obesityreviews

Volume 10 Supplement 1 MARCH 2009

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Obesity Reviews is covered by the Science Citation Index published by the Institute for Scientific Information. The Journal is also covered by EMBASE/Excerpta Medica, Current contents/Clinical Medicine, SciSearch, Research Alert, and CINAHL.
Typeset by SNP Best-set Typesetter Ltd, Hong Kong

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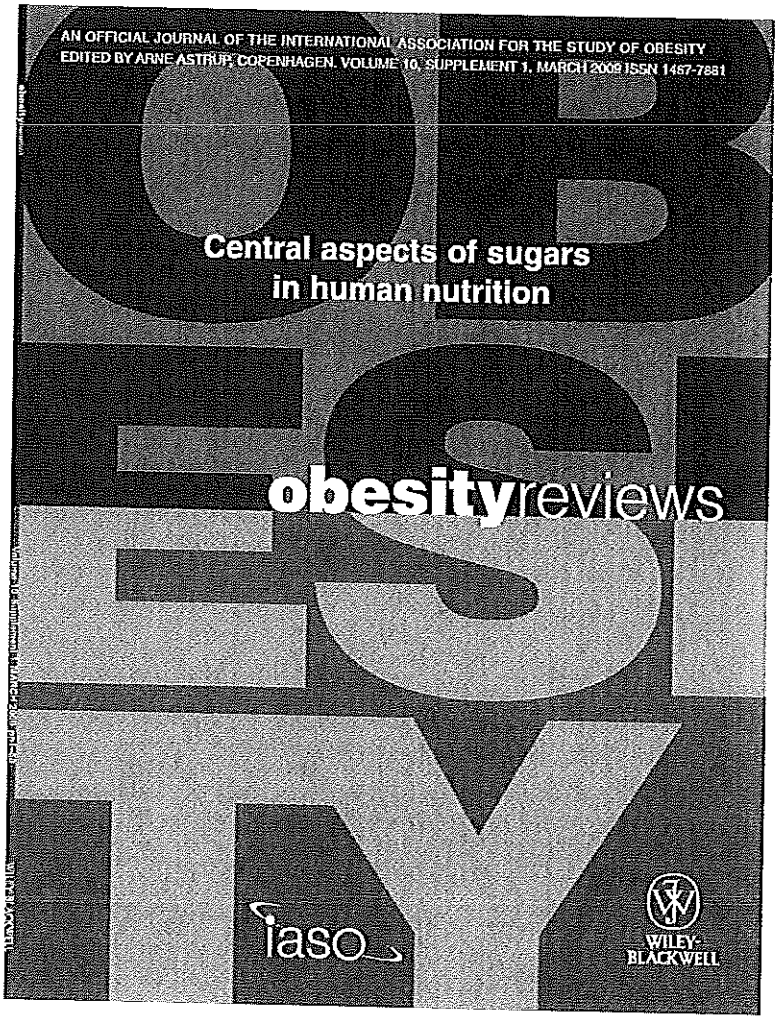

Overview

Summary and general conclusions/outcomes on the role and fate of sugars in human nutrition and health

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Received 30 October 2008; accepted 18 November 2008

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obesity reviews (2009) **10 (Suppl. 1)**, 55–58

A scientific expert workshop was organized to review the controversial aspects of the role of sugars in relation to human health (see paper by Palou *et al.* in this issue (1)). Particular attention was paid to the quality of the scientific evidence and to identifying areas where further research is required. Consideration was given to the following topics covering potential effects of dietary sugars on (i) overweight and obesity (see paper by van Baak and Astrup in this issue (2)); (ii) insulin resistance and diabetes (see paper by Laville and Nazare in this issue (3)); (iii) dental caries (see paper by Anderson *et al.* in this issue (4)) and (iv) micronutrient dilution (see paper by Livingstone and Rennie in this issue (5)).

The term 'sugars' generally refers to monosaccharides and disaccharides present from whatever source in a food excluding polyols (sugar alcohols), and was also the definition adopted for the purposes of this exercise.

The working method adopted was to discuss review papers prepared prior to the meeting and to assess the evidence according to guidelines recommended by the World Health Organization (WHO) in order to establish relationships between food and health. According to the WHO expert group, there is convincing evidence when consistent associations between exposure and disease have been found in epidemiological studies; when the relevance is estimated through the availability of a substantial number of studies – including prospective observational studies and, where relevant, randomized controlled trials of sufficient size, duration and quality – showing consistent effects; and when the associations have biological plausibility (6).

Sugars in overweight and obesity

The main conclusions on this topic are:

1. Epidemiological studies and randomized controlled trials (RCT) show fairly consistent inverse associations between the carbohydrate and sugar content of the diet, and body weight and adiposity. The evidence can be considered probable when fat in the diet is replaced by carbohydrates – either in the form of sugars or complex carbohydrates; a small weight loss occurs owing to a decreased energy intake.

2. There is insufficient evidence that an exchange of sugar for non-sugar carbohydrates in the context of a reduced-fat *ad libitum* diet or energy-restricted diet results in greater weight reduction. Additional RCT, strictly controlling macronutrient ratios and fiber content, are necessary to definitively assess the effect of exchange of sugars for non-sugar carbohydrates on body-weight control.

3. There is concern regarding a possible relationship between a high consumption of sugar-sweetened beverages (SSB) (including juices and nectars) and obesity, especially in children and young adults. This is suggested from cross-sectional data as well as cohort studies, showing that there is a possible association between SSB consumption and excess body weight. One underlying hypothesis is that the sugar calories in liquids have little effect on satiety and therefore easily lead to over-consumption although SSB consumption may also represent a marker of a particular lifestyle.

4. A limited number of RCT have compared changes in body weight when SSB are replaced with artificially sweetened drinks, but the results are equivocal. More RCT of sufficient size and duration would be required in this area to support the data from epidemiological studies.

5. There is a clear need for more RCT of sufficient size and duration to compare effects of liquid vs. solid sugars on satiety, energy intake, compensation responses and other functions related with body-weight control.

6. There is currently no evidence that an *ad libitum* diet with a low glycaemic index causes more weight loss than a diet with a high glycaemic index when total carbohydrate intake is not different. There is some limited evidence from randomized controlled trials that *ad libitum* and moderately energy-restricted diets with a low glycaemic load are associated with modest body-weight loss compared with diets with a high glycaemic load. Whether or not there is a specific effect of glycaemic load, or of total amount of carbohydrate, needs to be elucidated.

Sugars in insulin resistance and diabetes

It was judged that there is insufficient evidence to demonstrate an association between dietary intake of sugars and the development of insulin resistance and type 2 diabetes from human studies. It was noted that current dietary recommendations for the management of type 1 and type 2 diabetes do not specify restriction of sugar intake but focus on weight management and the pattern of total carbohydrate intake throughout the day to avoid large fluctuations in blood glucose levels.

Impact of many dietary and lifestyle factors such as physical activity, excessive calorie intake and weight gain has to be taken into account. Obesity and low physical activity are causally related to the development of insulin resistance and its progression towards type 2 diabetes. There is convincing evidence from RCT that weight loss and physical activity are beneficial in improving insulin sensitivity and preventing type 2 diabetes.

There is uncertainty about the long-term effects of fructose on insulin sensitivity and associated disorders compared with other sugars. The evidence is insufficient to support substitution of sucrose by fructose. Consideration should be given to assessing the potential impact on health of replacing sugar by other food components.

More studies are needed in order to determine the impact of strict restriction of simple carbohydrates intake on

glucose and insulin metabolism, and weight reduction in order to make dietary recommendations to limit the risk of diabetes.

Sugars in dental caries

Although it is generally agreed that fermentable carbohydrates are required for causation of dental caries, there is still ongoing debate of the exact role of dietary sugars in the modern society. This interrelation is influenced by a large number of factors of which an important one is the widespread use of fluoridated toothpaste. This has weakened the relationship and has reduced the impact of sugars on dental caries on a population level.

A systematic review of the literature was conducted to assess the relationship between quantity and pattern of sucrose intake and dental caries in children and young adults. The analysis showed that there is no clear relationship of quantity of sugar used to dental caries, while there is evidence for a relationship between frequency of sugar consumption and dental caries.

Future research should focus on the role of sugars in relation to dental caries taking into account lifestyle factors and the way sugar is consumed within the diet in the modern society and in different age groups. The interaction of diet with preventive methods, in particular fluoride, warrants further studies. Although we accept that given the length of time for caries to manifest and the complexity of the disease it is difficult to conduct RCT, it is important that well-designed studies are undertaken.

Sugars and micronutrient dilution

Debates about the role of added sugars in promoting micronutrient dilution have been longstanding. The overall conclusion to emerge from the existing evidence, based mainly on cross-sectional observational studies, is that associations between reported intakes of added sugars and intakes of micronutrients are inconsistent and often non linear, both across and within age groups, and between the genders. In the context of intake of a diet with appropriate energy it appears that the consumption of a wide range of added sugar is compatible with an adequate micronutrient intake; if a nutrient displacement effect does exist, a high consumption of added sugar does not necessarily compromise overall micronutrient intakes and similarly, consuming less added sugar is no guarantee that micronutrient intakes will be optimized.

The observed associations between added sugars and micronutrient intake have been heavily contingent on both the definition of sugars chosen and the analytical approach used for adjusting for differences in reported energy intake. These issues have been further compounded by misreporting of food intake of unknown direction and magnitude and the cut-offs used to determine 'inadequate' micronutrient intakes which vary over time and between studies and countries.

Recommendations for future research

Most information about the relationship between dietary carbohydrates/sugars and health comes from observational epidemiological studies that cannot prove causality and in which it is conceivable that, at least in part, carbohydrate in diets simply act as a marker of some other factors. There is in the field of RCT a clear need for studies of sufficient size and duration to contrasts the conclusions of epidemiological studies.

The evaluation of the effects (risks and benefits) of food on health is usually limited to only one potential target (or a few of them) for reasons of simplicity, but ideally all effects should be considered. Future studies addressing the integral role of sugars on human health should consider altogether the different targets (metabolic-obesity-insulin, energy/nutrient balance, dental caries) in long-term circumstances. Moreover, because specific carbohydrates, as other dietary chemicals, can entail both health benefits and risks, there is the need to obtain more complete biomarker profiles, rather than focusing on individual biomarkers or end-points. Approaches involving the use of post-genomic technologies (nutrigenomics) may be particularly useful in this context.

Specific effects of carbohydrates on regulatory circuitries controlling physiological responses and gene expression are progressively unveiled and need to be understood at the molecular level. The elucidation of the mechanisms of action might initially be performed using homogeneous animal models and subsequently be translated to, and analysed, in human situation. For instance, the increasing incidence of obesity and related diseases worldwide is nowadays enhancing an intensive study of the role of carbohydrates as potential regulators of energy balance (e.g. by regulating appetite and/or energy expenditure) or other processes specifically involved in obesity development, where specific cause–effects and mechanisms behind can be identified for defined chemical species and combinations.

All in all, it is recognized that new studies are required to help setting up more precise figures for sugar and carbohydrate intake recommendations.

Conflict of Interest Statement

T. Sanders has acted as a paid consultant to aspartame advisory service to Beneo T in respect of artificial sweeteners and as an advisor to the Breakfast Cereals Information Services; he has chaired Cadbury PLC Global Nutrition Advisory Board and has served as a member of the Scientific Advisory Committee on the

Malaysian Palm Oil Board and of the Global Dairy Platform. B. Livingstone has received a grant from Unilever; M. van Baak is recipient of research grants and honoraria as speaker from a number of Dutch and international companies and has no conflict of interest related to sugar.

M. Laville has received speaker fees from Benjamin Delessert Institute and from the European Scientific Workshop on Sugars. L. Arola, M.L. Bonet, N. Delzenne, C. Gómez-Candela, M.S. Duggal, A. Huyghebaert, A. Palou, C. Picó, G. Schaafsma, P. Lingström, C. van Loveren and E.M. van Schothorst have no conflict of interest to declare.

Acknowledgements

The funding for the organization of the scientific workshop was provided by an unrestricted grant from the Asociación General de Fabricantes de Azúcar de España (AGFAE) and the Comité Européen des Fabricants de Sucre (CEFS).

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