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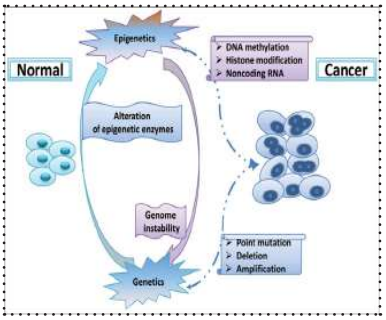
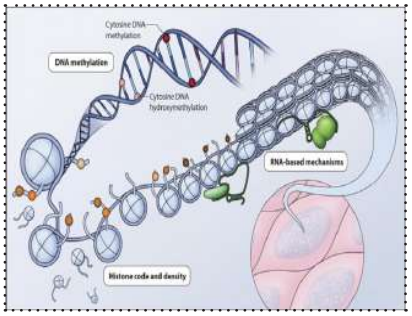
Consumption of hidden sugar in children

Page No. 10

Epigenetics in Human Health and Disease

Page No. 19





Brain Health

Page No. 23

GENERAL

Consumption of hidden sugar in children

SANJAY AGRAWAL

INTRODUCTION

There are two types of sugars in our diets: naturally occurring sugars and added sugars. Naturally occurring sugars are found naturally in foods such as fruits (fructose) and milk (lactose). Sugars added to foods during processing, preparation or at table (putting sugar in milk, tea, coffee or breakfast cereal), sweeten food and beverage taste, improve their palatability and are used to preserve foods and to confer property such as viscosity, texture and colour.

Added sugars can include natural sugars such as white sugar, brown sugar and honey as well as others that are chemically manufactured (such as high fructose corn syrup, corn syrup, dextrose, fructose, glucose, malt syrup, maltose, molasses, raw sugar, and sucrose.). Sugar-sweetened beverages (SSBs-flavoured milk, fruit juices, soft drinks) are the biggest source of added sugar in the diet. Other sources of added sugars are baked items (like cakes, muffins, cookies and pies), ice cream and desserts.

The American Heart Association recommends limiting added sugars to no more than 100 calories a day (6 teaspoons) for most women and no more than 150 calories a day (9 teaspoons) for most men. The 2015 World Health Organization guideline also advises that people should reduce the number of free sugars to <10% of their daily energy intake. (Ref.1). The World Health Organization further advises that a reduction to <5% of total energy intake per day would have additional benefits in reducing the risk of non-communicable diseases (specifically excess weight gain and dental caries) in adults and children. Five percent of total energy intake is equivalent to ≈25 g (≈6 teaspoons or ≈100 kcal) of sugar per day for an adult with a healthy body mass index (BMI).

The American Heart Association recommends that children, 2 years and older consume not more than 25 g of added sugars per day and no more than 8 oz of sugary drinks per week. Published data shows that these recommendations are not met in developed as well as developing countries (Ref.2).

HEALTH HAZARDS OF ADDED SUGARS

Children's diets are characterized by a low consumption of fruits and vegetables and an excessive consumption of products high in sugar, saturated fat and sodium (UNICEF, 2019). Sugar contributes to the daily energy intake, without providing additional nutritional value.

According to The American Heart Association (AHA) strong evidence supports the association of added sugars with increased cardiovascular disease risk in children through increased caloric intake, increased adiposity, and dyslipidaemia (Ref.3).

Excess consumption of sugary drinks, contributes to the high prevalence of childhood and adolescent obesity (Ref.4). Additionally, in randomized, controlled trials in which children and adolescents switched from SSBs to non-caloric beverages, reductions in weight were found, strengthening the likelihood that it is added sugars intake (at least in beverage form) that is responsible for increasing incidence of obesity in children. (Ref.5).

SSBs also increases the risk for dental decay (Ref.6), cardiovascular disease (Ref.3), hypertension (Ref.7), dyslipidaemia, (Ref.8), insulin resistance, (Ref.9), type 2 diabetes mellitus (Ref.10), fatty liver disease (Ref.11) and all-cause mortality (Ref.12).

Excessive consumption of sugar may also represent a threat to children's mental health as it has been linked to changes in neural systems, altered emotional processing, anxiety and depression (Ref.13).

PAEDIATRIC FORMULATIONS: HIDDEN SOURCE OF ADDED SUGARS

Apart from SSBs, paediatric formulations are an important source of added sugars. Sweetened oral medications are widely used for children to facilitate compliance. A variety of natural and artificial sweeteners are used in these drug formulations to augment the sweetness and thereby palatability of the product. Among the different dosage forms, liquid preparations are most popular and are easily accepted by both parents and children. Liquid preparations are preferred for oral administration in infants and children under 5 years of age.

The pharmaceutical industry uses a large quantity of sugars, especially sucrose, in the formulation of cough syrups, lozenges, gummies, oral-dispersible tablets, vitamin preparations, antibiotic syrups, and others. Sucrose is widely used because it is a low-cost, non-hygroscopic, easily processed substance and it also acts as a preservative, antioxidant, solvent, and thickening agent. (Ref.14). Fructose and glucose are added to increase bulk, palatability and, consequently, compliance (Ref.15). Acids are also added to medicines to maintain chemical

Dr. Sanjay Agrawal,
Leading Pharmaceutical Consultant and
Editor-in Chief of IJM Today
Post Graduation Diploma in Naturopathy and Yoga,
6/146, Malviya Nagar,
Jaipur -302017
Rajasthan

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Vol. 120 No. 09 & P : 10 - 11

stability, control tonicity and/or to ensure physiological compatibility. Because of these so called "inactive ingredients", many paediatric liquid medicines are characterized by having a high concentration of sugars, high titratable acidity and low pH. Because of these characteristics, various studies have pointed out the possible relationship between dental caries and frequent intake of liquid oral medicines (Ref.16). The presence of sucrose in medicines leads to pH drop of dental plaque, and it also acts as substrate for fermentation of oral microbiota, contributing to dental caries (Ref.17).

A study assessed the cariogenic and erosive potentials of 29 different paediatric antibiotic formulations. 83 % of formulations had high sucrose concentration, ranging from 26g% to about 100g%. Sucrose is considered the most carcinogenic dietary carbohydrate, because it is fermentable, and also serves as a substrate for the synthesis of extracellular and intracellular polysaccharides in dental plaque (Ref.18). The study concluded that many antibiotic formulations had high concentration of sugars, high titratable acidity, pH below the critical value and high viscosity which can be considered risk factors for dental caries and erosion, when consumed frequently. (Ref.19).

Because of the concern of sugar-containing paediatric products, pharmaceutical companies have introduced sugar-free medications into the market. Sugar-free medications are known to be as palatable and effective as sugar-containing medications and provide little or no calories. (Ref.20).

An in vitro study was carried out by Gaurao V.Mali, Arun S. Dodamani et al (Ref.21) to assess and compare the effect of conventional and sugar -free paediatric syrup formulations on primary tooth enamel hardness over a period of 14 days. 10 teeth in each group were dipped in 4 paediatric medicinal syrups (1 sugar-free and 3 conventional) for 1 min, thrice daily for 14 days and the enamel surface micro hardness was checked at baseline, 7th day and 14th day by Vickers hardness testing machine. The pH, titratable acidity and buffering capacity of the syrups were also assessed. ANOVA test indicated that the reduction in mean micro hardness was maximum in conventional syrup groups and least in sugar-free syrup on 7th and 14th day. **The study concluded that sugar- free paediatric medicines can be effective in reducing dental erosion and efforts should be made to incorporate sugar substitutes in formulation of paediatric medicines.**

A study (Ref.22) was conducted among 55 Indian paediatricians to assess their awareness and attitudes towards the use of liquid paediatric medicines and their relationship with dental caries and erosion. Majority of the respondents were unaware regarding the sweetening agents and acidity of prescribed products. Most of them neither recommended nor delivered oral hygiene instructions (OHI) after prescribing sweetened liquid medicaments.

CONCLUSION

As the medications prescribed to children are commonly available as drops and syrups in sweetened forms, it is important that health professionals, particularly paediatricians and paediatric dentists should make an effort to make the parents aware about the ill effects of these on children's teeth.

Despite the availability of many sugar substitutes, products in the market continue to include sweeteners with cariogenic potential. Sugar substitutes have been proved to be non-cariogenic and tooth- friendly. Though their use is minimal, efforts should be made to incorporate them in formulation of paediatric medicines by the pharmaceutical companies and health care professionals should start prescribing these sugar-free paediatric formulations, keeping in mind their benefits.

Alternative measures to improve the flavour or taste using techniques such as coating, complex formation, choice of vehicle, and adjustment of viscosity should be considered in the development of drug formulations. Paediatricians should be made aware of the potential harm to the teeth and general health of children due to sweetened drug formulations. Parents and children should be motivated to practice adequate oral hygiene measures.

REFERENCES

1. Guidelines: sugars intake for adults and children: WHO guidelines approved by the Guidelines Review Committee. 2015.
2. Afeiche, Koyratty, Wang, Jacquier, & Lê, Pediatric Obesity 2018; 13 (4), 204–212.
3. Vos MB, Kaar JL, Welsh JA, et al; Circulation. 2017;135(19):e1017–e1034.
4. Luger M, Lafontan M,et al. Obes Facts 2017;10(6):674–693.
5. De Ruyter JC, Olthof MR, Seidell JC, Katan MB. N Engl J Med. 2012; 367:1397–1406.
6. Moynihan P, Petersen PE. Public Health Nutr. 2004;7(1A):201–226.
7. Chen L, Caballero B, Mitchell DC, et al. Circulation. 2010;121(22):2398–2406.
8. Lee AK, Binongo JN, Chowdhury R, et al. J Am Heart Assoc. 2014;3(1):e000615.
9. Wang JW, Mark S, Henderson M, et al. Pediatr Obes. 2013;8(4):284–293.
10. Malik VS, Popkin BM, Bray GA, et al. Diabetes Care. 2010;33(11):2477–2483.
11. O'Sullivan TA, Oddy WH, Bremner AP, et al. J Pediatr Gastroenterol Nutr. 2014;58(5):624–631.
12. Shah NS, Leonard D, Finley CE, et al. Am J Med. 2018;131(1):48–55.
13. Jacques et al., Neuroscience & Biobehavioral Reviews, 2019; 103:178–199.
14. Bigeard L. Dent Clin North Am 2000;44:443.
15. Kenny DJ, Somaya P. J Can Dent Assoc 1989; 55(1): 43-6.
16. Neves BG, Farah A, Lucas E, de Sousa VP, Maia LC. Dent Health 2010; 27(1): 46-51.
17. Rekola M. Caries Res 1989; 23(6): 412-6.
18. Bowen WH. Crit Rev Oral Biol Med 2002; 13(2): 126-31.
19. Ana Carolina Valinoti , Luiz Carlos da Costa Jr. et al.The Open Dentistry Journal, 2016, 10, 420-430.
20.). Peres KG, Oliveira CT, Peres MA,et al. Rev Saude Publica. 2005;39:486–9.
21. J Indian Soc Pedod Prev Dent 2015;33:331-6.
22. S.V.S.G. Nirmala, Vimala Devi Popuri et al. Journal of International Society of Preventive and Community Dentistry January-February 2015, Vol. 5, No. 1;35-39.

mRNA - Therapeutic Considerations and Challenges - Part IV

JAYANTHI A

GOOD MANUFACTURING PRACTICE PRODUCTION

mRNA is produced by in vitro reactions with recombinant enzymes, ribonucleotide triphosphates (NTPs) and a DNA template; thus, it is rapid and relatively simple to produce in comparison with traditional protein subunit and live or inactivated virus vaccine production platforms. Its reaction yield and simplicity make rapid mRNA production possible in a small GMP facility footprint. The manufacturing process is sequence-independent and is primarily dictated by the length of the RNA, the nucleotide and capping chemistry and the purification of the product. However, it is possible that certain sequence properties such as extreme length may present difficulties (D.W., unpublished observations). According to current experience, the process can be standardized to produce any encoded protein immunogen, making it particularly suitable for rapid response to emerging infectious diseases.

All enzymes and reaction components required for the GMP production of mRNA can be obtained from commercial suppliers as synthesized chemicals or bacterially expressed, animal component-free reagents. Thhis helps avoiding safety concerns surrounding the adventitious agents that plague cell-culture-based vaccine manufacture. All the components, such as plasmid DNA, phage polymerases, capping enzymes and NTPs, are readily available as GMP-grade traceable components. However, some of these are currently available at only limited scale or high cost. As mRNA therapeutics move towards commercialization and the scale of production increases, more economical options may become accessible for GMP source materials.

GMP production of mRNA begins with DNA template production followed by enzymatic IVT and follows the same multistep protocol that is used for research scale synthesis, with added controls to ensure the safety and potency of the product. Depending on the specific mRNA construct and chemistry, the protocol may be modified slightly from what is described here to accommodate modified nucleosides, capping strategies or template removal. To initiate the production process, template plasmid DNA produced in Escherichia coli is linearized using a restriction enzyme to allow synthesis of runoff transcripts with a poly(A) tract at the 3′ end. Next, the mRNA is synthesized from NTPs by a DNA-dependent RNA polymerase from bacteriophage (such as T7, SP6, or T3). The template DNA is then degraded by incubation with DNase. Finally, the mRNA is enzymatically or chemically capped to enable efficient translation in vivo. mRNA synthesis is highly productive, yielding in excess of 2 g l^{-1} of full-length mRNA in multi-gram scale reactions under optimized conditions.

Once the mRNA is synthesized, it is processed though several purification steps to remove reaction components, including enzymes, free nucleotides, residual DNA and truncated RNA fragments. While LiCl precipitation is routinely used for laboratory-scale preparation, purification at the clinical scale utilizes derivatized microbeads in batch or column formats, which are easier to utilize at large scale. For some mRNA platforms, removal of dsRNA and other contaminants is critical for the potency of the final product, as it is a potent inducer of interferon-dependent translation inhibition. This has been accomplished by reverse-phase FPLC at the laboratory scale, and scalable aqueous purification approaches are being investigated. After mRNA is purified, it is exchanged into a final storage buffer and sterile-filtered for subsequent filling into vials for clinical use. RNA is susceptible to degradation by both enzymatic and chemical pathways. Formulation buffers are tested to ensure that they are free of contaminating RNases and may contain buffer components, such as antioxidants and chelators, which minimize the effects of reactive oxygen species and divalent metal ions that lead to mRNA instability.

Pharmaceutical formulation of mRNAs is an active area of development. Although most products for early phase studies are stored frozen (−70 °C), efforts to develop formulations that are stable at higher temperatures more suitable for vaccine distribution are continuing. Published reports suggest that stable refrigerated or room temperature formulations can be made. The RNActive platform was reported to be active after lyophilization and storage at 5–25 °C for 3 years and at 40 °C for 6 months. Another report demonstrated that freeze-dried naked mRNA is stable for at least for 10 months under refrigerated conditions. The stability of mRNA products might also be improved by packaging within nanoparticles or by co-formulation with RNase inhibitors. For lipid-encapsulated mRNA, at least 6 months of stability has been observed (Arbutus Biopharma, personal communication), but longer-term storage of such mRNA–lipid complexes in an unfrozen form has not yet been reported.

Ms. A.Jayanthi,
Nursing Tutor,
Nandha College of Nursing,
Erode - 52.

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