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RESEARCH ARTICLE

Altered taste threshold in chronic Type 2 diabetes mellitus

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ABSTRACT

Background: "Taste" is one of our basic senses. The prevalence of hypogeusia or ageusia is much more than what we are aware of, and hence it is addressed to a lesser extent. Diabetes mellitus (DM) is one such disease, which majorly contributes to the burden of taste dysfunction. **Aims and Objectives:** We have undertaken the present study to test and compare taste threshold in these patients with age and sex-matched healthy individuals. **Materials and Methods:** Sixty normal subjects with no DM were taken as controls and 60 known cases of Type 2 DM patients were taken as subjects in the present study. Taste threshold tests were performed in both these groups and were compared. **Result:** Chemical gustometry tests for five primary taste sensation were performed, it was observed that taste threshold for sweet and salty taste was higher and statistically significant ($P < 0.01$) in Type 2 diabetic patients compared to the control group. However, it was not significantly different for other taste modalities sour, bitter, and umami. **Conclusion:** Taste dysfunction was evident in Type 2 diabetic patients. The NJPPP_8(4)_27_RA increased taste threshold is specific, affecting salt and sweet modality mainly. Dysfunction of taste sensation should be detected in diabetics by screening. Measures to improve the food intake and supplementation for nutritional deficiencies can be given priority in diabetics.

KEY WORDS: Taste Threshold; Type 2 Diabetes Mellitus; Salt; Sweet; Umami; Sour; Bitter.

INTRODUCTION

Taste is the sensory modality that guides organisms to identify and consume nutrients while avoiding toxins and indigestible materials. For humans, this means recognizing and distinguishing sweet, umami, sour, salty, and bitter–the so-called "basic" tastes. There are likely additional qualities such as fatty, metallic, and others that might also be considered basic tastes. Each of these is believed to represent different nutritional or physiological requirements or pose potential dietary hazards. Thus, sweet-tasting foods signal the presence of carbohydrates that serve as an energy source. Salty taste governs intake of sodium and other salts, essential for maintaining the body's water balance and blood circulation. We generally surmise that umami, the taste of L-glutamate and a few other L-amino acids, reflects food's protein content. Bitter taste is innately aversive and is thought to guard against consuming poisons, many of which taste bitter to humans. Sour taste signals the presence of dietary acids.

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An important, unrecognized aspect of taste is that it serves 'functions' in addition to guiding dietary selection. Stimulating the taste buds initiates physiological reflexes that prepare the gut for absorption (releasing digestive enzymes, initiating peristalsis, and increasing mesenteric flow) and other organs for metabolic adjustments (insulin release, sympathetic activation of brown adipose tissue, increased heart rate, etc.). Collectively, these reflexes that are triggered by the sensory (sight, smell, and taste) recognition of food are termed as cephalic phase responses.[1]

The taste threshold alters by a number of factors such as age, ethnic backgrounds, drugs, local and systemic diseases, consumption of alcohol, smoking, and tobacco chewing. One of the factors, which alter the physiological taste threshold, is diabetes mellitus (DM). The pathophysiology of taste alteration in DM may be related to a decreased rate of turnover of the receptors.[2] Furthermore, an association between taste impairment and diabetic neuropathies has been described but remains disputed.[3]

Diabetes is a group of metabolic disorders, characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia in diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

Type 2 DM (ranging from predominantly insulin resistance with relative insulin deficiency to predominantly an insulin secretory defect with insulin resistance) is a form of diabetes, which accounts for ~90–95% of those with diabetes, previously referred to as non-insulin dependent diabetes, Type 2 diabetes or adult-onset diabetes, encompasses individuals who have insulin resistance and usually have relative (rather than absolute) insulin deficiency. At least initially, and often throughout their lifetime, these individuals do not need insulin treatment to survive. There are probably many different causes for this form of diabetes. Most patients with this form of diabetes are obese, and obesity itself causes some degree of insulin resistance.[4]

Many studies have been done on alteration of taste sensations in Type 2 DM, mainly on four primary sensations of taste, without considering the umami taste in their study frame.

Thus, the present study is undertaken with the objectives; to compare the alteration in taste threshold for five primary sensations in Type 2 DM. Most of the previous studies have used electrogustometry as the principal tool of investigation. However, we are using the "taste test" using chemical taste stimuli of different concentrations, which is a simple, cheap, and more feasible for testing patients on outpatient basis and so aids in timely management of decreased taste sensation.

MATERIALS AND METHODS

Source of Data

The taste threshold for five primary sensations of taste will be determined among the Type 2 DM patients, who are visiting the Medicine Department, Karnataka Institute of Medical Sciences (KIMS), Hubli, for follow-up and in the control groups, having age and sex-matched normal healthy individuals. The study and its conduct was cleared by the Ethical Committee KIMS Hubli.

Inclusion Criteria

1. Sixty, Type 2 diabetic subjects, of both sexes with the age ranging between 40 and 70 years, diagnosed at least 1 year before the study with normal kidney function and without any obvious clinical evidence, suggestive of a metabolic complication of diabetes
2. A group of 60 normal healthy individuals, having age and sex-matched with Type 2 DM subjects.

Exclusion Criteria

1. Those subjects, who are on prescribed medicines, which are known to cause taste alteration such as Sulfonylureas and angiotensin-converting enzyme inhibitors
2. Smokers and alcoholics
3. Pregnant and lactating women
4. Those subjects, with another taste altering, causes such as upper respiratory tract infection and herpes infection
5. Newly diagnosed (within, 1 year from the day/month of diagnosis) Type2 diabetics subjects.

After considering inclusion and exclusion criteria, the study groups were selected. The importance of the procedure was explained to the subject. Informed consent was taken from each subject before the commencement of the study.

Methods of Collection of Data

Determination of taste threshold

Stimulus representing the five classical basic tastes was included for testing the recognition of taste threshold for a particular taste. Seven serial half dilutions of the stock concentration were made for each taste solution, using deionized water and used for the experiment. The starting concentrations were glucose (2.00 M), sodium chloride (1.00 M), citric acid (0.05 M), quinine sulfate (0.001 M), and monosodium glutamate (1 M). The concentrations obtained after seven serial dilutions are given in Table 1. The taste sensitivity for each solution was investigated as per Harris and Kalmus method assisted by forced choice and up-down tracking procedure for better output and result.[5]

Subjects were tested with two or three drops of the solution of lowest concentration on the dorsum of the tongue to taste first and then made to taste successive higher solution until a definite taste was identified. Distilled water was used in between two solutions for rinsing. Rinsing of mouth was repeated till the subject volunteer said that no taste of the previously tasted concentration lingers on. Accordingly, the

Table 1: List of tastant concentrations used

Concentration number	Umami (M)	Salt (M)	Sweet (M)	Sour (M)	Bitter (M)
1	0.01562	0.01562	0.03125	0.000781	0.00001562
2	0.03125	0.03125	0.0625	0.001562	0.00003125
3	0.0625	0.0625	0.125	0.003125	0.0000625
4	0.125	0.125	0.25	0.00625	0.000125
5	0.25	0.25	0.5	0.0125	0.00025
6	0.5	0.5	1	0.025	0.0005
7	1	1	2	0.05	0.001

Source, physical and chemical nature of the tastants used in the study

Table 2: Different concentrations of monosodium glutamate solutions and taste response of control and Type 2 diabetic subjects

Concentrations number	Umami (M)	Control (*n*=60)	Type 2 DM (*n*=60)	*P*=0.29
1	0.01562	12	16	
2	0.03125	38	44	
3	0.0625	6	0	
4	0.125	2	0	
5	0.25	2	0	
6	0.5	0	0	
7	1	0	0	

(*P*<0.01=*significant). DM: Diabetes mellitus

Table 3: Different concentrations of sodium chloride solutions and taste response of control and Type 2 diabetic subjects

Concentrations number	Salt (M)	Control (*n*=60)	Type 2 DM (*n*=60)	*P*=0.001*
1	0.01562	0	2	
2	0.03125	14	4	
3	0.0625	32	22	
4	0.125	14	28	
5	0.25	0	4	
6	0.5	0	0	
7	1	0	0	

[*P*<0.01=*significant]. DM: Diabetes mellitus

actual threshold concentration was determined, and the bottle number was noted.[6]

The following sequence was followed for taste recognition threshold, i.e., Umami, followed by salt, sweet, sour, and bitter taste solution.[7]

1. Umami
   - Physical nature: White in color, solid crystal form
   - Chemical nature: L-glutamic acid monosodium salt
   - Molecular formula: $C_5H_8NNaO_4.H_2O$
   - Molecular weight: 187.13
   - Manufactured by An ISO 9001:2008 Certified Company Kemphasol, Mumbai.
2. Salt
   - Physical nature: White in color, solid powder form
   - Chemical nature: Sodium chloride, extra pure
   - Molecular formula: NaCl
   - Molecular weight: 58.44
   - Manufactured by HiMedia Laboratories Private Limited, Mumbai.
3. Sweet
   - Physical nature: White in color, solid powder form
   - Chemical nature: Dextrose anhydrous extra pure
   - Molecular formula: $C_6H_{12}O_6$
   - Molecular weight: 180.16
   - Manufactured by Thomas Baker Company, Mumbai.
4. Sour
   - Physical nature: White in color, solid crystal form
   - Chemical nature: Citric acid
   - Molecular formula: $Na_3C_6H_5O_7$
   - Molecular weight: 192
   - Manufactured by Alfa Chem Laboratories, Mumbai.
5. Bitter
   - Physical nature: White in color, solid, fine powder form

- Chemical nature: Quinine sulfate
- Molecular formula: $[C_2OH_{24}N_2O_2].H_2SO_4.2H_2O$
- Molecular weight: 782.95
- Manufactured by S.D. Fine Chemicals Limited, Mumbai.

All tastants were kept in airtight plastic bottles and stored as per recommended by the manufacturer.

About 2 ml Eppendorf tubes, 5 ml of sterile disposable syringes and deionized water was used to prepare the stock solution and seven serial dilutions. Fresh solutions were prepared and used within 24 h of preparation. Separate droppers were used for each tastant.

Statistical Analysis

Statistical analysis was done using the SPSS (Statistical Package for the Social Sciences) software. The statistical analysis was done using "Mann–Whitney U-test." This is a non-parametric test used to compare two unpaired groups. This test was used to compare the threshold of different taste parameters. $P < 0.01$ was taken as significant.

RESULT

In this study, we assessed the taste threshold for different taste modality in Type 2 diabetic subjects is compared with anthropometrically matched controls Tables 2-6.

It is observed that at 0.03125 M and lower concentration, 50 control subjects were able to recognize bitter taste properly, while all 60 Type 2 diabetic subjects recognize it properly at the same concentrations. Thus, the threshold for a bitter taste sensation in Type 2 diabetics is not significantly altered compared to control.

It is observed that at 0.0625 M and lower concentration, 56 control subjects were able to recognize salt taste properly,

Table 4: Different concentrations of glucose solutions and taste response of control and Type 2 diabetic subjects

Concentrations number	Sweet (M)	Control (*n*=60)	Type 2 DM (*n*=60)	*P*=0.000*
1	0.03125	0	0	
2	0.0625	16	12	
3	0.125	34	14	
4	0.25	8	26	
5	0.5	2	6	
6	1	0	2	
7	2	0	0	

[*P*<0.01=*significant]. DM: Diabetes mellitus

Table 5: Different concentrations of citric acid solutions and taste response of control and Type 2 diabetic subjects

Concentrations number	Sour (M)	Control (*n*=60)	Type 2 DM (*n*=60)	*P*=0.306
1	0.000781	2	2	
2	0.001562	18	16	
3	0.003125	30	26	
4	0.00625	8	10	
5	0.0125	2	6	
6	0.025	0	0	
7	0.05	0	0	

(*P*<0.01=*significant). DM: Diabetes mellitus

Table 6: Different concentrations of quinine sulfate solutions and taste response of control and Type 2 diabetic subjects

Concentrations number	Bitter (M)	Control (*n*=60)	Type 2 DM (*n*=60)	*P*=0.80
1	0.00001562	0	0	
2	0.00003125	8	14	
3	0.0000625	44	42	
4	0.000125	6	4	
5	0.00025	0	0	
6	0.0005	2	0	
7	0.001	0	0	

(*P*<0.01=*Significant). DM: Diabetes mellitus

while only 28 Type 2 diabetic subjects recognize it properly at the same concentrations. Thus, the threshold for salt taste sensation in Type 2 diabetics is significantly altered compared to control.

It is observed that at 0.0125 M and lower concentration, 50 control subjects were able to recognize salt taste properly, while only 26 Type 2 diabetic subjects recognize it properly at the same concentrations. Thus, the threshold for salt taste sensation in Type 2 diabetics is significantly altered compared to control.

It is observed that at 0.003125 M and lower concentration, 50 control subjects were able to recognize sour taste properly, while 44 Type 2 diabetic subjects recognize it properly at the same concentrations. Thus, the threshold for sour taste sensation in Type 2 diabetics is not significantly altered compared to control.

It is observed that at 0.00006125 M and lower concentration, 52 control subjects were able to recognize bitter taste properly, while 44 Type 2 diabetic subjects recognize it properly at the same concentrations. Thus, the threshold for bitter taste sensation in Type 2 diabetics is not significantly altered compared to control.

DISCUSSION

Diabetes is the most common cause of peripheral neuropathy. Distal symmetrical sensorimotor polyneuropathy is the most common form of diabetic neuropathy.[8] Duration of diabetes and peripheral neuropathy had the strongest association with taste impairment.[9] In this study, it was observed that taste threshold for sweet and salty taste was higher and statistically significant ($P < 0.01$) in Type 2 diabetic patients compared to their control. However, it was not significantly different for other taste modalities-sour, bitter, and umami.

These findings in the present study are well in agreement with the observations of the previous studies, conducted by many researchers. In a study conducted by Dey and Inamdar, it was revealed that there was significantly lowered tasting ability in the diabetic subjects for sweet, salt, sour, and bitter solutions as compared to the controls. Moreover, highly significant results were observed for sweet taste among the different sensations.[10] Similarly, Gondivkar *et al*. conducted a study in diabetics and concluded with the findings that Type 2 diabetic patients had a blunted taste response for sweet followed by sour and then salt tastes. They pointed out that the taste abnormality may influence the choice of nutrients, with a preference for sweet-tasting foods, thereby exacerbating hyperglycemia.[11] Similar study by Gaphor and Saeed, for evaluation of taste sensation showed that diabetic patients have less sensitivity to sweet and salty taste than healthy individuals. There were no differences in sour and bitter sensation sensitivity between diabetic and non-diabetic healthy individuals. Furthermore, they pointed out that the age, sex, and duration of the disease had no effect on taste disturbance.[12]

On the other hand, the present study was conducted in Type 2 diabetics, wherein the primary taste modality umami was also included, which was not considered previously by other researchers, who worked on taste threshold in Type 2 diabetics. Umami, the recently established fifth primary taste modality was included as a tastant. Kurihara and Kashiwayanagi conducted a study on umami taste, in which the canine taste system was sensitive to umami substance and showed a large synergism between monosodium glutamate and disodium guanylate or disodium inosinate. Single-fiber analysis on the responses of mouse glossopharyngeal nerve and monkey's primary taste cortex neurons also showed that the responses to umami substances are independent of other basic tastes. On the basis of these results, it was proposed that the umami taste is fifth basic taste, and there is a unique receptor for umami substances.[13]

The underlying cause for taste impairment in DM is unclear. However, the probable mechanism for the heightened taste thresholds in diabetes could be explained on the basis of a different school of thoughts. Taste impairment may be a degenerative complication of DM; due to neuropathy of the "taste nerves."[9] Increased intracellular glucose in diabetics leads to the formation of advanced glycosylation end products (AGEs), which bind to a cell surface receptor. AGEs have been shown to cross-link proteins (e.g., collagen and extracellular matrix proteins), accelerate atherosclerosis, promote glomerular dysfunction, reduce nitric oxide synthesis, induce endothelial dysfunction, and alter extracellular matrix composition and structure. Hyperglycemia increases glucose metabolism through the sorbitol pathway. Increased sorbitol concentration alters redox potential, increases cellular osmolality, generates reactive oxygen species, and likely leads to other types of cellular dysfunction. Hyperglycemia increases the formation of diacylglycerol leading to activation of protein kinase C (PKC). PKC alters the transcription of genes for extracellular matrix proteins in endothelial cells and neurons leading to complications such as neuropathy, retinopathy, and renal complications.[14] Inherent or acquired defect of the taste receptor, or abnormality of the mechanism underlying the central appreciation of taste within the brain, or microangiopathy involving the taste buds may also be responsible for the taste impairment.[15]

The other school of thought specifically points out toward a significant and specific impairment in glucose taste detection. It is said that in diabetics a taste abnormality for glucose might conceivably be due to a frequent elevation of the blood sugar ("satiation effect").[16]

CONCLUSION

So to conclude, taste threshold for five primary taste modalities was assessed in Type 2 diabetic patients. Sweet and salty taste threshold was significantly higher in Type 2 diabetic patients compared to controls. However, the threshold for other taste modalities, i.e., Umami, sour, and bitter did not show any difference in these two groups compared to controls. Therefore, it can be concluded that hypogeusia, especially for sweet and salty sensations in Type 2 diabetics, even though the glycemic status of the subjects was within the normal limits.

REFERENCES

1. Chaudhari N, Roper SD. The cell biology of taste. J Cell Biol 2010;190:285-96.
2. Schiffman SS. Taste and smell in disease (first of two parts). N Engl J Med 1983;308:1275-9.
3. Le Floch JP, Le Lievre G, Labroue M, Peynegre R, Perlemuter L. Early detection of diabetics patients at risk of developing degenerative complication using complication using electric gustometry: A five year follow-up study. Eur J Med 1992;1:208-14.
4. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010;33:62-3.
5. Harris H, Kalmus H, Trotter WR. Taste sensitivity to phenylthiourea in goitre and diabetes. Lancet 1949;2:1038.
6. Khobragade RS, Wakode SL, Kale AH. Physiological taste threshold in Type 1 diabetes mellitus. Indian J Physiol Pharmacol 2012;56:42-7.
7. Shi HB, Masuda M, Umezaki T, Kuratomi Y, Kumamoto Y, Yamamoto T, *et al.* Irradiation impairment of umami taste in patients with head and neck cancer. Auris Nasus Larynx 2004;31:401-6.
8. Kumar V, Abbas AK, Aster JC. Robbins Basic Pathology. 9th ed. Philadelphia, PA: Elsevier Saunders; 2013. p. 799.
9. Le Floch JP, Le Lièvre G, Verroust J, Philippon C, Peynegre R, Perlemuter L, *et al.* Factors related to the electric taste threshold in type 1 diabetic patients. Diabet Med 1990;7:526-31.
10. Dey CK, Inamdar RS. A comparative study of different taste parameters in diabetics and non-diabetics. Indian J Appl Basic Med Sci 2011;13B:1-11.
11. Gondivkar SM, Indurkar A, Degwekar S, Bhowate R. Evaluation of gustatory function in patients with diabetes mellitus Type 2. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:876-80.
12. Gaphor SM, Saeed RA. The evaluation of taste threshold for four main tastes between diabetic and healthy individuals. Eur Sci J 2014;10:434-9.
13. Kurihara K, Kashiwayanagi M. Physiological studies on umami taste. J Nutr 2000;130:931S-4.
14. Longo DL, Faucl AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J. In: Harrison's Principles of Internal Medicine. 18th ed., Vol. 2. New York: McGraw Hill; 2012. p. 2968-92.
15. Perros P, MacFarlane TW, Counsell C, Frier BM. Altered taste sensation in newly-diagnosed NIDDM. Diabetes Care 1996;19:768-70.
16. Schelling JL, Tetreault L, Lasagna L, Davis M. Abnormal taste threshold in diabetes. Lancet 1965;1:508-12.

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