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Artificially sweetened beverages: What does the latest evidence tell us on health benefits versus harm?

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Cristina Cleghorn, Amanda Jones , Andrea Teng, Tony Blakely, Nick Wilson

Reducing consumption of sugar-sweetened beverages (SSBs) is an important current policy issue internationally. One suggested strategy is for people to swap to artificially sweetened beverages (ASBs). But there are multiple concerns about potential health risks of ASBs – although limited evidence and hard data. This blog seeks to briefly summarise current evidence, to inform the public, public

health practitioners and policy makers.

In NZ there are numerous artificial sweeteners approved for use in beverages, including aspartame (brand names NutraSweet, Equal), cyclamate (Sucrayl, Assugrin, Sugar Twin), neotame (NutraSweet), saccharin (Sweet'N Low, Sweet Twin, Necta Sweet), Stevia, and Sucralose (Splenda, Sugar Free Natura). An artificial sweetener replicates the sensory properties of sugar (ie, it tastes like sugar). However, because artificial sweeteners are significantly sweeter than sugar, they are used in very small amounts and therefore contribute no or little energy. Other names for artificial sweeteners are non-nutritive sweeteners, high intensity sweeteners, low calorie sweeteners, and low energy sweeteners.

In this brief review* for this blog, the studies that we examined often referred to sweeteners as 'artificial sweeteners', and we'll mainly use this terminology throughout, noting this category may include some sweeteners that are from naturally occurring plant extracts (eg, steviol gylcosides from the stevia plant).

Association of ASBs with weight

Starting with the association between ASBs and weight, two meta-analyses have been published recently on this topic. In the first [1] it was found that the cohort studies reported inconsistent associations between Low Energy Sweetener (LES use and body mass index (BMI, -0.002 kg/m^2 per year, 95% confidence interval (CI): -0.009 to 0.005)). While the meta-analysis of sustained randomised controlled trials (RCTs), four weeks to 40 months, showed LES consumption led to a reduced body weight compared to those consuming sugar in nine studies of -1.35 kg (CI: -2.28 to -0.42). There was a similar reduction in body weight when LES were compared to water: -1.24 kg, (CI: –2.22 to -0.26). It should be noted however that this study was funded by the International Life Sciences Institute, which includes Coca-Cola, PepsiCo and other large food and beverage companies.

In the second meta-analysis by Azad et al [2], no statistically significant association was seen between non-nutritive sweeteners and BMI compared to controls (a placebo in two of the RCTs and water in the third) in the three included RCTs: –0.37 kg/m^2; (CI: –1.10 to 0.36). However, this meta-analysis did not make a comparison of ASBs with SSBs. Azad et al noted that weight differences between consumers of ASBs compared to controls tended to be stronger in RCTs with industry sponsorship of the research.

One meta-analysis focused on the association between consumption of ASBs specifically and obesity [3]. Only three studies (one cross-sectional and two cohort studies) were included. The pooled risk ratio (RR) of obesity in patients consuming ASBs was 1.59 (CI: 1.22 to 2.08), indicating that patients who consumed ASBs were at greater risk of developing obesity than those who did not. But again, no direct comparison was made with SSBs.

The studies included in all three of these meta-analyses suffer from a number of limitations. For the cohort studies, the most important in this context is reverse causality – people who are overweight or have a higher risk of disease may switch from SSBs to ASBs to improve their diet. This may explain the positive association between ASB consumption and BMI seen in cohort studies in two of these meta-analyses. So should we just focus on the results from the RCTs? The limited results included in meta-analyses so far show mixed results for association between non-nutritive sweeteners and body weight. Additionally, a review focused on the relationship between research outcomes and study sponsorship (and other sources of bias) in studies looking at ASBs and weight outcomes concluded that industry

sponsored reviews were more likely to have favourable results (3/4) than non-industry sponsored reviews (1/23), RR: 17.25 (CI: 2.34 to 127.29) [4]. Clearly more non-industry funded RCTs focusing on the effect of ASBs on weight are needed, particularly including comparison with SSBs – and industry-funded work should be treated with substantial scepticism.

Association of ASBs with chronic disease outcomes

What about research which is focused on longer term chronic disease outcomes? These reviews are limited to cross-sectional and prospective cohort studies due to the necessary time restrictions on RCTs. Narain et al (2017) found that high compared to low consumption of ASBs was associated with metabolic syndrome in cross-sectional (two studies, RR 2.45; (CI: 1.15 to 5.14)) and prospective studies (three studies, RR 1.32, (CI: 1.21 to 1.44)) [5].

Imamura et al (2016) conducted a meta-analysis using data from 10 cohort studies and found one serving per day higher consumption of ASBs was associated with a higher incidence of diabetes: 25% (CI: 18% to 33%) before adjustment for adiposity and 8% (CI: 2% to 15%) after adjustment. An earlier linear dose-response meta-analysis on four cohort studies of the association between ASBs and type 2 diabetes gave a pooled estimate of 1.13 (CI: 1.02, 1.25) per 330ml daily ASB consumption [6].

For associations between ASB consumption and hypertension, four prospective cohort studies were included in the reported meta-analysis [7]. The pooled RRs were 1.14 (CI: 1.10 to 1.18) for highest versus lowest consumption of ASBs and 1.09 (CI: 1.06 to 1.11) for every additional one serving per day increase in ASB consumption. Similar results were seen in an earlier meta-analysis of four studies (three cohort and one cross-sectional studies), the RR for hypertension in patients consuming ASBs was 1.15 (CI: 1.11 to 1.19) compared to patients not consuming ASBs [8].

In addition to the weight outcome discussed above, Azad et al (2017) found that consumption of non-nutritive sweeteners, in cohort studies, was associated with higher incidence of hypertension, metabolic syndrome, type 2 diabetes and cardiovascular events (excluding coronary heart disease) for the highest versus lowest quantiles of non-nutritive sweetener intake [2].

The same limitations of prospective cohort studies as discussed above are relevant for these studies. Narain et al (2017) concluded that the association seen in their meta-analysis may be driven by the fact that ASB intake may serve as a surrogate for an unhealthy lifestyle or an adverse risk factor profile at baseline [5] (ie, ASB consumption is confounded by other lifestyle factors also associated with health and disease). Imamura et al (2016) noted that publication bias and residual confounding were likely to impact on their results. Greenwood et al (2014) suggested that due to less consistent trends seen with ASBs (compared to SSBs) that the association may be due to an alternative explanation, such as lifestyle factors or reverse causality [6].

So where does this leave us? ASBs may possibly be a useful tool to replace SSB consumption with for weight loss, but meta-analyses on RCTs are so far inconclusive. Prospective cohort studies suggest that increased consumption of ASBs may lead to an increased risk of being overweight, metabolic syndrome, diabetes, hypertension and potentially some cardiovascular events. However, these results should be treated with marked scepticism due to such issues as reverse causation.

Possible cancer risk of aspartame

Historically there has been some concern about the link between a commonly used artificial sweetener, aspartame and cancer risk. Since then the US National Cancer Institute conducted a cohort study of nearly half a million people, comparing the risk of specific cancers in those who consumed drinks containing aspartame with those who did not over a five year follow up. Higher levels of aspartame intake were not associated with the risk of overall hematopoietic cancer (RR for >600 mg/d, 0.98; (CI: 0.76 to 1.27)) or glioma (RR for >400 mg/d, 0.73; (CI: 0.46 to 1.15)) [9]. The European Food Safety Authority has concluded that aspartame was not a safety concern at the current aspartame exposure estimates or at the 'Acceptable Daily Intake' of 40 mg/kg body weight/day [10].

ASB consumption and dental health

Apart from weight gain and chronic disease, there are other health considerations around ASB consumption. The acidity of beverages is a primary factor in the development of dental erosion [11]. Many ASBs are harmful to teeth because of their acidity and chemical composition [12]. In a study of beverages sold at Australian schools, all SSBs, ASBs and sports drinks contained phosphoric acid, citric acid, sodium citrate or a combination of these food acids [11]. For example, Coca-Cola Zero, Sprite Zero [11], Diet Coca-Cola and Diet Pepsi-Co [13] are all acidic. There was no statistical difference in the erosive potential of sugared and non-sugared soft drinks [11]. Carbonated beverages had significantly lower pH (more acidic) and greater potential impact on dental erosion compared to milk drinks, suggesting that ASBs are harmful to oral health, and milk and water are preferable.

Conclusions

ASBs may possibly be the healthier choice over SSBs due to their lower energy content but the current evidence does not allow us to make firm conclusions about the effects on weight or the long term health effects of ASB consumption. There is no convincing evidence of increased cancer rates with ASBs, but it is not possible to rule out other health risks (e.g. heart disease, diabetes); modest increased risks may be due to reverse causation or confounding, or perhaps some 'true' increased risk. Furthermore, the 'actual' policy question of interest here may be a head-to-head comparison of the risk of ASBs and SSBs, if the use of such results is to consider the *relative* benefits and harms of shifting people from SSBs to ASBs, or SSBs to water.

We can say that ASBs do contribute to dental erosion and choosing water is most certainly the best beverage choice from an oral health perspective. These conclusions are in line with the recommendations in NZ Ministry of Health's most recent Eating and Activity Guidelines for New Zealand Adults which recommends plain water as the best option, but adds 'diet drinks in moderation are a better option than sugary drinks'

Initiatives that support healthier choices of water over SSBs and ASBs, such as increasing the number of drinking water fountains in public places, are the best policy response in the face of residual uncertainty on health risks of ASBs. To make firmer conclusions on ASBs and chronic disease outcomes we need an improved research base eg, more non-industry funded RCTs and meta-analyses on this topic.

* Note: We conducted a basic Medline search on 'Non-Nutritive Sweeteners' (mesh term) or 'artificially sweet$', 'artificial sweet$', 'ASB', 'low energy sweetener$' (key words), and limited this to meta-analyses in humans. This provided us with a snap-shot of high quality

evidence on the potential role of ASBs in disease.

References

1. Rogers P, Hogenkamp P, De Graaf C *et al.* (2016) Does low-energy sweetener consumption affect energy intake and body weight? A systematic review, including meta-analyses, of the evidence from human and animal studies. *International Journal of Obesity* 40, 381.
2. Azad MB, Abou-Setta AM, Chauhan BF *et al.* (2017) Nonnutritive sweeteners and cardiometabolic health: a systematic review and meta-analysis of randomized controlled trials and prospective cohort studies. *Canadian Medical Association Journal* 189, E929-E939.
3. Ruanpeng D, Thongprayoon C, Cheungpasitporn W *et al.* (2017) Sugar and artificially sweetened beverages linked to obesity: a systematic review and meta-analysis. *QJM: An International Journal of Medicine* 110, 513-520.
4. Mandrioli D, Kearns CE, Bero LA (2016) Relationship between research outcomes and risk of bias, study sponsorship, and author financial conflicts of interest in reviews of the effects of artificially sweetened beverages on weight outcomes: a systematic review of reviews. *PLoS ONE* 11, e0162198.
5. Narain A, Kwok CS, Mamas MA (2017) Soft drink intake and the risk of metabolic syndrome: A systematic review and meta-analysis. *International Journal of Clinical Practice* 71, e12927.
6. Greenwood D, Threapleton D, Evans C *et al.* (2014) Association between sugar-sweetened and artificially sweetened soft drinks and type 2 diabetes: systematic review and dose–response meta-analysis of prospective studies. *British Journal of Nutrition* 112, 725-734.
7. Kim Y, Je Y (2016) Prospective association of sugar-sweetened and artificially sweetened beverage intake with risk of hypertension. *Archives of cardiovascular diseases* 109, 242-253.
8. Cheungpasitporn W, Thongprayoon C, Edmonds PJ *et al.* (2015) Sugar and artificially sweetened soda consumption linked to hypertension: a systematic review and meta-analysis. *Clinical and Experimental Hypertension* 37, 587-593.
9. Lim U, Subar AF, Mouw T *et al.* (2006) Consumption of aspartame-containing beverages and incidence of hematopoietic and brain malignancies. *Cancer Epidemiology and Prevention Biomarkers* 15, 1654-1659.
10. Additives EPoF, Food NSat (2013) Scientific Opinion on the re-evaluation of aspartame (E 951) as a food additive. *EFSA Journal* 11, 3496.
11. von Fraunhofer JA, Rogers MM (2004) Dissolution of dental enamel in soft drinks. General dentistry 52: 308-312.
12. Reynolds E, Dashper S, Morgen M, et al. (2015) BRIEFING PAPER: The potential of sugar-free beverages, sugar-free confectionery and sports drinks to cause dental erosion. In: Australian Government Department of Industy and Science, Oral Healthcrc (eds).
13. Cochrane NJ, Cai F, Yuan Y *et al.* (2009) Erosive potential of beverages sold in Australian schools. *Aust Dent J* 54, 238-244; quiz 277.

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