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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 hypoguesia or aguesia is much more than what we are aware of and hence it is addressed to a lesser extent. Diabetes mellitus is one such disease, which majorly contributes to the burden of taste
dysfunction. Thus, we have undertaken the present study to test and compare taste threshold in these patients with age and sex matched healthy individuals.

**Material and Methods**: Sixty, normal subjects with no diabetes mellitus were taken as controls and Sixty, known cases of type 2 diabetes mellitus 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 were 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 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.

**Keywords**: 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.
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, 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, taste) recognition of food are termed as cephalic phase responses.¹

The taste threshold alters by 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 Also, 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 Diabetes mellitus (ranging from predominantly insulin resistance with relative insulin deficiency to predominantly an insulin secretary 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 diabetes mellitus, 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 diabetes mellitus. Most of the previous studies have used electrogustometry as the principle 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 diabetes mellitus patients, who are visiting the Medicine department, KIMS, HUBLI for follow up and in the control groups, having age and sex matched normal healthy individuals. The study and its conduct were cleared by the ethical committee KIMS Hubli.

Inclusion Criteria

1. Sixty, type 2 diabetic subjects, of both sexes with the age ranging between 40 to 70 years, diagnosed at least one year prior to the study with normal kidney function and without any obvious clinical evidence, suggestive of metabolic complication of diabetes.

2. A group of sixty normal healthy individuals, having age and sex matched with type 2 diabetes mellitus subjects.

Exclusion Criteria

1. Those subjects, who are on prescribed medicines, which are known to cause taste alteration like Sulfonylureas, ACE inhibitors.
2. Smokers and alcoholics.
3. Pregnant and lactating women.
4. Those subjects, with other taste altering causes like upper respiratory tract infection, Herpes infection.

5. Newly diagnosed [within, one 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 prior to the commencement of 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 particular taste. Seven serial half dilutions of the stock concentration were made for each taste solution, by using deionised water and used for experiment. The starting concentrations were Glucose (2.00 M), Sodium chloride (1.00 M), Citric acid (0.05 M), Quinine sulphate (0.001 M) and Monosodium glutamate (1M). The concentrations obtained after seven serial dilutions are given in the 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 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 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

**TABLE 1: List of tastant concentrations used.**

<table>
<thead>
<tr>
<th>CONC N0</th>
<th>UMAMI (M)</th>
<th>SALT (M)</th>
<th>SWEET (M)</th>
<th>SOUR (M)</th>
<th>BITTER (M)</th>
</tr>
</thead>
</table>

Source, Physical and Chemical nature of the tastants used in the study

1. Umami

Physical nature: White in colour, Solid crystal form.
Chemical nature: L-Glutamic acid monosodium salt
Molecular formula: C₅H₈NNaO₄.H₂O
Molecular Weight: 187.13

2. Salt

Physical nature: White in colour, 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 colour, Solid powder form.
Chemical nature: Dextrose anhydrous extra pure.
Molecular formula: C₆H₁₂O₆
Molecular Weight: 180.16
Manufactured by Thomas Baker Company, Mumbai.

4. Sour

Physical nature: White in colour, Solid crystal form.
Chemical nature: Citric Acid
Molecular formula: Na$_3$C$_6$H$_5$O$_7$
Molecular Weight: 192
Manufactured by Alfa Chem Laboratories, Mumbai.

5. Bitter

Physical nature: White in colour, Solid, Fine powder form.
Chemical nature: Quinine Sulphate.
Molecular formula: [C$_2$OH$_{24}$N$_2$O$_2$].H$_2$SO$_4$.2H$_2$O
Molecular Weight: 782.95
Manufactured by S.D. Fine Chemicals limited, Mumbai.

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

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

Statistical Analysis

Statistical analysis was done by using the SPSS (Statistical package for social sciences) software. The statistical analysis was done by 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 value <0.01 was taken as significant.

RESULT

In the present study, we assessed the taste threshold for different taste modality in type 2 diabetic subjects are compared with anthropometrically matched controls.
TABLE 2: Different concentrations of Monosodium glutamate solutions and taste response of control and type 2 diabetic subjects.

<table>
<thead>
<tr>
<th>Conc. No</th>
<th>Umami (M)</th>
<th>Control (n=60)</th>
<th>Type2 DM (n=60)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.01562</td>
<td>12</td>
<td>16</td>
<td>0.29</td>
</tr>
<tr>
<td>2</td>
<td>0.03125</td>
<td>38</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.0625</td>
<td>6</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0.125</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.25</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

[P <0.01 = *Significant ]

It is observed that at 0.03125 M and lower concentration, fifty control subjects were able to recognize bitter taste properly, while all sixty type 2 diabetic subjects recognize it properly at the same concentrations. Thus, the threshold for bitter taste sensation in type2 diabetics is not significantly altered compared to control.

TABLE 3: Different concentrations of Sodium chloride solutions and taste response of control and type 2 diabetic subjects.

<table>
<thead>
<tr>
<th>Conc. No</th>
<th>Salt (M)</th>
<th>Control (n=60)</th>
<th>Type2 DM (n=60)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.01562</td>
<td>0</td>
<td>2</td>
<td>0.001*</td>
</tr>
<tr>
<td>2</td>
<td>0.03125</td>
<td>14</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.0625</td>
<td>32</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0.125</td>
<td>14</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.25</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

[P <0.01 = *Significant ]

It is observed that at 0.0625 M and lower concentration, fifty six control subjects were able to recognize salt taste properly, while only twenty eight 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.

**TABLE 4: Different concentrations of Glucose solutions and taste response of control and type 2 diabetic subjects.**

<table>
<thead>
<tr>
<th>Conc. No</th>
<th>Sweet(M)</th>
<th>Control (n=60)</th>
<th>Type2 DM (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.03125</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0.0625</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>0.125</td>
<td>34</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>0.25</td>
<td>8</td>
<td>26</td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

[P <0.01 = *Significant ]

It is observed that at 0.0125 M and lower concentration, fifty control subjects were able to recognize salt taste properly, while only twenty six 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.

**TABLE 5: Different concentrations of Citric acid solutions and taste response of control and type 2 diabetic subjects.**

<table>
<thead>
<tr>
<th>Conc. No</th>
<th>Sour(M)</th>
<th>Control (n=60)</th>
<th>Type2 DM (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.000781</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>0.001562</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>0.003125</td>
<td>30</td>
<td>26</td>
</tr>
<tr>
<td>4</td>
<td>0.00625</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>0.0125</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>0.025</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>0.05</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

P = 0.306
It is observed that at 0.003125 M and lower concentration, fifty control subjects were able to recognize sour taste properly, while forty four 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.

**TABLE 6: Different concentrations of Quinine sulphate solutions and taste response of control and type 2 diabetic subjects.**

<table>
<thead>
<tr>
<th>Conc. No</th>
<th>Bitter (M)</th>
<th>Control (n=60)</th>
<th>Type2 DM (n=60)</th>
<th>P= 0.80</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.00001562</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>0.00003125</td>
<td>8</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.0000625</td>
<td>44</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0.000125</td>
<td>6</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.00025</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0.0005</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>0.001</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

It is observed that at 0.00006125 M and lower concentration, fifty two control subjects were able to recognize bitter taste properly, while forty four 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. Duration of diabetes and peripheral neuropathy had the strongest association with taste impairment. In the present study, it was observed that taste threshold for sweet and salty taste were 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 Chandan Dey et al., it was revealed that, there was significantly lowered tasting ability in the diabetic subjects for sweet, salt, sour & bitter solutions as compared to the controls. Moreover, highly significant results were observed for sweet taste among the different sensations. 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. Similar study by Shanaz Mohammad Gaphor et al., 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.

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. Kenzo Kurihara and Makoto 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 diabetes mellitus is unclear. However, the probable mechanism for the heightened taste thresholds in diabetes could be explained on the basis of different school of thoughts. Taste impairment may be a degenerative complication of diabetes mellitus; 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, extracellular matrix proteins etc), accelerate atherosclerosis, promote glomerular dysfunction, reduce nitric oxide synthesis, induce endothelial dysfunction and alter extracellular matrix composition and structure. Hyperglycemia increases glucose metabolism via 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 like neuropathy, retinopathy, renal complications etc.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.\textsuperscript{15}

The other school of thought specifically points out towards 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 frequent elevation of the blood sugar (“satiation effect”).\textsuperscript{16}

So to conclude, Taste threshold for five primary taste modalities were assessed in type 2 diabetic patients. Sweet and Salt taste threshold were 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 hypoguesia, especially for sweet and salt sensations in type 2 diabetics, even though the glycemic status of the subjects was within the normal limits.

REFERENCES


