Cola intake and serum lipids in the Oslo Health Study

Arne Torbjørn Høstmark and Sissel Erland Tomten

Abstract: Soft drinks can be a major source of sucrose, which may influence serum lipid concentration. We have examined the association between intake frequency of various types of soft drinks and the concentration of serum triglycerides (TG) and high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol in the cross-sectional Oslo Health Study. A total of 14 188 subjects of the altogether 18 770 participants of the study had data on intake frequency of colas and non-colas, with or without sugar. The population sample consisted of both sexes and 3 age groups: group1 (30 years of age), group 2 (40 and 45 years of age), and group 3 (59–60 years of age). In both sexes, HDL decreased and TG increased significantly \((p < 0.001)\) with increasing intake frequency of colas. In contrast, no consistent associations were found between the reported intake of non-cola soft drinks and the serum lipids. We found no significant differences related to the reported presence or absence of sugar in the soft drinks. In multiple linear regression analyses, the colas vs. serum lipid associations prevailed \((p < 0.001)\) after including 13 possible confounders: sex; age group; time since last meal; physical activity; intake of alcohol, coffee, cheese, fruit and (or) berries, and fatty fish; smoking; length of education; use of cholesterol-lowering drugs; and intake of non-colas. Thus, the self-reported intake frequency of colas, but not other soft drinks, was negatively associated with serum HDL, and positively associated with TG and LDL.

Key words: HDL cholesterol, LDL cholesterol, triglycerides, serum, cola, carbonated soft drinks, men, women, cross-sectional study.

Introduction

Intake of carbohydrates has been associated with increased serum triglyceride (TG) levels and low concentrations of high-density lipoprotein (HDL) cholesterol (Merchant et al. 2007). Sugar-sweetened soft drinks can be a major source of carbohydrates, if used frequently. Conceivably, increased sugar intake via soft drinks might have an effect on blood lipid levels. This line of reasoning seems to be supported by an epidemiological study (Dhingra et al. 2007) showing a positive association between soft drink intake and serum TG, and a negative relationship with HDL. However, this study did not differentiate among various types of soft drinks.

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Whether intake of colas could give special health problems has been considered because these soft drinks contain caffeine and phosphoric acid in addition to sucrose and carbonic acid (Jensdottir et al. 2006; Kapiclog˘lu et al. 2000). High doses of caffeine stimulate fatty acid release from adipose tissue (Mayes 2000), thereby possibly promoting hepatic synthesis and release of very low-density lipoprotein (VLDL). However, Carson et al. (1993) found no consistent relation between caffeine consumption and serum lipids in elderly women.

The purpose of the present work was to study the association between the intake frequency of colas and other carbonated soft drinks, with and without sugar, and serum lipids (i.e., TG, HDL cholesterol, and low-density lipoprotein (LDL) cholesterol) using data of the cross-sectional Oslo Health Study.

Materials and methods

Main project

In 2000–2001, the Oslo Health Study was conducted under the joint collaboration of the National Health Screening Service of Norway (now the Norwegian Institute of Public Health), the University of Oslo, and the Municipality of Oslo. The study population included all individuals in Oslo County born in 1970, 1960, 1955, 1940–1941, and 1924–1925. At the time of the data collection, the subjects were 30, 40, 45, 59–60, and 75–76 years of age. A total of 18 770 individuals (45.9% of the invited) participated.

One self-administered questionnaire was part of the letter of invitation, to be returned in a prestamped self-addressed envelope (The Oslo Health Study 2006); 2 supplementary questionnaires were handed out at the screening units. The questionnaires provided information on health status, symptoms, diseases, and various other aspects of health-related behavior. The main questionnaire items used in the present study were

A. “How often do you drink colas?” There were 5 response alternatives: (1) never–rarely; (2) 1–6 glasses per week; (3) 1 glass per day; (4) 2–3 glasses per day; and (5) 4 or more glasses per day.

B. “How often do you drink non-cola soft drinks?” This question had the same response alternatives as (A).

C. “Do you drink colas–other soft drinks with or without sugar?” There were 2 response alternatives: (1) with sugar and (2) without sugar.

Up to 2 reminders were sent to the nonresponders. The second reminder invited those living in the suburban parts of the city to mobile screening units parked in their neighborhoods.

The responders consisted of 8404 men (42.4% of the invited) and 10 366 women (49.3% of the invited) who attended the physical examination and (or) filled in at least one of the questionnaires. When weighted by the inverse of probability of attendance, the values of self-rated health, smoking, body mass index, and mental health in the responders differed only slightly from the estimated values in the target population (Søgaard et al. 2004).

At the screening unit, a simple clinical examination was conducted, and measurements and analyses were performed according to a standard protocol (The Oslo Health Study 2006). A venous nonfasting blood sample was analyzed for total cholesterol (mmol·L⁻¹), HDL cholesterol (mmol·L⁻¹), glucose (mmol·L⁻¹), and TG (mmol·L⁻¹) in serum using an enzymatic method (Hitachi 917 auto analyzer; Roche Diagnostic, Basel, Switzerland). Seronorm Lipoprotein (Nyc­comed AS, Oslo, Norway) was used as reference material for the lipid analyses and Autonorm Human Liquid (Nyc­comed AS) for the glucose analyses. These 2 control sera were analyzed at regular time intervals throughout the day. The day-to-day coefficient of variation for the quality controls was 3% for glucose, cholesterol, and TG, and 4% for HDL cholesterol. All the laboratory investigations were performed by the Department of Clinical Chemistry, Ullevål University Hospital, Oslo, Norway. The results were registered and transferred on data files to the National Health Screening Service. LDL cholesterol was estimated using the Friedewald formula (Friedewald et al. 1972). (For further details, see http://www.fhi.no/hubro.) The study protocol was approved by the Regional Committee for Medical Research Ethics and by the Norwegian Data Inspectorate. The study was conducted in full accordance with the World Medical Association Declaration of Helsinki.

Population sample in the present investigation

Because the prevalence of metabolic disturbances increases with increasing age, and the intake of carbonated soft drinks is relatively rare in older people, the oldest age group (75–76 years) was excluded from the study. The present study is therefore confined to the 14 750 participants in the 3 youngest age groups of The Oslo Health Study (i.e., group 1 (30 years), group 2 (40 and 45 years), and group 3 (59–60 years)). Among these, there were 14 188 participants (96%) who answered the questions about their soft drink intake frequency (6422 men and 7766 women).

Statistical methods

In the 5 cola intake groups, there were 7294, 4799, 913, 836, and 346 subjects, respectively. To obtain a high number of respondents in those with frequent cola intake, we pooled the 3 highest levels of intake (≥7 glasses per week), which totaled 2095 subjects.

The bivariate association between intake frequency of soft drinks (3 levels) and the 3 serum lipids (HDL, LDL, TG) was estimated using Spearman’s correlation coefficient (ρ). First we calculated ρ in each age group of the whole group of respondents (n = 14 188). Next, the material was divided into 4 main subgroups: (i) sugar-cola drinkers (with no or rare intake of non-cola soft drinks, n = 3827, 1751 men and 2076 women); (ii) sugar-free cola drinkers (with no or rare intake of non-cola soft drinks, n = 2506, 736 men and 1770 women); (iii) users of non-cola soft drinks with sugar (with no or rare intake of cola, n = 3374, 1418 men and 1956 women); and (iv) users of non-cola soft drinks without sugar (with no or rare intake of cola, n = 1991, 598 men and 1393 women). We finally subdivided each of the 4 groups of men and women in the 3 age groups, so as to obtain 24 subgroups in total; however, to limit the number of tables, the results of these analyses are mentioned only briefly.

We performed multiple linear regression analyses to study the association between intake frequency of various soft drinks and serum lipids. To identify possible confounders,
we explored the possible bivariate associations between serum lipids (HDL, LDL, TG) and factors that might influence the lipids, such as sex, age, and nutritional and lifestyle factors, using Spearman’s correlation analyses. Variables that were found to be significantly associated with serum lipids (HDL, LDL, TG) in the correlation analyses were included as additional independent variables in a stepwise linear regression model, with each of the 3 serum lipids as the dependent variable and with cola (non-cola) intake frequency as the main independent variable.

The variables that were found to be significantly associated with all 3 serum lipids in the first regression analysis and with intake frequency of cola (non-cola) in the second one constituted a set of potentially confounding variables that was included in the final regression analysis. The possible confounders were sex; age group; physical activity; intake of alcohol; intake of cheese, fruit and (or) berries, and fatty fish; length of education; use of cholesterol-lowering drugs; smoking; and intake of additional soft drinks; and because the blood samples were nonfasting, we also controlled for time since last meal (1–9 h). Intake of coffee (cups per day) was not found to be significantly associated with HDL levels in the total group but it was found to be positively, although weakly, associated with HDL when males and females were analyzed separately. The association between coffee intake and TG was observed only in the female group.

Five linear regression models (dependents: HDL, LDL, TG) with cola (non-cola) intake frequency (3 levels) as the independent under investigation were created. In model 1, we adjusted for sex and age group; model 2 = model 1 + adjustments for time since last food intake, use of cholesterol-lowering drugs, and diet items (intake of cheese, fruit and (or) berries, and fatty fish); model 3 = model 2 + adjustments for physical activity, years at school, use of sugar in the soft drinks, and intake of the alternative soft drink (non-colas); model 4 = model 3 + adjustments for smoking and frequency of alcohol intake the last year; model 5 = model 4 + body mass index (kg·m⁻²).

SPSS, version 15.0 (SPSS Inc., Chicago, Ill.) was used for the statistical analyses. Analysis of variance (ANOVA) was used to compare groups. The significance level was 0.05.

### Results

#### Serum HDL cholesterol and triglyceride concentrations by sex and age group

HDL was higher in women than in men (p < 0.001), and was higher in group 3 than in the younger age groups (Table 1). Mean serum HDL was higher in women than in men in all age groups (p < 0.001). Serum TG concentration increased with increasing age in women but was higher in men than in women in all age groups (p < 0.001). Men in groups 1 and 3 had similar TG values, which were lower than those found in group 2.

#### Bivariate associations

In the total sample, in all age groups and in both sexes, there were, in general, highly significant (p < 0.001) positive correlations between the reported intake frequency of colas and TG and LDL, and negative associations with HDL, but for non-cola soft drinks, these associations were not consistent (results not shown).

To obtain homogenous groups, only those reporting no or rare intake of non-colas were included in the studies of possible effects of different levels of cola intake, and only those reporting no or rare intake of colas were included in studies regarding possible non-cola effects. The associations between blood lipids and intake frequency of soft drinks are shown in Figs. 1 and 2.

Cola intake frequency correlated positively with serum TG concentration (Fig. 1, TG, upper panels) and negatively with serum HDL (Fig. 1, lower panels). The exception was found in women reporting use of artificially sweetened colas.

#### Intake of sugar-containing colas

Subjects with the highest intake frequency of sugar-containing colas had HDL concentrations that were 10.4% lower (men) and 12.5% lower (women) than subjects in the lowest intake group (p < 0.001; ANOVA). The serum TG concentration was 20.8% higher (men) and 22.7% higher (women) (p < 0.001) in the highest intake group compared with the lowest.

### Table 1. Serum HDL cholesterol and triglyceride concentration, by sex and age group.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th>Mean</th>
<th>SD</th>
<th>n</th>
<th>Group</th>
<th>Age</th>
<th>Mean</th>
<th>SD</th>
<th>n</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Men</td>
<td></td>
<td></td>
<td>Women</td>
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<tr>
<td>HDL (mmol·L⁻¹)</td>
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<tr>
<td>1</td>
<td>30</td>
<td>1.25</td>
<td>0.29</td>
<td>1770</td>
<td>0.36</td>
<td>2154</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2</td>
<td>40–45</td>
<td>1.28</td>
<td>0.33</td>
<td>2735</td>
<td>1.59</td>
<td>3457</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3</td>
<td>59–60</td>
<td>1.38*†</td>
<td>0.38</td>
<td>1917</td>
<td>1.71*†</td>
<td>2155</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Triglycerides (mmol·L⁻¹)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>30</td>
<td>1.77</td>
<td>1.15</td>
<td>1770</td>
<td>1.10</td>
<td>0.70</td>
<td>2154</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>40–45</td>
<td>2.01*</td>
<td>1.42</td>
<td>2735</td>
<td>1.24</td>
<td>0.82</td>
<td>3457</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>59–60</td>
<td>1.87†</td>
<td>1.13</td>
<td>1917</td>
<td>1.47*†</td>
<td>0.88</td>
<td>2155</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: HDL, high-density lipoprotein; SD, standard deviation.

* p < 0.01 vs. group 1.
† p < 0.001 vs. group 2. Serum HDL was higher in women than in men in all age groups (p < 0.001).

*p < 0.001 vs. group 1.
Intake of artificially sweetened colas

In subjects reporting the highest intake of artificially sweetened colas (Fig. 2), HDL values were 7.5% lower (men) and 7.8% lower (women) and TG was 11.7% higher (men) and 8.1% higher (women) than in the lowest intake group. There was no significant difference in the cola vs. serum lipid association related to the use of sugar.

Correlation coefficients for sugar-containing cola intake vs. TG and HDL in men (Fig. 1, closed circles) were 0.109 ($p < 0.001$) for TG and –0.145 ($p \leq 0.001$) for HDL. Correlation coefficients for intake of artificially sweetened cola vs. TG and HDL (Fig. 1, open circles) were 0.092 ($p = 0.01$) and –0.133 ($p < 0.001$), respectively. Corresponding values for women were TG: 0.072 ($p = 0.001$), HDL: –0.158 ($p = 0.001$), and TG: 0.034 ($p = 0.150$), HDL: –0.122 ($p = 0.001$). There were no significant differences between sugar-containing colas and artificially sweetened colas with regard to the association between intake frequency and TG or HDL (ANOVA).

Intake of non-cola soft drinks with and without sugar (Fig. 2)

No significant correlation was found between the reported intake frequency of non-cola soft drinks and serum TG or HDL concentrations, irrespective of the absence or presence of sugar.

Linear regression models for the association between serum lipids (HDL, LDL, TG) and intake frequency of colas and non-colas, as influenced by other factors

We found a significant negative association between cola intake and serum HDL, and a positive association with LDL and TG (Table 2). The associations were weakened when models with an increasing number of independents were introduced, but the cola vs. serum lipid associations prevailed even after including 13 possible confounders. In contrast to this, the associations between intake of non-cola soft drinks and serum lipids were no longer significant when going from model 2 to 3.

We studied the soft drink vs. serum lipid association by multiple linear regression after dividing the soft drink intake frequency into 4 or 5 levels; the outcome was, however, always the same, as was the conclusion using multiple logistic regression models (results not shown).

Discussion

To our knowledge, the present work is the first to suggest that frequent intake of colas with, and even without, sugar is associated with increased serum TG and LDL, and decreased HDL cholesterol. The associations were robust; the same pattern was found in several subgroups of men and women, and they were assessed by many statistical approaches controlling for several possible confounders. Previ-
Table 2. Linear regression models for the association between serum HDL, LDL, TG (dependent variables) and intake frequency of colas or non-colas (3 levels*), as influenced by other factors (n = 14 188).

<table>
<thead>
<tr>
<th>Model† †</th>
<th>HDL (mmol·L⁻¹)</th>
<th>LDL (mmol·L⁻¹)</th>
<th>TG (mmol·L⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B (SE)</td>
<td>β</td>
<td>p</td>
</tr>
<tr>
<td><strong>Main independent = colas</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-0.018 (0.001)</td>
<td>-0.112</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>-0.017 (0.001)</td>
<td>-0.102</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>-0.012 (0.001)</td>
<td>-0.074</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4</td>
<td>-0.010 (0.002)</td>
<td>-0.063</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5</td>
<td>-0.006 (0.002)</td>
<td>-0.039</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Main independent = non-colas</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-0.010 (0.002)</td>
<td>-0.051</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>-0.009 (0.002)</td>
<td>-0.047</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>-0.003 (0.002)</td>
<td>-0.016</td>
<td>0.082</td>
</tr>
<tr>
<td>4</td>
<td>-0.002 (0.002)</td>
<td>-0.013</td>
<td>0.199</td>
</tr>
<tr>
<td>5</td>
<td>-0.001 (0.002)</td>
<td>-0.006</td>
<td>0.509</td>
</tr>
</tbody>
</table>

Note: HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; B, unstandardized regression coefficient; SE, standard error.

*Grouped frequency of cola (non-cola) soft drink intake: level 1: 0 times per week; level 2: 3.5 times per week; level 3: ≥7 times per week.
† Model 1 = adjusted for sex and age group. Model 2 = model 1 + adjustments for time since last food intake, use of cholesterol-lowering drugs, and intake frequency of diet items (cheese, fruit and (or) berries, fatty fish). Model 3 = model 2 + adjustments for physical activity, years at school, use of sugar in the soft drink, and use of the alternative soft drink (non-colas or colas). Model 4 = model 3 + adjustments for smoking and frequency of alcohol intake. Model 5 = model 4 + body mass index (kg·m⁻²).

**Possible explanations for the findings**

Frequent use of sugar-sweetened carbonated beverages would provide a considerable amount of sucrose. This disaccharide may increase the serum TG concentration and lower the serum HDL (Høstmark and Blom 1985; Archer et al. 1998). Dhingra et al. (2007) found a positive association between soft drink intake and serum TG, and a negative relationship between soft drink intake and HDL. Because their study did not discriminate between colas and other soft drinks, the question is open as to whether their observations relate to soft drinks in general. Although we cannot exclude the possibility that sugar is involved, our results do not seem to favour attributing the cola vs. lipid associations solely to the disaccharide, because we found similar associations for colas with and without sugar.

Colas contain caffeine, which is a methyl xanthine known to inhibit cyclic AMP phosphodiesterase (Mayes 2000). Inhibiting the inactivation of cyclic AMP should enhance adipose tissue lipolysis, because the cyclic nucleotide stimulates the hormone-sensitive lipase in adipose tissue, thereby promoting release of fatty acids that could be used for hepatic TG and VLDL synthesis. However, Carson et al. (1993) found no consistent relation between caffeine consumption and serum lipids in elderly women. If caffeine in cola is a major factor in our findings, we would anticipate that adjusting for coffee intake should weaken the cola vs. lipid association. However, entering coffee intake into the multiple regression analysis did not significantly influence the associations between cola intake and blood lipids, thus rendering the caffeine hypothesis less plausible.

Because colas contain phosphoric acid yielding pH 2.6 (Jensdottir et al. 2006; Kapicloğlu et al. 2000), our results raise the question of whether an increased inorganic acid load caused by cola intake could partly explain the negative association between cola and HDL. In general, an acid load would not appear to influence serum HDL, because we did not account for variation in time since last meal.
not find that intake of fruit juice was related to serum HDL (results not shown). We suspect, however, that organic and inorganic acids have different impacts. Metabolism of many organic acids will result in the formation of water and carbon dioxide, which can be quickly removed through the respiratory system without affecting the bicarbonate pool, as shown by the carboxylic acid–bicarbonate equilibrium: $\text{CO}_2 + \text{H}_2\text{O} = \text{H}^+ + \text{HCO}_3^-$. Unlike the acid load of organic acids, protons of inorganic acids, such as the phosphoric acid present in colas, would tend to lower the bicarbonate concentration. Protons of inorganic acids will mainly have to be excreted in the urine, and may also react with ammonia and $\text{HPO}_4^{2-}$ to be excreted as ammonium and $\text{H}_2\text{PO}_4^-$ ions. Bone mass may be influenced by the release of calcium and phosphorus in response to an inorganic acid load. In keeping with these considerations, high intakes of colas, but not other soft drinks, has been shown to be associated with osteoporosis and bone fractures (Wyshak 2000; Tucker et al. 2006), although the association between cola and reduced bone mineral density was not found by McGartland et al. (2003).

Interestingly, intake of bicarbonated mineral water has been reported to increase serum HDL and decrease postprandial lipaemia in postmenopausal women (Schoppen et al. 2004; Schoppen et al. 2005). If an inorganic acid load is involved in the cola vs. lipid association, it would appear that the presence of bicarbonate in colas is insufficient to counteract the effect of phosphoric acid. Also, our preliminary data from a diet trial in rats given colas ad libitum suggest a serum lipid effect related to phosphoric acid.

In conclusion, this study shows a direct positive association between cola intake frequency and serum TG and LDL concentration, and a negative association with serum HDL cholesterol, but the data do not clarify whether the associations are causal ones.

Acknowledgements

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References


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