Open Access
Full Length Article

ORIGINAL ARTICLE

Effect of an Artificial Sweetener on Rat's Pancreas and Body Weight

Hina Kundi [1], Naureen Waseem [2], Maria Yousaf [3]

[1] Assistant Professor of Anatomy, Fazaia Medical College, Air University. Islamabad
[2] Assistant professor of Anatomy, Islam Medical and Dental College. Sialkot
[3] Assistant professor of Anatomy, Army Medical College, Rawalpindi

ABSTRACT

Objective: To observe the effects of an artificial sweetener on rat's pancreas and body weight.

Material and Methods: This Laboratory based randomized control trial was carried out at Anatomy department, Army Medical College Rawalpindi, in collaboration with NIH, Islamabad, from March to May 2014. Forty male and female Sprauge dawley rats were used in the experiment. Ten males and 10 female served as control group C and 10 males and 10 female served as an experimental group E (n = 20 animals in each group). The rats were randomly allocated by using a random selection table. Control group C was given normal diet for two months whereas experimental group E was provided artificial sweetener (sodium cyclamate) 60mg/kg/day through oral gavage tube for two months. Animals were weighed before and at the end of experiment. Pancreas were dissected out, examined and weighed. Histological sections of pancreas were studied under light microscope. Fatty infiltration was calculated in three slides per specimen. Results were analyzed on SPSS version 20.

Results: The pancreas of rats showed fatty infiltration and weight of animals were significantly higher in experimental group.(p-Value<0.001)

Conclusion: Artificial sweetener brings significant fatty infiltrations in rat's pancreas and also induces weight gain in animals.

Key words: Artificial sweetener, Fatty infiltration, Pancreas, Sodium cyclamate.

Author`s Contribution
[1]Conception, synthesis, planning of research and manuscript writing Interpretation and discussion
[2] Data analysis, interpretation and manuscript writing, [3] Active participation in data collection.

Address of Correspondence
Hina Kundi
Email: drhinazaid@gmail.com

Article info.
Received: September 20, 2017
Accepted: January 11, 2017

Cite this article. *Kundi H, Waseem N, Yousaf M. Effect of an Artificial Sweetener on Rat's Pancreas and body weight. JIMDC.2018; 7(2): 84-87*

Funding Source: *Nil*
Conflict of Interest: *Nil*

Introduction

Humans have a sweet tooth for deserts and sweet items. It is for this reason that such products are consumed much more than the body's nutritional requirement. Natural sugars and sweeteners are a part and parcel of human diet and having them in appropriate amount is very important as it may influence health.[1] Over the last few decades, a wide range of sweeteners has been introduced in market. [2] Among food additives, artificial sweeteners are considered most important as they are low in calories, intensely sweet and maintain the taste of sweet foods and drinks.[3]

The first generation sweeteners are saccharine, cyclamate and aspartame while acesulfame-K, sucralose, alitame and neotame are referred as second or new generation artificial sweeteners.[4] They bind with taste receptors and exceed sweetness of sucrose from 30 to

13000 times.[5] Artificial sweeteners are widely used in beverages, multivitamins, breakfast cereals, dairy products and pharmaceuticals. The safety for the consumption of products like artificial sweeteners, coloring, flavoring agents and preservatives is still controversial.[6] It is generally thought that artificial sweeteners are not harmful and are helpful in weight reduction but few recent studies showed alteration in glucose metabolism and appetite by the use of these sweeteners. There are various studies, which showed unfavorable metabolic effects, and included increase in weight, diabetes mellitus and other metabolic disorders.[7]

Sodium cyclamate is being used in several artificial sweetened foods, beverages, medicines and cosmetics since it is easily available and cheap.[8] Not much work has been done regarding its effect on histology of pancreas. A long-term study on primates showed alteration in blood glucose levels as well as histology of pancreas showed hyalinization of pancreatic islets of Langerhans.[9] A study conducted on children by giving them sodium cyclamate sweetened beverages showed no alteration in diet, hunger or body weight. The effects of sodium cyclamate on body weight and weight of pancreas have not been seen simultaneously. The rationale of current study was to identify the effects of sodium cyclamate on the body weight and weight of pancreas.

Material and Methods

This randomized control trial was carried out at the Anatomy department, Army Medical College Rawalpindi, in collaboration with NIH (National Institute of Health) Islamabad. The duration of study was three months from March 2014 to May 2014. Forty *Sprauge dawley* rats, both male and female, were used in the experiment.[1] Weight of the experimental animals was between 175gm to 205gms. They were kept in controlled environment of Animal house of NIH, Islamabad. Pelleted diet prepared in NIH was given to them for two months. Rats were randomly divided into two groups, each having equal number of male and female rats by using a random selection table. They were kept in separate cages to avoid pregnancy. Group C served as control group in which animals were given 1ml plain water with normal diet. Group E served as experimental group in which animals were given 60mg/kg body weight sodium cyclamate once daily orally for two months by a gavage tube.[10,11] After two months, the animals were weighed and dissected. Pancreas was removed and their weight was recorded. Specimens were fixed and three sections/specimen (intestine, middle and spleen region) were placed in tissue cassettes.[12] Automated processing of all the sections obtained was done. Sections were cut and stained with routine Hematoxylin and Eosin to observe the histology of pancreas. Four fields were selected per slide randomly and images were taken at 10X. Fatty infiltration in pancreas was observed. The fatty infiltration was scored as global score by adding the scores of (a) perilobular fat and (b) intralobular fat.[13] For perilobular fat, zero score was marked for no fat cells, score one was given to few fat cells and score two was assigned to more than 10 fat cells between two lobules. For intralobular fat zero score was given to no fat cells, one score was marked for few scattered fat cells and two score was given to numerous fat cells within lobules in the form of clusters of more than 10 cells. Global score was given by adding (a) and (b). Global score 0 to 2 indicate fatty infiltration. Global score 3 to 4 indicate fatty infiltration. Statistical package SPSS version 20 was used to analyze data. To find out intergroup differences, independent sample T test was applied on quantitative data and chi square was applied on qualitative data. P value < 0.05 was considered significant. Results were represented as mean ± standard deviation (mean ±SD) and number with percentages.

Results

At the start of study, weight of the experimental animals was between 175gm to 205gms and it was statistically non-significant between two groups. After two months, the mean change in weight of animals in control and experimental group was found be statistically significant with p value <0.001 (Table 1). Histologically the pancreas of group C showed normal architecture consisting of glandular parenchyma and stroma. There was a loose connective tissue capsule covering the gland. The glandular parenchyma was divided into irregular lobules by septa originating from the capsule. Lobules showed tubuloacinar gland consisting of pancreatic acinar cells and duct system. The small islets of Langerhans of variable sizes were scattered through the pancreatic parenchyma. (Figure 1A). The stroma comprising of large

Table 1: Comparison of weight and fatty infiltration in control and experimental groups (n=40)			
Variable	**Group C (n = 20)**	**Group E (n = 20)**	**P value**
	Mean±SD		
Animal weight (gms)	291.18±10.82	307.64±7.05	< 0.001*
	Number (%)		
Fatty infiltration			
Yes	0(0%)	6(30%)	0.020
No	20(100)	14(70)	

amount of loose connective tissue was present between each lobule containing arteries, vein, nerves, ducts and few fat cells. Fat cells present between lobules were considered as perilobular fatty infiltration. While the fat cells present in the lobule were considered as intralobular fatty infiltration. Perilobular fatty infiltration was present in 5 animals of control group, whereas intralobular fatty infiltrate was present in 2 animals of control group. Global scoring showed no fatty infiltration in any animal of control group. In experimental group E, perilobular fatty infiltration was found in 13 animals, whereas intralobular fatty infiltration was found in 9 animals. Global scoring showed that fatty infiltration was present in 6 (30%) rats, while it was absent in 14 (70%) rats. Frequency of fatty infiltration was significantly higher in experimental group E as compared to control group C (p = 0.020) (Figure 1B, Table 1).

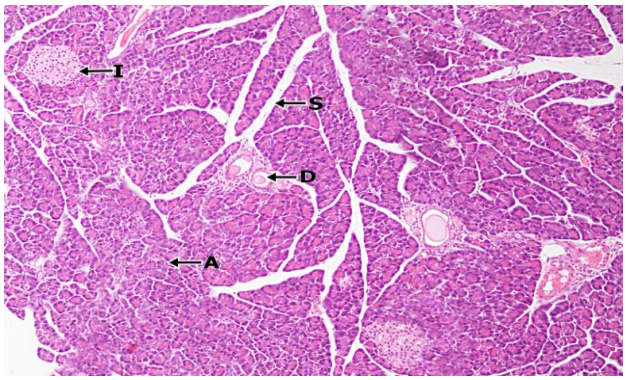

Figure 1 (A) Photomicrograph of histological section of pancreas of control group showing; pancreatic acinus (A), islets of Langerhans (I), duct (D) and connective tissue septa (S). [H&EX300]

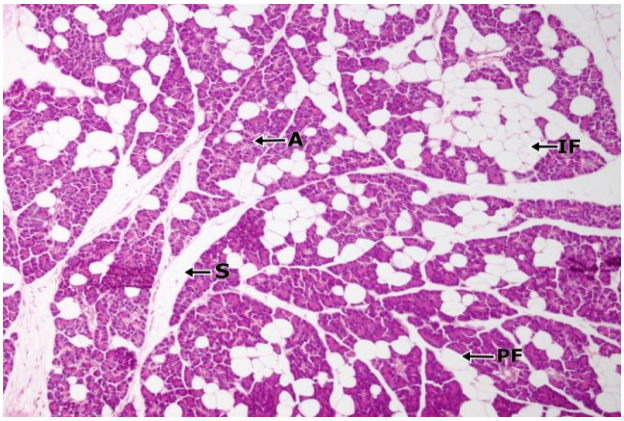

Figure 1 (B) Photomicrograph of histological section of pancreas of animal in experimental group showing; fatty infiltration with perilobular fat cells (PF), intralobular fat cells (IF), connective tissue septa (S) and acinus (A). [H&EX300]

Discussion

Sugar free food items are gaining a lot of attention these days for being low in calories but with sweet taste. It is for this reason many artificial sweeteners are being used by the food industry as a substitute of sugars. Diseases like hypertension, diabetes, obesity and other cardiovascular diseases are growing day by day. High sugar content in diet could be alarming to health.[14] Sugar sweetened beverages are considered to play a negative impact on weight and health. Non-caloric sweeteners are grabbing more attention in order to avoid the risks of these out comes. However evidences have proved that regular users of these non-caloric sweeteners may also be at a high risk of diseases like metabolic syndrome, diabetes mellitus, obesity and heart disease.[15]

The change in body weight of rats was statistically significant when both the groups were compared. It has been reported that artificial sweeteners may induce hunger and thus encourage food intake, which may affect the body weight.[16,17] Use of artificial sweeteners and weight gain are positively correlated in a prospective cohort study.[18] A review on artificial sweeteners suggested that non nutritive sweeteners intensify the appetite especially when it is taken with other non-caloric products. The reason being when artificial sweeteners are replaced by nutritive sweeteners they are unable to provide energy to the body which leads to increased hunger and appetite.[19] A perspective study carried out on

women showed that intake of artificial sweetener such as sodium cyclamate and saccharin for one year didn't help in weight reduction when compared with non user group. The study proved a negative correlation between long-term use of sodium cyclamate and weight reduction.[20]

The pancreases of experimental group showed significant fatty infiltration. Which has also caused increase in organ weights, as shown in previous study.[21] The results of the current study were in agreement with the findings of Gaujoux et al, reporting that increase in the body weight and obesity leads to increase in weight of abdominal organs and risk of morbidity.[13] In the current study, fatty infiltration also caused increase in weight of pancreas as well as of the animals. The mean weight of six cases with pancreatic fatty infiltration in experimental group was higher than that of six cases without fatty infiltration in control group. This lipomatosis of pancreas is directly related to increase in body weight.[22]

This study has shown that the artificial sweetener tends to increase body weight as well as induce fatty infiltration in pancreas, may thus induce obesity.

Conclusion

The use of artificial sweeteners like sodium cyclamate induces fatty infiltration in rat's pancreas and is also responsible for weight gain.

Future recommendations: The artificial sweeteners effects can also be seen in other organs like kidney and liver.

Acknowledgment: Special thanks to Dr Hussain Ali, Scientific officer animal house, National Institute of Health, for his support in animal handling and care.

References

1. Dell RB, Holleran S, Ramakrishnan R. Sample size determination. ILAR journal. 2002;43(4):207-13.
2. O'Donnell K, Kearsley M. Sweeteners and Sugar Alternatives in Food Technology. 2nd ed: Wiley Blackwell; 2012.137-163
3. Abhilash M, Paul MV, Varghese MV, Nair RH. Effect of long term intake of aspartame on antioxidant defense status in liver. Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association. 2011;49(6):1203-7.
4. Weihrauch MR, Diehl V. Artificial sweeteners--do they bear a carcinogenic risk? Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2004;15(10):1460-5.
5. Shastry CS, Yatheesh CK, Aswathanarayana BJ. Comparative evaluation of diabetogenic and mutagenic potential of artificial sweeteners aspartame, acesulfame-k and sucralose. Nitte University Journal of Health Science. 2012;2(3):80-4.
6. Soffritti M, Belpoggi F, Esposti DD, Lambertini L, Tibaldi E, Rigano A. First experimental demonstration of the multipotential carcinogenic effects of aspartame administered in the feed to Sprague-Dawley rats. Environmental Health Perspectives. 2006;114(3):379-85.
7. Brown RJ, Rother KI. Non-nutritive sweeteners and their role in the gastrointestinal tract. The Journal of clinical endocrinology and metabolism. 2012;97(8):2597-605.
8. O'Brien-Nabors L. Alternative Sweeteners, Third Edition, Revised and Expanded: Taylor & Francis; 2001.63-66
9. Takayama S, Renwick A, Johansson S, Thorgeirsson U, Tsutsumi M, Dalgard D, et al. Long-term toxicity and carcinogenicity study of cyclamate in nonhuman primates. Toxicological Sciences. 2000;53(1):33-9.
10. Reagan-Shaw S, Nihal M, Ahmad N. Dose translation from animal to human studies revisited. The FASEB journal. 2008;22(3):659-61.
11. Martins AT, SANTOS FdSd, Scannavino FLF, Pires JR, Zuza EP, Padovani Junior JA, et al. Effect of sodium cyclamate on the rat fetal exocrine pancreas: a karyometric and stereological study. International Journal of Morphology. 2010;28(3):899-904.
12. Farrokhi B, Rostamkhani F, Zahediasl S, Zardooz H. Effects of acute and chronic psychological stress on isolated islets' insulin release. 2012.11: 163-175
13. Gaujoux S, Cortes A, Couvelard A, Noullet S, Clavel L, Rebours V, et al. Fatty pancreas and increased body mass index are risk factors of pancreatic fistula after pancreaticoduodenectomy. Surgery. 2010;148(1):15-23.
14. Chattopadhyay S, Raychaudhuri U, Chakraborty R. Artificial sweeteners–a review. Journal of food science and technology. 2011:1-11.
15. Swithers SE. Artificial sweeteners produce the counterintuitive effect of inducing metabolic derangements. Trends in Endocrinology & Metabolism. 2013;24(9):431-41.
16. Fowler SP, Williams K, Resendez RG, Hunt KJ, Hazuda HP, Stern MP. Fueling the Obesity Epidemic? Artificially Sweetened Beverage Use and Long-term Weight Gain. Obesity. 2008;16(8):1894-900.
17. Kroger M, Meister K, Kava R. Low-calorie Sweeteners and Other Sugar Substitutes: A Review of the Safety Issues. Comprehensive reviews in food science and food safety. 2006;5(2):35-47.
18. Yang Q. Gain weight by "going diet?" Artificial sweeteners and the neurobiology of sugar cravings.
The Yale journal of biology and medicine. 2010;83(2):101-8.
19. Mattes RD, Popkin BM. Nonnutritive sweetener consumption in humans: effects on appetite and food intake and their putative mechanisms. The American journal of clinical nutrition. 2009;89(1):1-14.
20. Vermunt S, Pasman W, Schaafsma G, Kardinaal A. Effects of sugar intake on body weight: a review. obesity reviews. 2003;4(2):91-9.
21. Kundi H, Butt SA, Hamid S. Variation in the area of islets of langerhans in sodium cyclamate treated rats. Pakistan Armed Forces Medical Journal. 2015;65(5):656-9.
22. Schmitz-Moormann P, Pittner P, Heinze W. Lipomatosis of the pancreas: A morphometrical investigation. Pathology-Research and Practice. 1981;173(1):45-5