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**CONSUMPTION OF CARBONATED BEVERAGES AND THE RISK FOR GASTROINTESTINAL DISEASE: A SYSTEMATIC REVIEW
(KONSUMSI MINUMAN BERKARBONASI DAN RISIKO SAKIT SALURAN PENCERNAAN: REVIEW SISTEMATIS)**

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ABSTRACT

Issues of different effects of carbonated soft drinks to human health have been circulated and analyzed in both scientific and non-scientific approaches. However, there is few publications discussing the specific effect of carbonation on human health and, more often than not, studies have largely concentrated on the effect of sugar or calorie content in carbonated beverages in affecting our health. Thus the effect of carbonation itself on human health is then lost in arguments contradicting or reaffirming the effect of carbonated soft drinks. We conducted this systematic review to specifically observe current findings on the effect of carbonation in beverages on human health. This systematic review was conducted using Scirus search engine to list articles relevant with keywords such as CO₂, carbonated beverage, carbonation, sparkling water, gastrointestinal, gastro-esophageal and adenocarcinoma. Next, articles were obtained from numerous databases and screened for their relevance and context. Finally, peer reading and discussion were conducted for the writing of this article. The results of this systematic review observed three major article subjects currently correlated with exclusive effect of carbonation on gastrointestinal health. Published studies indicate that oral cavity/dental health, gastro-esophageal reflux and most recently esophageal adenocarcinoma are discussed frequently and observed in population studies in different countries consuming significant quantities of carbonated beverages. Eight articles (40%) discussed dominant factors not correlated with carbonation which significantly affect dental erosions. Six (33%) articles observed no clear clinical significance carbonation promotes or exacerbate gastro-esophageal reflux. Interestingly, five (27%) articles reported insignificant correlation, even inverted, of carbonation on esophageal carcinoma. Currently available scientific studies on populations in multiple countries show that the effect of carbonation in beverages has non-significant (statistically) effect on the health of the gastrointestinal tract.

Keywords: Carbonated beverages, gastrointestinal, GERD, esophageal adenocarcinoma

ABSTRAK

Isu mengenai dampak karbonasi pada minuman ringan terhadap kesehatan, terutama kesehatan saluran pencernaan, telah banyak beredar beserta pembahasannya, baik secara ilmiah maupun tidak. Efek kesehatan dari unsur karbonasi pada minuman ringan sangat jarang dibahas dan dipublikasikan pada jurnal ilmiah. Melakukan systematic review status ilmiah terkini khusus mengenai dampak karbonasi dalam berbagai produk minuman terhadap kesehatan saluran pencernaan. Scirus search engine digunakan untuk melacak artikel ilmiah dengan kata kunci khusus, yakni CO₂, carbonated beverage, carbonation, sparkling water, gastrointestinal, gastro-esophageal and adenocarcinoma. Tahap ini dilanjutkan dengan penapisan (screening) untuk kesesuaian subjek artikel dan akses. Tahap terakhir adalah focus group discussion bersama peer/ahli dalam bidang gizi, kesehatan dan keamanan pangan. Hasil dari systematic review memperlihatkan bahwa terdapat tiga kelompok pembahasan utama yang berhubungan dengan efek karbonasi terhadap kesehatan saluran pencernaan, yaitu kesehatan pada gigi/rongga mulut, refluks esofagus dan kanker esofagus. Hasil skrining menunjukkan 40 persen published articles membahas dental health, 33 persen membahas gastro-esophageal health dan 27 persen membahas esophageal adenocarcinoma. Delapan artikel yang membahas dental health menunjukkan erosi yang dapat terjadi disebabkan oleh faktor lain di luar karbonasi. Enam artikel yang membahas gastro-esophageal health menunjukkan tidak ada korelasi antara faktor karbonasi dengan refluks ataupun refluks kronis yang terjadi. Sementara 5 artikel memperlihatkan observasi yang berkorelasi terbalik dengan risiko munculnya kanker esofagus. Systematic review menunjukkan bahwa saat ini berbagai artikel ilmiah relevan yang sudah dipublikasikan menyimpulkan dampak karbonasi pada minuman terhadap kesehatan saluran pencernaan tidak signifikan secara statistik klinis. [Penel Gizi Makan 2014, 37(1): 69-76]

Kata kunci: Minuman berkarbonasi, penyakit saluran pencernaan, GERD, esophageal adenocarcinoma

INTRODUCTION

Carbonation of water and its development into a myriad of carbonated beverages or soft drinks is ubiquitous in the consumer's market in recent times, available in caloric and non-caloric, flavored and non-flavored drinks. These carbonated beverages contain carbon dioxide at low concentration (up to 1.0%), but enough to create carbonic acid (H_2CO_3) to decrease its pH and give the sensation of effervescent or *sparkle* as a desirable sensory attribute¹. The acidity of carbonated beverages, excluding other parameters such as calorie, could be perceived to have an effect on human health.

Limited scientific studies and results show inconsistent data with regard to the effects of carbonation on the gastrointestinal tract. Different groups have suggested a negative influence while others have described beneficial effect when consuming carbonated beverages under different conditions¹. The typical carbonated beverage would most likely be composed of three main constituents: (1) the carbon dioxide dissolved in the liquid; (2) the sugar, sweetener and/or flavors; (3) other substances such as colorants. Recent and numerous arguments have highlighted the effect of sugar or calorie contained in these carbonated drinks on increased risks of obesity and other metabolic syndromes, however the onset of this disease is complex and compounded by factors closely related to lifestyles, such as diet and exercise². From this perspective, carbonated beverages containing calories could be seen as equally influential as other calorie containing drinks in increasing the risks of obesity. What would make carbonated beverages distinct is the presence of dissolved carbon dioxide, which should make this the main factor in assessing the effect it has on human health.

We have determined that carbonation is the main focus in studying the effect of carbonated beverage on human health, more specifically its effect on the gastrointestinal tract. Carbon dioxide occurs naturally in the body as the waste product of respiration in all cells. However, as bicarbonate ions (HCO_3^-) it has diverse roles in the human body including affecting blood's pH balance, contributes to vasodilation, inflammation and tissue regeneration, and the stimulation of breathing³. Upon the consumption of carbonated beverage, only dissolved CO_2 will

continue to reach the later stages of the gastrointestinal tract, as most of CO_2 is lost in the sudden drop of pressure when opening the beverage container. However, the concentration of dissolved CO_2 which reaches the stomach is sufficient to induce lancinating stimulus which is thought to induce the gastrocolic reflex and activate intestinal peristalsis, a mechanism in which carbonated beverage is credited for the treatment of constipation⁴. Furthermore, as the gastrointestinal tract begins with the oral cavity the effect of carbonation on dental health will also need to be included in this study.

Other observed effect of carbonated beverages consumption is the induction of gastro-esophageal reflux (GER), a condition in which stomach acid and/or bile would flow back up the esophagus as a result of ingested carbonated liquid⁵⁻⁷. This condition is commonly observed in the consumption of large quantities of carbonated beverage. It has also been established that chronic GER is one of the many other major factors contributing to the development of esophageal carcinoma⁸. Thus, there was emerging assumption that the increased consumption of carbonated beverage, which parallels increased incidence of esophageal adenocarcinoma, observed in recent years, is positively correlated and even assumed to have causal association.

METHODS

This systematic review was conducted using internet scientific search engine at www.scirus.com which is capable to access numerous journal repositories and databases. Articles included in this study were limited to English, peer-reviewed, relevant to keywords entered and accessible to the author. The keywords entered in the search engine include CO_2 , carbonated beverage, carbonation, sparkling water, gastrointestinal, gastro-esophageal and adenocarcinoma. The number of hits was then followed up to obtain the relevant articles from various different journal sources/databases is then checked for duplicate entries which were removed. From this number, articles with little or no relevance (opinions, theoretical articles, letters etc. published in journals) were excluded from being evaluated resulting in a final number of peer-reviewed articles which are then further evaluated.

RESULTS

Entering keyword of interest (*carbonated beverage, carbonation, sparkling water, gastrointestinal, gastro-esophageal and adenocarcinoma*) in the scirus search engine resulted in 156 published scientific articles, which were then screened for duplicate entries, which result in 108 articles. These 108 articles were then matched to the specific context of *carbonation effect* which removed a further 88 articles.

Evaluations with our peers in nutrition, health and food safety removed 2 other articles (Figure 1A). Of the 20 articles found relevant to the specific effect of carbonation on health, it was observed that 40 percent of the articles discussed oral and dental health, 33 percent of the articles discussed gastro-esophageal reflux and its chronic disease, and interestingly 27 percent of articles presented observations on the effect of esophageal adenocarcinoma (Figure 1B).

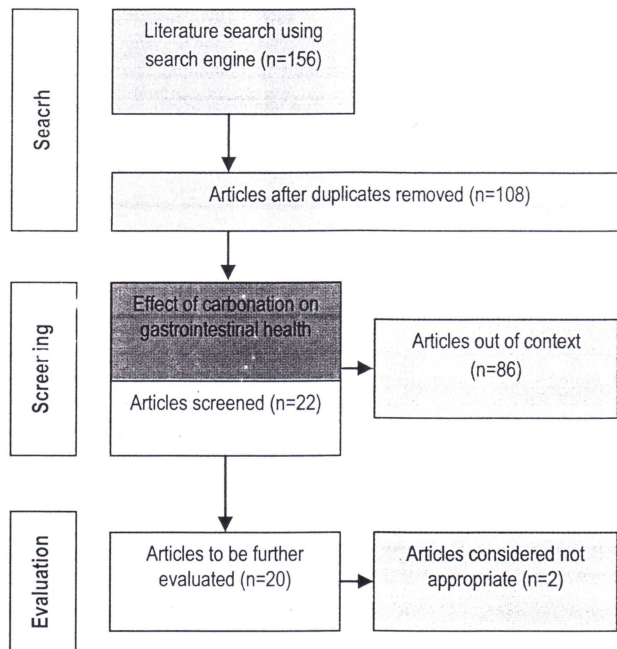


Figure 1A.
Search Of Articles Using The Scirus Serach Engine And Subsequent Screening By Peers

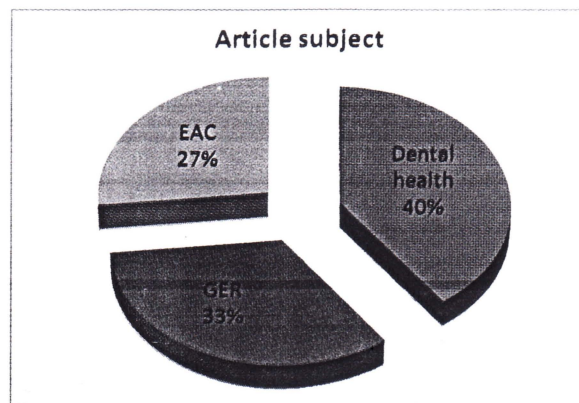


Figure 1B
Result Of Screening Categorized By Article Subject

Table 1
Results of studies included in the systematic review

Year	Author	Subjects	Study Type	Main Outcomes
2001	Parry <i>et al.</i>	-	<i>in vitro</i>	Very low level dissolution of human enamel, carbonation not an important factor in erosive potential
2003	Sanchez <i>et al.</i>	30 children with caries, 30 age and sex matched caries free subjects	Cross-sectional salivary pH monitoring	Decrease of salivary pH was observed higher in subjects with dental erosion after beverage consumption.
2004	Jensdottir <i>et al.</i>	80 adults (57 age 19-23; 23 GERD patients age 25-45)	Cross-sectional study interview and examination	No significant difference in prevalence of dental erosion with GERD
2007	Kitchens <i>et al.</i>	-	<i>In vitro</i> test on 28 extracted human teeth	No difference between carbonated and non-carbonated beverages in affecting dental erosion
1999	Oliviera <i>et al.</i>	GERD Subjects (n=2000)	Prospective survey	Inconclusive relationship to GER
2005	Fass <i>et al.</i>	Subjects with Nocturnal GERD (n=3806)	Prospective survey	Inconclusive relationship to GER during sleep
2006	Pehl <i>et al.</i>	GERD subjects (n=25)	Prospective pH monitoring	Intra-esophageal pH <4 – exposure time insignificant
2008	Dore <i>et al.</i>	GERD subjects (n=300)	Prospective survey	Inconclusive relationship to GER
2006	Mayne <i>et al.</i>	282 subjects with EAC, 206 subjects with esophageal squamous cell carcinoma – ESCC	Case-control study	Diet carbonated soft drink showed significant inverse correlation (OR = 0.47, 95% CI = 0.29 to 0.76; p = 0.005), or at least no correlation with regular carbonated soft drink.
2006	Lagergren <i>et al.</i>	820 control subjects and 189 EAC patients	Case-control study	Showed non significant inverse correlation (OR = 0.80, 95% CI = 0.60 – 1.90, p= 0.87) between carbonated drink and EAC.
2007	Gallus <i>et al.</i>	304 subjects with ESCC, grouped by carb. drink consumption	Case-control study	Showed less significant correlation (OR = 0.86, 95% CI = 0.62 – 1.20) between carbonated drinks with ESCC.
2008	Ibibebe <i>et al.</i>	population-based multicenter	Case-control study	Inverse correlation between carbonated beverage consumption and ESCC risk (OR = 0.40, 95% CI = 0.20 – 0.78; p = 0.04)

DISCUSSION

It was inadvertently apparent that health effects to the gastrointestinal tract became the main focus as a result of this systematic review as carbonation (CO₂) is not adsorbed, and its associated effects (such as increased pressure or decrease of pH) renders the mucosal surface of this tract. Thus the three main areas of concern in the gastrointestinal tract: oral cavity, esophageal reflux and esophageal carcinomas became the topic of concern.

Oral cavity

The hypothesis that carbonation in beverage is potent to cause and promote dental erosion stems from the notion that dissolved CO₂ in liquids enhance its acidity and lowering its pH. This is correctly noted as many of the commercially available carbonated beverages yield pH ranging from 2.4 to 4.0⁷. The aspect of carbonation excludes the factor of dissolved sugar which further compounds the problem with additional calorie yield. This also excludes other aspects such as colorants added to carbonated beverages which may contribute to the cause of teeth discoloration.

The majority of articles obtained presumed that carbonation of beverage is indicative for potential dental erosion²². This is due to the high acidity commonly found in these beverages. A clinical study conducted in Iceland indicated that there is significant association between carbonated cola and dental erosions⁹. However this study was limited by its small size and could not isolate the cause of promoted erosion was due only to one factor, the carbonation of beverage. However, it was noted that these observations could only conclude that the carbonation effects are potential¹⁰, again only in carbonated water with the addition of flavoring. While in carbonated non flavored water, no promoted erosion was observed^{1,22}.

It was found that when compared to control groups, subjects who have drank carbonated soft drinks, including carbonated water, showed lower salivary pH. However, this observation was only found in subjects who already have tooth decay, indicating that their basal salivary pH is readily or easily influenced by the presence of carbonated liquid, thus promoting further erosion^{1,21}. Similarly, the consumption of all other highly acidic foods and drinks has been observed to significantly promote dental erosions, not only due to their low pH but also because of their

higher titratable acid contents and calcium chelating ingredients^{11,12}.

Gastro-esophageal reflux disease (GERD)

The effect of carbonated beverages on lower esophageal sphincter (LES) has been evaluated by one study⁶. This study involved nine healthy young subjects, in which esophageal manometry was performed on the subjects after ingesting water and different carbonated beverages. All carbonated beverages resulted in a minimum of 20 minutes reduced resting pressure (30-50% decrease) of the LES, overall length and intra-abdominal length. This decrease of resting pressure was observed to be mediated by the distension of the stomach because of the carbonation in the liquids consumed, thus making it probable for GER. The limitation of this study was the small size of healthy subject.

As the consumption of carbonated beverages was demonstrated able to contribute to the occurrence of GER, a systematic review of the effect of consuming these beverages to patients of GER disease (GERD) was performed by Johnson *et al.* (2009). This study reaffirmed that the consumption of carbonated beverages result in transient reduction of LES resting pressure, but further noted that little damage to the esophagus were to occur. It was observed that from the relevant peer-reviewed articles included in the study that even with the increase consumption of carbonated beverages there is little support for the association of between the consumption and GERD, including GERD related complications⁷. While the consumption of carbonated beverages is probable for the occurrence of GER, there is no direct evidence that it promotes or exacerbates GERD.

Esophageal cancer

Esophageal cancer is determined to be the eighth most common cancer worldwide and rank as the sixth most common cause of death by cancer¹³. The incidence of esophageal cancer or esophageal adenocarcinoma (EAC) has been attributed to several factors including male gender, caucasian race, obesity and dietary fats⁸. Dominant risk factors for EAC include tobacco smoking and gastro-esophageal reflux disease (GERD)^{8,14}.

Chronic GER and GERD is thought to play a major role in the progress and development of EAC, although the

mechanisms are still unclear. There are two proposed mechanisms, first is that the reflux of stomach acids and/or bile injures the esophageal epithelium, inducing cytokine production and the onset of inflammation thus initiating cell proliferations and the metaplasia-dysplasia-neoplasia sequence¹⁵. The second proposed mechanism is that the reflux may cause increased production of nitric oxide (as a result of inflammatory response or from the ingested nitrites), thus promoting further DNA damage and enhanced risk of genetic change¹⁶.

The consumption of carbonated beverages have been increasing in recent years concurrent with the increase of EAC incidence (over 350% increase since mid-1970s), suggesting a contributory link¹⁶. This was presumably because of the observation that carbonated beverages could increase the risk of GER, thus the natural inquiry of whether increased consumption of carbonated beverages correlates positively with the incidence and development of EAC.

Several epidemiological studies conducted in the US¹⁷, Sweden¹⁸, Italy¹⁹ and Australia²⁰ have observed no positive correlation between consumption of carbonated beverages and EAC. On the contrary there have been observations of significant inverse correlation¹⁷, not significant inverse correlation^{18,19} and no correlation whatsoever between consumption of carbonated beverages and the risk of EAC.²⁰

A study conducted by Mayne *et al* in multiple medical centers population-based case-control involved 687 control subjects and 488 subjects with esophageal carcinoma (282 subjects with EAC, 206 subjects with esophageal squamous cell carcinoma-ESCC). After adjusted for age, gender, race, body mass index (BMI), caloric intake, intake of alcoholic beverages, meat consumption, cigarettes, education and income; the study found that the Odds Ratio (OR) between consumption of diet carbonated soft drink and esophageal carcinoma risk showed significant inverse correlation (OR = 0.47, 95% confidence interval = 0.29 to 0.76; $p = 0.005$). However, there was no association between regular carbonated soft drink intake. Furthermore, this team acknowledge the importance of consuming fruit and vegetables, decreasing smoking, and decreasing BMI as important factors in decreasing the risk of esophageal carcinoma.

An independent study conducted by Gallus *et al* in Italy used data from one hospital involving 743 control subjects and

304 subjects with ESCC. Subjects (control and ESCC patients) were grouped according to the frequency of their carbonated soft drink consumption. The association between carbonated soft drink consumption and ESCC risk was again adjusted for age, gender, education, cigarette smoking BMI, physical exercise and total caloric intake, showed less significant correlation (OR = 0.86, 95% confidence interval= 0.62 – 1.20). This finding does not show significant inverse correlation between carbonated soft drink consumption and ESCC risk, but it does reinforce the finding that carbonated beverage consumption does not increase esophageal carcinoma risk.

A study conducted in Sweden by Lagergren *et al*. nationwide population-based case-control model involved 820 control subjects and 189 EAC patients. The association between carbonated soft drink consumption and EAC risk was again adjusted for age, education, income, cigarette smoking and alcohol intake; and showed non significant inverse correlation (OR = 0.80, 95% confidence interval = 0.60 – 1.90, $p = 0.87$). Similarly, a study conducted by Ibiebele (2008) using data from population-based multicenter case-control in Australia provided similar conclusion (OR = 0.94, 95% confidence interval = 0.53 – 1.66, $p = 0.86$) of no correlation between carbonated beverage consumption and EAC risk. On the contrary, they observed inverse correlation between carbonated beverage consumption and ESCC risk (OR = 0.40, 95% confidence interval = 0.20 – 0.78; $p = 0.04$).

These epidemiological studies indicate that the risk of EAC increased by the consumption of carbonated soft drinks via increased GER is not correlated nor associated. There are other factors which could contribute highly to the risk of EAC such as compounding factors like cigarette smoking and overweight. These findings confirm that the worldwide increase of EAC incidence is not associated to the increase of carbonated soft drink consumption.

CONCLUSIONS

This systematic data acquisition and review study is easily reproducible and robust to show repeated similar results by anyone with access to the relevant scientific publications. Results from our systematic data acquisition and review study show that current data and publications indicate there is no correlation of carbonation in carbonated beverage consumption with risks in dental

erosion, gastro-esophageal reflux and esophageal adenocarcinoma. Available clinical studies data showed that carbonated beverage does not promote dental erosion more than non-carbonated soft drinks or other beverages containing sugar. Similar observation was made in that carbonated beverage does not promote GERD and its complication when viewed from epidemiological studies. Data from case-control studies also indicate non association findings in the effect of carbonation on the development of esophageal carcinomas. Thus, it could be concluded that carbonation in beverages consumed by the general population shows no association with health issues in the gastrointestinal tract.

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