Carbonated Soft Drinks and Diabetic Retinopathy- Are there Any Effects?

by

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ABSTRACT

The purpose of this study is to test whether or not drinking moderate quantities of carbonated soft drinks has any effects on diabetic retinopathy in patients with Insulin-dependent diabetes Mellitus. Based on personal observations, diabetic retinopathy, especially if accompanied with diabetic macular edema, seems to improve when discontinuing moderate quantities of carbonated soft drinks. Therefore it was hypothesized that carbonated beverage consumption may have an adverse effect on patients with diabetic retinopathy, specifically those with diabetic macular edema.

Diabetic Macular Edema

Dietary salt is responsible for raising blood pressure, thickens and stiffens conduit arteries and thickens and narrows resistance arteries. It also increases the number of strokes, and the tendency for platelet aggregation. An increased total body sodium and enhanced vascular reactivity are found in people with diabetes and most type 2 diabetics are salt sensitive. Similar to a subset of patients with essential hypertension, type 2 diabetics manifest dietary salt-induced exacerbation of hypertension. Sympathetic nerve overactivity is crucial in the pathogenesis of hypertension in diabetes. It is related to the activation of the rennin-angiotensin-aldosterone (RAA) system in. Sympathetic overactivity stimulates RAA activity, promotes sodium reabsorption, and increases heart rate, stroke volume, and peripheral vascular resistnce, thus inducing hypertension and increasing cardiovascular risk.
Diabetic Retinopathy

Diabetic retinopathy remains a major cause of loss of vision. Overall, diabetic retinopathy is estimated to be the most frequent cause of new blindness in the U.S. among adults between the age of 20-74 years. Diabetic retinopathy is characterized by microaneurysms, hemorrhages, and lipid accumulation referred to as hard exudates, within the retina. Microaneurysms are thin-walled dilations of the capillaries that develop in diabetic patients as the pericyte cells which line the capillaries, die off and weaken the capillaries, causing a "ballooning", of the capillaries, or microaneurysm. Macular edema (retinal thickening) is an important manifestation of diabetic retinopathy as it is the leading cause of legal blindness in diabetic patients. Retinal thickening of macular edema is a result of intercellular fluid derived from both leaking microaneurysms and diffuse capillary leakage. Patients with diabetic macular edema have a significant impaired visual acuity. Diabetic maculopathy is closely associated with diabetic nephropathy and neuropathy and with several atherosclerotic risk factors which suggest that these factors may have an important role in the pathogenesis of maculopathy.

Medical treatment of macular edema with carbonic anhydrase inhibitors have been known effective treatment of cystoid macular edema in patients with diabetic macular edema in nonproliferative retinopathy, even though mechanisms remain obscure, although it may facilitate the transport of water across the retinal pigment epithelium from the subretinal space. Carbonic anhydrase inhibitors have also been shown to have other direct effects both on retinal and retinal pigment epithelial function by inducing an
acidification of the subretinal space, a decrease of the standing potential as well as an increase in the retinal advesiveness25. The enzyme carbonic anhydrase catalyzes the conversion of carbon dioxide and hydroxide ion into bicarbonate22. Acetazolamide, a diuretic, is a carbonic anhydrase inhibitor, primarily effects the kidneys by inhibiting carbonic anhydrase. Its mechanism of action is inhibits carbonic anhydrase, which in turns catalyzes the hydration of bicarbonate at the proximal tubule in the kidneys, facilitating the resorption of virtually all of the sodium21. By inhibiting hydrogen ion secretion by the renal tubules, carbonic anhydrase inhibitors cause increased excretion of electrolytes, sodium, potassium, bicarbonate, and H2O, thus producing alkaline diuresis23. As carbonic anyhydrase inhibitors increase the excretion of sodium, potassium, bicarbonate, and water, and improve diabetic macular edema, discontinuation of carbonated soft drinks (which contain the above electrolytes), may have a similar effect1. Carbonated soft drinks have been part of American lifestyle for more than 100 years. Soft drinks contain between 90% water in regular soft drinks, up to 99% water in diet soft drinks. Carbon dioxide is the essential ingredient in all carbonated beverages. Soft drinks also contain flavors, coloring, caffeine, acidulants, preservatives, potassium, phosphorous, sodium, sucrose or high fructose corn syrup in regular (non-diet) soft drinks, and aspartame, saccharin, sucralose and acesulfame K in diet soft drinks. One out of every four beverages consumed in America is a carbonated soft drink, which averages to over 57 gallons of soft drinks per year for every man, woman and child7. This is equivalent to more than 576 12-oz. servings per year or 1.6 12 oz. cans per day for every man, woman, and child28. Carbonated soft drinks account for more than 27% of Americans’ beverage consumption7. Artificially sweetened diet sodas account for 24% of
sales. Carbonated soft drinks are the biggest source of refined sugars in the American diet.

**Caffeine in soft drinks**

Caffeine in soft drinks varies by brand, from 0 mg. in caffeine-free and 7-Up, to 58 mg per 12 oz. in Josta Cola. Most standard brands (Pepsi, Coca-cola) contain between 37.5 to 46.5 mg per 12 oz.

**Caffeine, sodium, hypertension, and diabetes**

Diabetes and hypertension are both relatively common diseases in westernized countries. Both diseases increase with age. Hypertension is twice as frequent in diabetic patient than in the general population. Essential hypertension accounts for the majority of hypertension in people with type 2 diabetes, which means Type 2 diabetes or essential hypertension? constitutes more than 90% of those with dual diagnosis of diabetes and hypertension. The benefit conferred per mmHg of Blood pressure reduction is greater in persons with type 2 diabetes than with hypertensive patients without diabetes. Recent guidelines have recommended that target blood pressure levels in patients with diabetes should be lower than in other hypertensive groups. It is currently recommended that individuals with diabetes maintain a blood pressure of less than 130/85 to maximize renal protection. An increased total body sodium and enhanced vascular reactivity are found in people with diabetes, and most type 2 diabetic patients are salt sensitive.
Caffeine raises blood pressure by elevating vascular resistance, and this effect is more pronounced and prolonged in hypertensive patients than in normotensives. Regular coffee drinking raised blood pressure in older hypertensives.

**Known Risk Factors in Diabetic Retinopathy**

The best predictor of diabetic retinopathy is the duration of the disease. Patients who have had insulin-dependent diabetes mellitus (IDDM) for 5 or less years rarely show evidence of diabetic retinopathy. However, 27 of those who have had IDDM for 5-10 years and 71 to 90% of those who have had IDDM greater than 10 years have diabetic retinopathy. After the diagnosis of Non-insulin-dependent diabetes mellitus (NIDDM), 67% of patients had retinopathy and 10% had proliferative diabetic retinopathy (PDR).

**Systemic Factors**

**Control of blood glucose**

The Diabetes Control and Complications Trial (DCCT), published in 1993, was the first large, scientific, and clinical trial demonstrated a marked reduction in the development and progression of diabetic complications in intensively treated patients. More recently, the U.K. Prospective Diabetes Study confirmed that intensively controlled patients with type 2 diabetes had a significantly reduction in microvascular complications.

**Renal Disease**
Patients with renal disease (proteinurea, elevated blood urea nitrogen, and elevated blood creatine) almost always have retinopathy\textsuperscript{13}. However, only 35\% of patients with retinopathy have proteinuria, elevated blood urea nitrogen, or elevated creatine\textsuperscript{14}. [I don't understand this]

**Body Mass Index (BMI)**

Body mass index, or BMI, [higher? Lower?] is a positive risk factor for diabetic retinopathy\textsuperscript{19}. Body mass index is expressed as weight in kilograms divided by the square of the height in meters.

**Systemic Hypertension**

Elevated systolic blood pressure is a moderate risk for diabetic retinopathy\textsuperscript{14}, whereas other studies have shown that diastolic blood pressure is important for the development of retinopathy in type 1 diabetes\textsuperscript{15}. Control of systemic hypertension reduces the risk of new onset diabetic retinopathy and slows the progression of existing diabetic retinopathy\textsuperscript{15}. Pulse rate [high? Low?] may be an indicator of overall risk of diabetic retinopathy, but is not an independent association with the condition\textsuperscript{16}.

**Race**

The prevalence of diabetic retinopathy is more prevalent in blacks compared to whites\textsuperscript{17}. In addition, blacks have a higher rate of severe macular edema and blindness, probably because of a higher incidence of severe systemic hypertension and because of poorer medical care\textsuperscript{18}.
These studies demonstrate evidence that good metabolic control protects diabetic patients against complications. However, clinicians are faced with individual variability of diabetic patients in their practices, often wonder why some patients under good metabolic control develop complications while others remain free of complications, despite poorly controlled diabetic, remain control. Studies have shown that retinopathy develops in about 10% of patients with type 1 diabetes under good metabolic control, whereas over 40% of patients with type 1 diabetes remain retinopathy-free despite poor metabolic control.

The present study is to observe if moderate consumption of carbonated soft drinks has any effects on diabetic retinopathy.

RESEARCH DESIGN AND METHODS

Records from a retina specialist’s office were reviewed. Only patients with insulin-dependent diabetes mellitus with diabetic retinopathy and macular edema during the period of 1998-2003 were selected. A computer program was written in Hypercard 2.4 (Apple™) was designed to perform searches in patient records for all patients within the retina practice that include patients with IDDM, have documented word with “sodas” or “carbonated drinks” and a diagnosis of “macular edema”. All patients had diabetic retinopathy at baseline and patients with previous laser treatments at initial visit were excluded. Efforts were made to include women and minorities. A retrospective or
historical cohort study design was within on patients within the retina clinic; using patients with insulin-dependent diabetes mellitus with diabetic retinopathy who drink carbonated drinks compared to a similar group of diabetic patients with retinopathy, but did not drink carbonated beverages. The prevalence of diabetic macular edema in each group was then compared.

From approximately 10,000 medical records, about 3,500 patients with Insulin-dependent Diabetes Mellitus (IDDM) were extracted. Of those patients, 1,849 patient records had “soda” or “carbonated beverages” documented within the record. 1,278 patients had macular edema and drank at least 1 -12 oz. can of soda per day, and had the diagnosis of diabetic macular edema. 158 patients drank at least 1 can of soda per day and did have diabetic macular edema. 355 patients had diabetic macular edema, but did not drink sodas. 49 patients had IDDM and no macular edema, and had documented “no sodas” or “does not drink sodas” in their medical records.

Calculation of the prevalence of disease in persons with exposure (sodas) and compare it with the prevalence of disease (macular edema) without exposure. Odds Ratio in a 2 X 2 table was tabulated and calculated (table 1).
Table 1.

Odds Ratio - Macular Edema and Sodas

<table>
<thead>
<tr>
<th>Sodas</th>
<th>Cases (exposed)</th>
<th>Controls (not exposed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macular edema</td>
<td>1278</td>
<td>158</td>
</tr>
<tr>
<td>No macular edema</td>
<td>355</td>
<td>46</td>
</tr>
</tbody>
</table>

Odds Ratio = \( \frac{a}{b} \div \frac{c}{d} = \frac{ad}{bc} \)

\[
\text{Odds Ratio} = \frac{58788}{56090} = 1.048101266
\]

In addition, a survey was performed to estimate the carbonated beverage drinking habits of diabetics, compared to non-diabetics. The survey included categories of age, sex, race, no. of years having diabetes if diabetic. Efforts were made to include an adequate sample of race, age and both sexes. Carbonated soft drink consumption was estimated per day, soda use was categorized as regular or diet, caffeinated or caffeine-free. Data was entered using Access (Microsoft®), statistics were calculated, including
average soda consumption, categories of sodas were tabulated, and pie graphs were generated.

The study design has been submitted to the Institutional Review Board for approval.

**Definition of carbonated soft drink users**

In this study, the definition of a carbonated soft drink user was anyone who drinks 1 or more, 12 oz. cans of soda or equivalent, each day.

**Results**

Of the sample surveyed, 88% of non-diabetics drank sodas, averaging 1.4 sodas per day, while 70% of diabetics drank sodas, averaging 1.4% sodas per day. 60% of non-diabetics drink regular sodas, 28% drank diet, while in the diabetic group, 52% drank diet, and 18% drank regular sodas. (Figures 1 and 2).
Fig. 1

**Soda Consumption: Non-diabetics**

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>% non-diabetics who do not drink sodas</td>
<td>12%</td>
</tr>
<tr>
<td>% non-diabetics who drink diet sodas</td>
<td>28%</td>
</tr>
<tr>
<td>% non-diabetics who drink regular sodas</td>
<td>60%</td>
</tr>
</tbody>
</table>

Fig. 2

**Soda Consumption: Diabetics**

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>% diabetics who do not drink sodas</td>
<td>30%</td>
</tr>
<tr>
<td>% diabetics who drink diet sodas</td>
<td>52%</td>
</tr>
<tr>
<td>% diabetics who drink regular sodas</td>
<td>18%</td>
</tr>
</tbody>
</table>
Risk- Odds Ratio

The Odds Ratio in our group studied, or the ratio of the odds of development of disease in exposed (to sodas) persons to the odds of development of disease (macular edema) in non-exposed (no sodas), was 1.05 demonstrating that there is not an apparent association between soda drinking and diabetic macular edema. If the exposure is not related to the disease, the odds ratio will be equal to 1.

Conclusions

From this study, there is no clear association between drinking sodas and diabetic macular edema, demonstrating a spurious association from observation noted above within the retina clinic. However, due to confounding, we cannot rule out an association between macular edema and soda consumption. As soda consumption was not quantified, no dose-response was measured. Errors from selection bias may have a major impact on the internal validity of the study. Information bias or inaccuracies of data acquisition may have, at times, misclassified information regarding exposure status. Further studies—prospective, case-controlled, and clinical trials studies are needed for more conclusive evidence whether there is no association between carbonated beverage consumption and diabetic macular edema.
Acknowledgments

1. Personal communications, Peter Van Houten, M.D., retina specialist, East Carolina Retina Consultants, Greenville, NC 27834


27. http://www.cspinet.org/new/cachart.htm Caffeine Content of Foods and Drugs


37. de Wardener HE, MacGregor GA. Harmful effects of dietary salt in addition to hypertension. 16(4):213-23, 2002 Apr.