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Original Research Article

Taste dysfunction in type 2 diabetes mellitus patients with autonomic neuropathy and its relation with HbA1C level and disease duration

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a multifactorial, complex disease associated with chronic hyperglycemia, resulting from the interplay of genetic, environmental, and epigenetic factors. T2DM can causes various disabling complications. Diabetic autonomic neuropathy (DAN) is one of the common complications in diabetes. The taste threshold affected by various factors such as age, ethnic backgrounds, drugs, local and systemic diseases, consumption of alcohol, smoking, and tobacco chewing.
Method: The present study is undertaken with the objectives to compare the taste dysfunction of four primary sensations in Type 2 DM with autonomic neuropathy and its relation with glycemic control. The 60 patients of T2DM with autonomic neuropathy and 60 healthy controls were taken for the study. Autonomic neuropathy was assessed clinically. Chemical taste test using four solutions of basic tastes (sweet, sour, salty, bitter) were done.
Results: Taste dysfunction for sweet was significant in T2DM with uncontrolled hyperglycemia. The taste dysfunction in T2DM patients was not related to gender, disease duration, and type of treatment taken. The study found a significant correlation between taste dysfunction, HbA1C level and blood sugar fasting level in T2DM patients.
Conclusions: The taste dysfunction was mainly for sweet. Sour and bitter did not show any difference in case groups compared to controls.

Keywords: Diabetes, Taste dysfunction, Autonomic neuropathy

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is caused a defect in insulin secretion insulin action or both which results in hyperglycemia. Pathogenic processes involved in the development of diabetes ranges from autoimmune destruction of Beta cells of pancreas to abnormalities that result in resistance to insulin action. Resulting defects lead to abnormalities in carbohydrates, protein, fat metabolism. This chronic hyperglycemia is associated with long term damage, dysfunction and failure of different organs and result into various microvascular and macrovascular complications. Macrovascular complications include cardiovascular disease, stroke and peripheral vascular disease. Microvascular complication include neuropathy (i.e., both peripheral and autonomic neuropathy), nephropathy, retinopathy.

Diabetes represents one of the most challenging health problems of the 21st century: according to a survey by the international diabetes federation, there were 463 million adults with diabetes in 2019 worldwide, which corresponds to a striking 9.3% prevalence; this number is expected to increase to 700 million by 2045, with an economic impact on personal medical expenditure and on the healthcare system.[1]

DAN is one of the common complications in diabetes. DAN may manifest with gastrointestinal (GI) symptoms like gastroparesis, esophageal dysmotility, constipation, diarrhea, fecal incontinence, or gallbladder atony.

For humans, the so-called “basic” tastes are sweet, umami, sour, salty, and bitter. Abnormalities in any or several taste receptors are known to influence intake of specific food

components or ingredients related to the taste receptor.[2] To date, there very few reports describing changes in overall taste sensitivity in T2DM. Whether/ not environmental influences, such as habitual diet, can alter taste sensitivity, or vice versa, is still unclear. Thus present study was aimed at determining taste dysfunction in a population of T2DM subjects and its correlation with HbA1c level.

METHODS

This was a observational cross sectional study which was carried over a period of one and half year (January 2020 to November 2021) in the department of medicine, K.P.S institute GSVM medical college, after taking clearance from institutional ethical committee.

Patients of age above than 30 years and known case of T2DM for more than 5 years of any sex included in study.

Type 1 diabetes mellitus patients, smokers and alcoholics, patients on prescribed medicines known to cause taste alteration like sulphonylureas, ace inhibitors, pregnant and lactating women, patients with upper respiratory dysfunction and herpes infection excluded from studies.

Written informed consent was obtained from all enrolled subjects after the procedures were fully explained and prior to the anthropometric parameter measurements and taste test execution. The controls were healthy, non-T2DM volunteers, selected in the same period among hospital healthcare professionals and their relatives, and they were matched for sex, age, and body mass index with patients.

All required details about cases such as demographic data (Age, gender, address, registration number etc.), clinical presentation (signs and symptoms) general examination findings, systemic examination taste test were carried out. Blood sample were taken from all patients to check HbA1C, fasting blood sugar, post prandial blood sugar.

Diabetes mellitus was defined as an HbA1C>6.5 g% or history of receiving treatment for diabetes mellitus or previously diagnosed diabetes mellitus.

Tastant preparation

solutions was prepared as directed below.[3] Each solution were made using a volumetric flask to ensure precision of concentrations to ±0.0002 M. The compounds included were: 1. Quinine (bitter): Place 0.011 g of quinine HCl dihydrate in a 500 ml volumetric flask. Add water to bring the volume to 500 ml, producing a solution with a final concentration of 56 µM. 2. Sodium chloride (salty): Place 7.5 g of sodium chloride in a 500 ml volumetric flask. Add water to bring the volume to 500 ml, producing a solution with a final concentration of 0.25 M. 3. Sucrose (sweet): place 60 g of sucrose in a 500 ml volumetric flask. Add water to bring the volume to 500 ml, producing a solution with a final concentration of 0.35 M and 4. Citric acid (sour): place 25 g of citric acid in 500 ml volumetric flask. Add water to bring volume to 500 ml, producing a solution with a final concentration of 0.26 M.

Subjects were provided with 4 solutions, a bottle of water, empty cup, pen, and pen-and-paper taste questionnaire samples, 2 subjects were instructed to rate both the intensity and quality (e.g., salty, sour, bitter, sweet, or no flavor) of each tastant and 3 subjects were asked to rinse mouth twice with water and spit it out in the cup provided. After that 5 ml of sample was provided whose nature was kept unknown to the subject and asked to hold it there for 5 seconds before spitting the solution into the cup. After which they were asked to mark the quality and intensity of solutions in the questionnaire scale as mild, moderate and very. Afterward, was asked to rinse mouth with water twice before proceeding to the next sample.

Statistical analysis

Data was collected and entered in Excel spreadsheet for statistical analysis. Free trial version of SPSS software was downloaded and used for statistical analysis. A $p<0.05$ was deemed as significant. The variables were not normally distributed in the 2 subgroups of the variable group. Thus, non- parametric tests (Wilcoxon-Mann-Whitney U test) were used to make group comparisons.

RESULTS

The variable HbA1c (%) was not normally distributed in the 2 subgroups of the variable chemical taste dysfunction: sweet. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U test) were used to make group comparisons.

There was a significant difference between the 2 groups in terms of HbA1c (%) ($W=695.500$, $p\leq0.001$), with the median HbA1c (%) being highest in the chemical taste dysfunction: sweet: yes group.

Strength of association (Point-Biserial correlation)=0.49 (Large effect size).

Chi-squared test was used to explore the association between 'group' and 'chemical taste dysfunction: sweet'.

There was a significant difference between the various groups in terms of distribution of chemical taste dysfunction: Sweet ($\chi^2=7.548$, $p=0.006$).

Strength of association between the two variables (Cramer's V)=0.25 (Low association).

Strength of association between the two variables (Bias corrected Cramer's V)=0.23 (Low association).

Participants in the group group: case had the larger proportion of chemical taste dysfunction: sweet: yes. Participants in the group group: control had the larger proportion of chemical taste dysfunction: sweet: no.

Table 1: Association between group and parameters.

Parameters	Group (%)		P value
	Case, (n=60)	Control, (n=60)	
Age (Years)* **	54.22±9.89	38.20±10.06	<0.001[1]
Age* (Years)**			
21-30	1 (1.7)	22 (36.7)	<0.001[2]
31-40	4 (6.7)	14 (23.3)	
41-50	19 (31.7)	15 (25.0)	
51-60	22 (36.7)	9 (15.0)	
61-70	13 (21.7)	0 (0.0)	
71-80	1 (1.7)	0 (0.0)	
Gender			
Male	35 (58.3)	43 (71.7)	0.126[2]
Female	25 (41.7)	17 (28.3)	
Height (cm)* **	160.68±8.21	165.65±8.24	0.001[1]
Weight (kg)* **	64.60±10.10	68.63±9.72	0.025[1]
BMI (kg/m^2)	24.53±3.34	24.91±2.38	0.490[1]
BMI (Kg/m^2)			
<18.5	2 (3.3)	0 (0.0)	0.535[3]
18.5-22.9	12 (20)	8 (13.3)	
23.0-24.9	17 (28.3)	22 (36.7)	
25.0-29.9	24 (40)	25 (41.7)	
30.0-34.9	4 (6.7)	5 (8.3)	
35.0-39.9	1 (1.7)	0 (0.0)	
Systolic BP (mmHg)* **	137.70±13.93	120.40±9.93	<0.001[4]
Diastolic BP (mmHg)* **	85.50±9.79	76.70±6.31	<0.001[1]
Duration of T2DM (years)	9.53±4.50	-	-
Taking treatment (yes)	51 (85.0)	0 (NaN%)	1.000[2]
Duration of treatment (years)	9.25±4.44	-	-
Type of treatment: OHA (yes)	51 (85.0)	0 (NaN%)	1.000[2]
Type of treatment: insulin (yes)	10 (16.7)	0 (NaN%)	1.000[2]
History of hospitalistion (yes)	19 (31.7)	0 (NaN%)	1.000[2]
Blood sugar fasting (mg)* **	157.13±48.61	86.53±8.34	<0.001[1]
Blood sugar post-prandial (mg)* **	249.08±89.12	115.35±9.95	<0.001[1]
HbA1c (%)* **	9.26±2.86	5.26±0.41	<0.001[1]
Chemical taste assessment: sweet* **			
Mild	26 (43.3)	12 (20.0)	0.023[2]
Moderate	24 (40.0)	33 (55.0)	
Very	10 (16.7)	15 (25.0)	
Chemical taste assessment: salty			
Mild	14 (23.3)	8 (13.3)	0.338[2]
Moderate	31 (51.7)	33 (55.0)	
Very	15 (25.0)	19 (31.7)	
Chemical taste assessment: sour			
Mild	1 (1.7)	3 (5.0)	0.536[3]
Moderate	34 (56.7)	36 (60)	
Very	25 (41.7)	21 (35.0)	
Chemical taste assessment: bitter			
Mild	0 (0.0)	1 (1.7)	0.097[3]
Moderate	39 (65.0)	29 (48.3)	
Very	21 (35.0)	30 (50.0)	
Chemical taste dysfunction: sweet (yes)* **	26 (43.3)	12 (20.0)	0.006[2]
Chemical taste dysfunction: salty (yes)	14 (23.3)	8 (13.3)	0.157[2]
Chemical taste dysfunction: sour (yes)	1 (1.7)	3 (5.0)	0.619[3]
Chemical taste dysfunction: bitter (yes)	0 (0.0)	1 (1.7)	1.000[3]

***Significant at p<0.05, 1: Wilcoxon-Mann-Whitney U test, 2: Chi-Squared test, 3: Fisher's exact test, 4: t test.

Table 2: Comparison of the 2 subgroups of the variable chemical taste dysfunction: sweet in terms of HbA1c (%), (n=60).

HbA1c (%)	Chemical taste dysfunction: sweet		Wilcoxon-Mann-Whitney U Test	
	Yes	No	W	P value
Mean (SD)	10.83 (3.17)	8.05 (1.87)		
Median (IQR)	10.55 (8.32-12.97)	7.6 (7-9.05)	695.500	<0.001
Range	5.6 - 18.5	4.1 - 13.4		

Table 3: Comparison of the 2 subgroups of the variable chemical taste dysfunction: sweet in terms of duration of T2DM (Years), (n=60).

Duration of T2DM (Years)	Chemical taste dysfunction: sweet		Wilcoxon-Mann-Whitney U Test	
	Yes	No	W	P value
Mean (SD)	9.50 (3.44)	9.56 (5.22)		
Median (IQR)	9.5 (7-11.75)	8 (5-12)	490.000	0.474
Range	5 - 15	5 - 25		

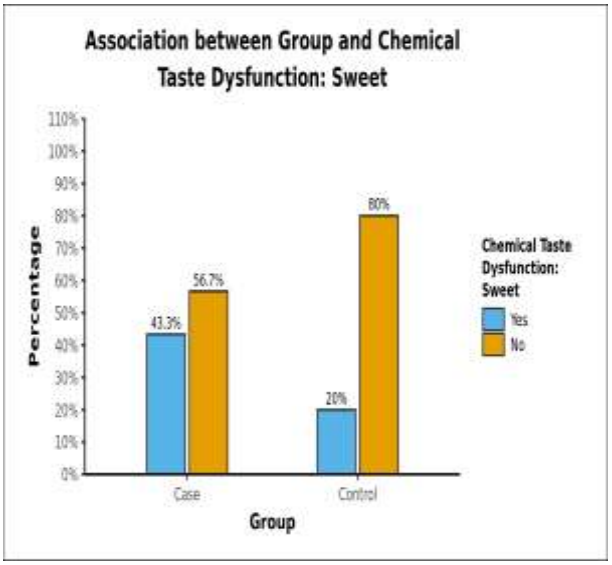

Figure 1: Association between group and chemical taste dysfunction: sweet.

The variable duration of T2DM (years) was not normally distributed in the 2 subgroups of the variable chemical taste dysfunction: sweet. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U test) were used to make group comparisons.

There was no significant difference between the groups in terms of duration of T2DM (years) (W=490.000, p=0.474).

Strength of association (Point-biserial correlation)=0.01 (little/no association).

DISCUSSION

In this study, we evaluated the perception of basic tastes in 60 subjects with T2DM out of which 35 (58.3%) male and 25 (41.7%) female compared to 60 healthy volunteers in which 43 (71.7%) male and 17 (28.3%) female.

It has been noticed that the taste sensation is an important factor in the regulating type of food ingestion, in digestive process control, and in the release of neuroendocrine hormones for hunger and satiety. Our results are not in accordance with those studies showing that taste function in humans decreases with age.[4] Fishers exact test was used to find correlation (χ^2=5.149, p=0.415).

In our study, we found a decrease in taste function in patients with diabetes, particularly concerning the sweet taste.[5] There were no differences in sour and bitter sensation sensitivity between diabetic and non-diabetic healthy individuals. A rise in taste threshold has been shown to be related with hyperglycemia.[6] A significant correlation between taste thresholds and plasma glucose concentration has been described in many previous studies, indicating that patients with T2DM are almost insensitive to the sweet taste response.[7] Our result are in accordance with study of Bustos-Saldana et al which shows relationship between fasting blood sugar and taste alteration in type 2 DM.

Our results show significant relationship between taste dysfunction and HbA1c levels. Patients with good glycemic control have preserved taste sensation. Non-parametric tests (Wilcoxon-Mann-Whitney U test) were used to make group comparisons (W=695.500, p≤0.001), it was not in accordance with the findings of Pugnaloni et al study which did not show any relationship between taste dysfunction and HbA1c levels. In our study there was a strong positive correlation between blood sugar fasting (mg) and HbA1c (%), and this correlation was statistically significant (rho=0.7, p≤0.001). For every 1 unit increase in blood sugar fasting (mg), the HbA1c (%) increases by 0.04 units. Conversely, for every 1 unit increase in HbA1c (%), the blood sugar fasting (mg) increases by 10.68 units.

More interestingly, we didn't find any correlation between the taste dysfunction and disease duration. The decreased sensitivity to sweet taste might explain the increase intake of sweet by the patients which leads deterioration of

glycemic control. Different nutritional surveys have described the presence of a significant prevalence of sweet (habitually soft and palatable) foods in the diet of elderly people.[8]

Our study didn't show any correlation between taste dysfunction and type of treatment being taken by the patients.

Though some previous studies showed some gender-related differences in taste function among healthy and diseased individuals.[9] In our study, we did not find any significant effect of gender on the differences in taste function between healthy subjects and T2DM patients. Chi-squared test was used to explore the association between 'gender' and 'chemical taste dysfunction: Sweet ($\chi 2$=0.939, p=0.333).

Some limitations, however, apply to our findings, that need to be addressed. Firstly, the sample size of our study was relatively small, so the subject pool may not be entirely representative of general population. Secondly, no validated questionnaire on food nutrients consumption was administered. Third, we used chemical tastant to test taste dysfunction which was very subjective test to be carried out.

CONCLUSION

In our study we found a significant correlation between taste dysfunction and HbA1C level and blood sugar fasting level in type 2 diabetes mellitus patients. Alteration in taste was mainly for sweet. Sour, and bitter did not show any difference in case groups compared to controls. The taste dysfunction was not related to gender, duration of T2DM or type of treatment being taken.

Our study was carried out at a tertiary care center of Kanpur. So, the subject pool may not be entirely representative of general population. Also, the sample size was not large enough with only 60 cases and 60 controls.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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