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Original Research Article

Assessment of the use of low-calorie sweeteners amongst Indian population and their awareness about their adverse effects

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ABSTRACT

Introduction: Obesity is one of the leading causes for morbidity and mortality worldwide and various countermeasures to tackle this global malice have been implemented, one of these being low-calorie sweeteners (LCS). However, unbeknownst to many, habitual use of such sweeteners could potentially have several detrimental effects on health of the consumer. The present research was undertaken to assess the awareness about these adverse effects in Indian population.

Materials and Methods: An online questionnaire-based survey was carried out on a sample size comprising of 607 individuals of Indian nationality. The questionnaire comprised of 18 closed-ended questions pertaining to use of LCS and awareness about their adverse effects.

Results: While majority of respondents declared that they added sugar in their food/beverages regularly, 51.65% of respondents preferred 'Diet/Low calorie' products containing LCS in the market over sugar-added products. Sucralose was found to be most popular amongst various commercially available artificial sweeteners. There was a statistically significant difference seen for the responses pertaining to awareness about artificial sweeteners and their uses or benefits between various educational groups ($p<0.01$, 0.05) wherein respondents that were graduates or above had greater cognizance about the subject as compared to respondents with lower educational qualification.

Conclusion: Although artificial sweeteners are presently being marketed widely as health substitutes, data regarding the possible adverse effects associated with their frequent use is still limited. Case-control studies are required to establish causal relationship between various artificial sweeteners and elicited adverse effects. The general population needs to be cautioned against unwarranted and injudicious use of LCS.

1. Introduction

Obesity is an adverse condition wherein there is excess of body adiposity that has numerous grave consequences on health. Practically, it is defined in terms of abnormally high body weight or a high Body Mass Index (BMI).[1] Excess body weight is the sixth most important risk factor contributing to the overall burden of disease worldwide.[2] The risks of diabetes, hypertension, and dyslipidemia increase from a BMI of about 21·0 kg per square meter area of the body thereby reducing life expectancy and greatly increasing the health and societal economic burden.[3] The number of deaths per year attributable to obesity is roughly 0.3 million in the USA,[4] where obesity is set to overtake smoking in 2005 as the main preventable cause of illness and premature death.[5] WHO describes obesity as one of the most blatantly visible, yet most neglected, public-health problems that threatens to overwhelm both more and less developed countries.[6] A recent systematic review of longitudinal studies on obesity has inferred that obesity leads to depression over time through various mechanisms such as negative effect on self-image, inflammation, HPA-

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axis dysregulation and physical pain.[7]

WHO guidelines have recommended that the dietary energy provided by added sugars should be restricted to less than 10% of the total amount thereby advising the public to choose foods and beverages that would keep their intake of added sugars in check.[8] The mean intake of added sugar has been estimated to constitute approximately 15.8% of the total energy intake, 47% of which are accounted for by non-diet soft drinks.[9] A review of literature on obesity has provided evidence linking the intake of sweetened beverages with obesity.[10] The various mechanisms suggested for this association include less physiological satiation after consumption of calorically sweetened beverages and less thermogenesis, both of which would result in increased daily caloric intake and inadequate compensation of energy intake[11] [Figure 1]. To tackle the global concern of obesity, there has been a rise in consumption of Low-calorie sweeteners (LCS) that have been approved by FDA such as Saccharine, Acesulfame, Aspartame, Neotame, Sucralose and Stevie.[12] The American Heart Association (AHA) and American Diabetes Association (ADA) have given a cautious nod to the use of artificial sweeteners in place of sugar to combat obesity, metabolic syndrome, and diabetes, and all risk factors for heart diseases.[13]

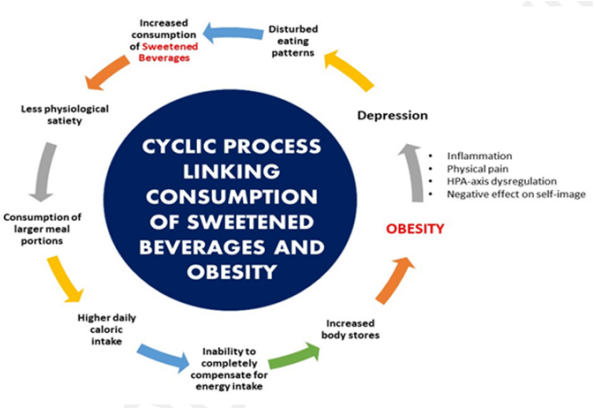

Fig. 1: Cyclic association of consumption of sweetened beverages, obesity and depression.

As indeed, even these so-called LCS are not free of side effects. Overstimulation of sugar receptors from their frequent use may develop tolerance for more complex tastes thereby resulting in shunning of healthy, filling, and highly nutritious foods for more artificially flavored foods with less nutritional value.[14] Also, these sweeteners have been reported to be addictive with increased risk for metabolic syndrome and type 2 diabetes.[15,16] Despite being a natural sugar substitute, Stevia is contraindicated in people with low blood pressure, pregnancy, breast-feeding woman and people allergic to ragweed.[17] Use of LCS is being widely promoted through various media with little light being shed upon their possible detrimental effects on health. The scientific literature hinting on the side effects of consumption of artificial sweeteners are also limited. Thus, the present questionnaire-based survey was conducted amongst Indian population aiming to assess the current demographics associated with the use of artificial sweeteners while objectively gauging their knowledge about artificial sweeteners and the side effects associated with their consumption.

2. Materials and Methods

2.1. Study Design

A self-constructed questionnaire of 18 closed-ended questions relating to awareness about LCS and their consumption (attached as annexure 1) was pilot tested for face and content validity with a team of four researchers, including a public health expert. A total of 20 respondents matched for demographic variables were included in the pilot study, the data of which were not included in the final study. Before commencement of the questionnaire, a screening question was incorporated to obtain the participant's informed consent. Following the initial pilot, on subjection to Cronbach's alpha analysis of the questions, the resultant value of 0.815 indicated adequate internal consistency and validity. Shortcomings in construction of questionnaire as discerned by the pilot study were amended.

The sample size was determined using a single proportion formula and a sample size of n=600 respondents was determined to be appropriate for the completion of the study. The respondents were sampled by utilizing a purposive sampling method. Participants above 18 years were included in the study whereas those providing responses to less than 10 questions or ambiguous data were excluded. The process of inclusion of respondents in the study has been delineated in Figure 2. Ethical clearance for the conduction of research was obtained from Institutional Ethical Committee. The survey was conducted by means of QuestionPro (Survey Analytics LLC, USA) software and the obtained results were compiled in a datasheet. (MS Office Excel, 2016, Microsoft Redmond Campus, Redmond, Washington, United States).

2.2. Statistical procedures

Data was subjected to statistical analysis using Statistical package for social sciences (SPSS v 26.0, IBM). Descriptive statistics like frequencies and percentage for categorical data, Mean & SD for numerical data has been depicted. Comparison of frequencies of categories of variables with groups was done using chi square test. For all the statistical tests, $p<0.05$ was considered to be statistically significant, keeping α error at 5% and β error at 20%, thus giving a power to the study as 80%.

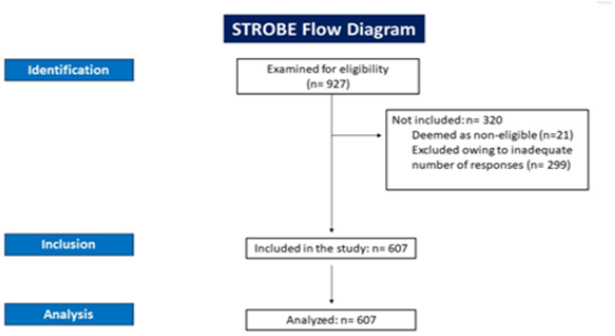

Fig. 2: STROBE Diagram illustrating the flow of inclusion of respondents for analysis

3. Results

3.1. Characteristics of respondents

The total number of respondents (n=607) comprised of 213 females and 394 males of age ranging from 18-70 years with a mean age of 30.53 years. The mean BMI of all the respondents was observed to be 21.23 with a standard deviation of 5.28. According to the criterion of education, 87.3% of respondents had completed their graduation while the groups of respondents with high secondary and university education included a similar number of members. The majority of respondents were from urban areas wherein 77.4% of respondents had visited a dentist at least once before. They declared good (41.13%) or average income (41.78%).

3.2. Awareness about LCS and their consumption

The majority of respondents declared that they added sugar in their food/beverages regularly (59.5%) or occasionally (37.7%). A small percentage (2.5%) of those surveyed avoided inclusion of sugar in their diet. With the exception of a tiny fraction of respondents, 91.1%. There was a statistically significant difference seen for the responses pertaining to awareness about artificial sweeteners and their uses or benefits between various educational groups ($p<0.01$, 0.05) wherein respondents that were graduates or above had greater cognizance about the subject as compared to respondents with lower educational qualification. Additionally, there was a statistically significant difference seen for the frequencies between the groups ($p<0.01$, 0.05) with higher frequency of responses from respondents belonging to 'Overweight' (>25.00) category of BMI having more familiarity with the LCS as compared to the 'Normal' (18.5-24.9) and 'Underweight' (<18.5) groups. Of these, Sucralose was found to be most popular, followed by Saccharin, Aspartame and Stevia[Figure 3]. 66.9% of respondents opined that use of artificial sweeteners is a better dietary option rather than sugar while 51.65% preferred 'Diet/Low calorie' products containing LCS in the market over sugar-added products (37.62%).

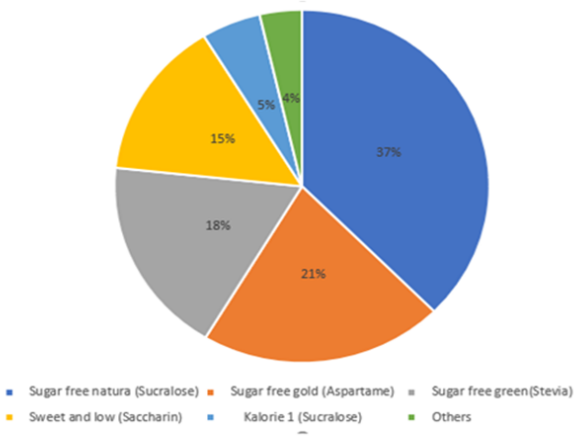

Fig. 3: Percentage of respondents using various types of LCS

About 35.3% (214) used LCS on a daily basis and similar number of respondents (37.2%) used them occasionally. It was alarming that 50.2% respondents that consumed LCS did not consult a physician or nutritionist before. This could largely be attributed to frank marketing of artificial sweeteners by the manufacturers and their over-the-counter availability. Nearly half of respondents (45.6%) found artificial sweeteners readily available when they went to restaurants for dining.

3.3. Responses related to adverse effects of LCS

Being marketed as 'health substitutes', the general population unhesitatingly add artificial sweeteners to their foods/beverages without any consideration of their possible adverse effects. With a significant portion of population being unaware about this issue, only 34.65% of respondents were aware or cautioned about the possible side effects of long-term consumption of artificial sweeteners. Various side effects as perceived or experienced by the respondents consuming LCS have been denoted in **[Table 1]**

Although there was no significant difference noted for a particular type of sweetener being used with an individual or a group of side effects. Furthermore, the study presents a limitation wherein the experienced adverse effects declared by the respondents could not be entirely attributed to the use of LCS. Such an association could only be confirmed by means of a prospective controlled trial.

4. Discussion

Owing to the sedentary lifestyle along with marked increase in consumption fast food and sweetened beverages by majority of population, obesity is on the rise throughout the world. In line with the rise in prevalence of obesity,

Table 1: Number of responses for elicited side effects by respondents

Perceived Side Effects	No.of respondents	Percentage
None	143	27.03%
Headache	82	15.50%
High blood pressure	32	6.14%
High sugar glucose	30	5.58%
Blurred vision	27	5.10%
Seizure	14	2.55%
Rashes	11	2.08%
Dizziness	37	6.99%
Anxiety	37	6.99%
Depression	32	5.95%
Fatigue	36	6.90%
Insomnia	30	5.67%
Numbness	14	2.65%
Others	4	0.85%

numerous weight reduction strategies have been adopted by the affected individuals in order to keep their weight under check. Since sugar-sweetened beverages have been demonstrated to be a major component of daily caloric intake and thus, strongly associated with weight gain, use of LCS could definitely be an effective tool in weight maintenance plans.[18] LCS have become a choice of management strategy to tackle the rising pandemic of obesity, wherein they are ubiquitously incorporated in numerous food products. However, the increased demand has led to competition and subsequent extensive marketing by various manufacturers.[19] of LCS which explain the high level of awareness about them in our results and their judicious use without recommendation by a physician. Another finding supported by our results is that a significant number of individuals prefer "sugar-free" or "diet" version of foods and beverages, leading to their overuse that is not only restricted to diabetic individuals but extends to involve general population, consumed by both lean and obese alike.

Presently, LCS have come into vogue of which Sucralose is most commonly used which is in accordance with the results of a recent systematic review on trends in the consumption of LCS conducted by Sylvetsky et al.[20] Another report has suggested that tabletop packets of Saccharin, primarily marketed as Sweet 'N' Low are the worldwide market leaders of sugar substitutes, however, a relatively lower fraction of population was found to be using Saccharin in our results. Concurrently, natural sweeteners such as Stevia or 'Sugarfree Green' are also gaining popularity owing to the present-day global emphasis on natural food products. Despite the FDA approval on six high-intensity sweeteners - saccharin, aspartame, acesulfame potassium (Ace-K), sucralose, neotame, and advantame as food additives.[21] they may not actually free of adverse effects that the consumers are not often cautioned about by the manufacturers.

Undoubtedly, artificial sweeteners are useful in controlling blood sugar levels in diabetics. However, their exact role is controversial when it comes to the subject of obesity.Under normal conditions, a sweet taste initiates insulin response which results in storage of blood glucose in the body tissues. However, since glucose levels do not increase on consumption of artificial sweeteners, it results in hypoglycemia and increased caloric intake. This would ultimately lead to increased body weight and obesity, which was proven through experimentation on rats.[22] Additionally, saccharin has been linked to obesity by means of its interference with bodily homeostatic mechanisms.[23] Results of a crossover design study have suggested that individuals with mood disorders could be sensitive to Aspartame and thus, should avoid its consumption.[24] Owing to their sweet taste, LCS stimulate G-protein-coupled subunit receptors - T1R2 and T1R3, that are present within the taste buds of the tongue. Stimulation of these receptors generates a sensation that mammals, in general, find rewarding subsequently leading to their over-consumption.[25]

Another concern that is invariably associated with any type of drug or food product is invocation of an allergic reaction. Aspartame may eventually break down into formic acid resulting in metabolic acidosis and is capable of causing hypersensitivity reactions such as hives and swelling in individuals that are sensitive to formaldehyde.[26] Another decomposition product of aspartame that has been suggested as the cause for allergic reactions is diketopiperazine.[27] Additionally, over-consumption of aspartame has also been linked to headaches or migraines and induction of seizures.[28].

The gravest consequence of consumption of artificial sweeteners can rightly be stated as development of cancer. Cyclamate was the first artificial sweetener to be banned due to risk of carcinoma. Systematic reviews on cancer risk associated with artificial sweeteners suggest that there is no definitive evidence that LCS increase the risk of cancer incidence.[29–31] However, certain studies have produced contradictory results wherein daily large doses of LCS consumption have been associated with bladder cancer.[32] Other significant correlations observed were those between LCS and laryngeal cancer and hematopoietic cancers such as leukemia or lymphoma.[33] Daily consumption of soft drinks with added LCS by pregnant women has been reported to increase likelihood of prematurity and development of asthma in children.[31]

The adverse effects of LCS may not only be limited to those on the consumer's health but also extend to involve the environment. Regular wastewater treatment procedures are unable to remove these non-nutritive sweeteners effectively from the discharged water. Significant concentrations of

LCS in widespread quantities have been detected in the environment.[34] This could point out towards the ensuing accumulation of LCS in the environment in line with the increase in their demand.

Our study, however, holds certain limitations wherein the adverse effects declared by the respondents could not be entirely attributed to the use of LCS which necessitates further experimental studies to determine the nature of cause-effect relationship precisely. Furthermore, the population in general belonged predominantly to above average socioeconomic classes. In a developing country such as India, wherein the lower socioeconomic classes constitute a significant portion of the population, our results may not accurately represent the national population.

5. Conclusion

Our study calls attention to be emphasized on possible adverse effects of LCS, particularly when consumed judiciously without any purpose. Further research in order to determine precise correlation of LCS consumption and prevalence of their associated side effects. Health authorities must strictly implement policies and promote awareness campaigns to prevent injudicious use of artificial sweeteners. Health care providers must meticulously discern the overall benefit of prescribing LCS after assessing purported beneficial effects versus their actual requirement and associated risks. Additionally, health care providers need to update themselves with evidence-based information pertaining to use of LCS and inform the patients as well.

6. Source of Funding

None.

7. Conflict of interest

None.

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