levels found in the same group at baseline[6].

Consumption of cola drinks had no significant effect on uricemia (data not shown).

Table 2 Body weight and nutritional facts (food, liquid, calories and sodium daily intake per 100 g body weight) after treatment and washout periods (mean ± SD)

	Treatment (6 mo)			Washout (12 mo)		
	W6 (n = 15)	C6 (n = 14)	L6 (n = 15)	W12 (n = 7)	C12 (n = 6)	L12 (n = 8)
Body Weight (g)	626 ± 8	669 ± 9[b]	630 ± 9	689 ± 10[d]	703 ± 27	699 ± 61
Intake (mL or g/100 g BW)						
Liquid	8.7 ± 1.2	14.7 ± 2.8[c]	8.5 ± 1.7	7.1 ± 1.1	11.3 ± 1.8[c,d]	6.5 ± 1.5
Solid	4.9 ± 0.6	3.4 ± 0.6[c]	5.1 ± 0.4	5.5 ± 0.6	3.8 ± 0.6[a]	4.9 ± 0.6[a]
Energy (Kcal/100 g BW)						
Liquid	0	6.17 ± 0.5[c]	0.09 ± 0.00	0	0	0
Solid	14.7 ± 1.1	10.2 ± 1.3	15.3 ± 0.9	16.5 ± 1.0	11.4 ± 0.9	14.7 ± 0.9
Total	14.7 ± 1.1	16.4 ± 1.2[b]	15.4 ± 0.9	16.5 ± 1.5	11.4 ± 1.1[d]	14.7 ± 0.9
Sodium (mg/100 g BW)						
Liquid	0	0.59 ± 0.2[c]	0.34 ± 0.1[c]	0	0	0
Solid	9.8 ± 1.0	6.8 ± 0.7[a]	10.2 ± 0.9	11.0 ± 0.1	7.6 ± 0.7	9.8 ± 1.0
Total	9.8 ± 1.0	7.4 ± 1.2	10.5 ± 1.0	11.0 ± 0.1	7.6 ± 0.7[a]	9.8 ± 1.0

Calculations based on: (1) kcal/g or mL: 3 (food), 0.42 (Coke) and 0.01 (Light coke); (2) Na^+ mg/g or mL: 2 (food), 0.075 (Coke or Light coke). [a]$P < 0.05$, [b]$P < 0.01$, [c]$P < 0.001$ *vs* W for the same period (i.e. treatment or washout); [d]$P < 0.01$ *vs* respective group after treatment.

Table 3 Systolic blood pressure and biochemical data at 6 and 12 mo (mean ± SD)

	Treatment (6 mo)			Washout (12 mo)		
	W (n = 15)	C (n = 14)	L (n = 15)	W (n = 7)	C (n = 6)	L (n = 8)
SBP (mmHg)	134 ± 2	145 ± 3[b]	135.5 ± 2	131 ± 9	142.5 ± 15	144 ± 8
Glycemia (mg/dL)	128 ± 3	139 ± 3[a]	126 ± 3	128 ± 10.5	127 ± 34	119 ± 16
Triglyceridemia (mg/dL)	90 ± 9[c]	196 ± 24[b]	107 ± 20	132 ± 73	206.5 ± 77[a]	149 ± 60

[a]$P < 0.05$, [b]$P < 0.01$ *vs* W group; [c]$P < 0.05$ *vs* same group after washout. SBP: Systolic blood pressure.

Table 4 Echocardiographic parameters at 6 and 12 mo (mean ± SD)

	Treatment (6 mo)			Washout (12 mo)		
	W (n = 15)	C (n = 14)	L (n = 15)	W (n = 7)	C (n = 6)	L (n = 8)
LVDD (mm)	6.8 ± 0.4	7.4 ± 0.3[a]	7.3 ± 0.5[a]	7.2 ± 0.5	7.4 ± 0.4	7.8 ± 0.6
RWTh	0.40 ± 0.03[c]	0.37 ± 0.03[a]	0.36 ± 0.05[a]	0.35 ± 0.04	0.36 ± 0.02	0.35 ± 0.04
ESD (mm)	2.7 ± 0.5[c]	3.1 ± 0.6	3.1 ± 0.5	3.4 ± 0.4	3.4 ± 0.4	3.2 ± 0.3
IVSd (mm)	1.2 ± 0.1	1.1 ± 0.1	1.1 ± 0.1	1.1 ± 0.1	1.1 ± 0.1	1.1 ± 0.1
LVPWd (mm)	1.6 ± 0.1	1.6 ± 0.1	1.5 ± 0.2	1.4 ± 0.1	1.6 ± 0.2	1.6 ± 0.1
LVPWs (mm)	3.6 ± 0.6	3.6 ± 0.6	3.1 ± 0.6	3.7 ± 0.4	3.1 ± 0.5	3.7 ± 0.5
HR (bpm)	469 ± 36	470 ± 46	457 ± 44	469 ± 23	472 ± 26	452 ± 52
Aorta (mm)	3.5 ± 0.3	3.5 ± 0.3	3.5 ± 0.3	3.4 ± 0.2	3.4 ± 0.2	3.6 ± 0.1
LA (mm)	3.3 ± 0.3	3.4 ± 0.4	3.2 ± 0.4	3.3 ± 0.3	3.4 ± 0.5	3.3 ± 0.2
Sf (%)	59.9 ± 7.2	58.5 ± 8.6	57.2 ± 7.4	52.1 ± 4.6	54.3 ± 6.3	58.9 ± 2.9
EDV (mL)	0.27 ± 0.04	0.34 ± 0.04[b]	0.33 ± 0.06[a,c]	0.32 ± 0.06	0.34 ± 0.06	0.41 ± 0.09[b]
ESV (mL)	0.02 ± 0.01	0.03 ± 0.02	0.03 ± 0.02	0.04 ± 0.01	0.03 ± 0.01	0.03 ± 0.01
Ef (%)	93.0 ± 4	92.0 ± 4.9	91.5 ± 3.8	88.8 ± 2.9	90.1 ± 3.7	92.9 ± 1.4
SV (mL)	0.25 ± 0.04	0.31 ± 0.04[a]	0.31 ± 0.07[a]	0.28 ± 0.06	0.31 ± 0.07	0.37 ± 0.08[a]
CO (mL/min)	118 ± 21	148 ± 21[a]	138.5 ± 33	132 ± 26	146 ± 29	172 ± 46

[a]$P < 0.05$, [b]$P < 0.01$ *vs* W; [c]$P < 0.05$ *vs* same group after washout. LVDD: Left ventricular diastolic dimension; RWTh: Relative wall thickness; ESD: End-systolic dimension; IVSd: Interventricular septal end-diastolic dimension; LVPWd: Left ventricular end-diastolic posterior wall dimension; LVPWs: Left ventricular end-systolic posterior wall dimension; HR: Heart rate; Aorta: Aorta diameter; LA: Left atrial dimension; Sf: Shortening fraction; EDV: End diastolic volume; ESV: End systolic volume; Ef: Ejection fraction; CO: Cardiac output; SV: Systolic volume.

Echocardiographic evaluation

Chronic drinking of either cola beverage induced an increase in LVDD (C: +9%, L: +7%, $P < 0.05$ *vs* W) and LV volume (diastolic C: +26%, L: +22%, $P < 0.01$ *vs* W; systolic C: +24%, L: +24%, $P < 0.05$ *vs* W), and a reduction in RWTh (C: -8%, L: -10%, $P < 0.05$ *vs* W). An increase in cardiac output was also observed, which became significant in group C rats (C: +25%, $P < 0.05$ *vs* W; L: +17%, $t = 1.985$, NS *vs* W). Heart rate was not affected (Table 4).

After the washout period a regression of most alterations was observed with the exception of end diastolic

and systolic volumes in group L, which remained elevated compared with W (Table 4).

Histopathological study

Necropsy findings in heart, aorta, pancreas and skeletal muscle were scarce, and mainly due to the aging process. In liver, different degrees of hepatic steatosis were found as described by Kleiner *et al*[11], and were related to aging in all washout groups. A few animals showed kidney lesions attributable to the aging process, which were consistent with chronic progressive nephropathy.

DISCUSSION

In the present study, long-term drinking of regular cola beverage resulted in weight gain, mild hyperglycemia and marked hypertriglyceridemia. Changes in plasma triglycerides were also associated with the consumption of diet cola. Importantly, reversal of most parameters was observed after switching back from cola to water. Both cola beverages induced increases in diastolic and systolic volumes, and thinning of the left ventricular posterior wall, resulting in greater cardiac output without a change in HR.

The hypothesis that regular cola drinking could induce weight gain because of solid food overeating, which would be secondary to perceived low satiety (due to the fact that calories were mostly provided as liquid)[5] was not confirmed in this study. Actually, weight gain observed after regular cola drinking occurred in spite of a net decrease in solid food consumption. This was likely the result of drinking large volumes of regular cola which provided excess caloric intake.

Regarding the diet cola group, the biochemical profile induced by low-calorie sweet beverage drinking revealed only mild changes in triglycerides and total cholesterol, which were not different from those found in the other experimental group.

A review of the literature suggests that consumption of non-nutritive sweeteners may heighten appetite[12]. Interestingly, in this study diet cola drinking did not increase food intake, suggesting that an increase in food consumption associated with aspartame-sweetened drinks in man might be due to other, non-nutritional factors. Indeed, it is appreciated that overeating may also be subject to psychological influences. Also, awareness of fewer calories provided by drinking light beverages might induce individuals to eat in excess. As mentioned above, this apparently did not occur in our rats.

Sustained hypertriglyceridemia observed 6 mo after washout could not be accounted for by the increase in triglycerides with time (i.e. W_{12} *vs* W_6). As observed previously in relation to the antioxidant concentration in plasma, long-term hypercaloric consumption resulted in changes similar to those found as a result of normal aging[6].

Both cola beverages induced an increase in LVDD, EDV and ESV, accompanied by a reduction in relative wall thickness. These ventricular changes induced a concomitant increase in cardiac output, without significant changes in HR. These cardiac ventricular changes could be likely related to the effect of increased fluid load associated with drinking larger volumes. Of note, a regression of these alterations was observed in both groups following washout.

Regular cola is a hypertonic solution (493 mOsm/L) due to its high carbohydrate content, while both tap water (3 mOsm/L) and light cola (38 mOsm/L) are hypotonic solutions compared with plasma (285-295 mOsm/L). Ingestion of regular cola is supposed to stimulate antidiuretic hormone secretion causing hypervolemia so as to maintain plasma osmolarity within normal values.

Decreased CoQ_{10} levels have been suggested to be a useful biomarker of oxidative stress[13]. CoQ_{10} mainly accumulates in the liver and in cell membranes, where it acts as an endogenous antioxidant[14], and plasma levels of CoQ_{10} are well correlated with liver stores. It is conceivable that reduced plasma levels of CoQ_{10} found after 6 mo of cola drinking in our rats might reflect the exhaustion of the protective response mechanism to sustained oxidative stress induced by chronic carbohydrate ingestion. Long-term ingestion of a hypercaloric hyperglycemic diet (as in C rats) leads to obesity and increased lipid peroxidation and induces oxidative stress by compromising the mitochondrial redox metabolism[14]. Considering that ubiquinone allows regeneration of α-tocopherol[15], and that α-tocopherol levels did not show substantial variations among treatments in our study, it seems reasonable to assume that α-tocopherol was preserved as the main antioxidant source at the expense of CoQ_{10} consumption, so that α-tocopherol levels remained largely unchanged while CoQ_{10} levels substantially decreased.

Interestingly, there is evidence that decreases in CoQ_{10} and α-tocopherol levels may cause impairment of LV function[14,16]. This is in agreement with our echocardiographic findings of LV dilation and remodeling in this model.

Systolic hypertension might result from an increase in adrenergic activity elicited by caffeine. However this is unlikely in the present study, as the calculated caffeine doses provided by the cola drinks were in the order of 2.5 μg/kg (regular cola) and 1.6 μg/kg (diet cola), which was far below (1/1000th) pharmacologically effective levels in male rats[17].

In summary, in this animal model, oxidative stress, overweight, hypertriglyceridemia, mild hyperglycemia, systolic hypertension and echocardiographic alterations occurred as a consequence of chronic drinking of cola beverages in rats. Most of these changes reversed after washout to tap water. This model may be useful in view of its clinical significance in relation to the high consumption of cola beverages.

COMMENTS

Background

Epidemiological and experimental evidence indicate that excessive consumption of sweet carbonated beverages is associated with overweight and obesity

by virtue of the high sugar content, low satiety, and incomplete compensation for total energy in subsequent meals. The health impact of soft drink consumption is becoming alarming, particularly among adolescents. The present paper aims at investigating possible biochemical, echocardiographic and pathological alterations associated with chronic consumption of cola in rats.

Research frontiers

This experimental model has the advantage of being able to dissect out potentially confounding factors usually associated with soft drinks consumption in human subjects, such as increased smoking, increased junk food consumption, and sedentary lifestyle, which might all indirectly contribute to development of metabolic syndrome. Furthermore, compared with previous animal models of metabolic syndrome, this approach has the potential advantage that it lends itself well to a direct comparison with the situation commonly found in real life.

Innovations and breakthroughs

In spite of the existence of multiple experimental data with fructose-induced model of metabolic syndrome, there are few reports on the effects of cola drinking in animal models. We are well aware that soft drinks are compound substances, making difficult the assertion of the effect of each component. However, soft drink consumption has increased by 300% in the past 20 years, and 56%-85% of children in school consume at least one soft drink daily. In this regard, our aim was to study the effect of chronic cola beverage drinking taking into account the major public health issue involved.

Applications

This model could be used not only to study metabolic syndrome but to raise awareness of the serious problems that high consumption of soft drinks can generate, especially in children and young people.

Terminology

Metabolic syndrome: A cluster of risk factors for developing cardiovascular disease and diabetes comprising obesity, insulin resistance, hypertension, dyslipidemia, and hyperglycemia. Cola beverage: A carbonated soft drink flavored with caramel and frequently containing caffeine. It also contains sugar or non-nutrient sweeteners, phosphoric or citric acids and a combination of flavoring substances and preservatives. Chronic progressive nephropathy: A progressive disease of the renal tissue that results in degeneration and regeneration of the epithelium lining the tubules, a thickening of basement membranes in the capsule, interstitial inflammation and fibrosis, and lesions which may be found in the glomeruli that tend to be generalized with variability in the amount present. It is commonly an age-related disease in rats. Coenzyme Q10: Also known as ubiquinone, ubidecarenone, coenzyme Q, is found in all membranes, particularly in mitochondria and acts as an important antioxidant in the body. α-tocopherol: is the form of vitamin E that is preferentially absorbed and accumulated in humans. Vitamin E may help prevent or delay coronary heart disease by limiting the oxidation of LDL-cholesterol, and also may help prevent the formation of blood clots.

Peer review

The study is very interesting, however there are still some questions to be answered.

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