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Evaluation of factors related to taste function in type 2 diabetics

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ABSTRACT

Aim: The sense is an important driver of diet choice, which can lead to the development of chronic diseases such as diabetes. Although factors affecting differences in taste function between individuals have been evaluated in healthy individuals, there are limited studies investigating them in patients with type 2 diabetes. The aim of the present study was to analyse the factors affecting taste function in individuals with type 2 diabetes.

Material and Method: Sixty-one participants with a history of type 2 diabetes lasting at least one year and aged 19 to 75 years were enrolled. The taste function was tested using impregnated filter paper strips.

Results: The mean taste strip scores of the participants for sweet, salty, bitter, sour, and overall were 2.38 ± 0.88 , 1.91 ± 0.92 , 2.28 ± 0.76 , 2.18 ± 1.01 , 8.7 ± 1.81 , respectively. Age was significantly associated with the taste score for salty ($r = -0.225$ $p = 0.041$) and sour ($r = -0.252$ $p = 0.040$). It was determined that there was no effect of other confounders (gender, body mass index, fasting plasma glucose, glycosylated hemoglobin and duration of diabetes), except age, on the overall taste score in participants.

Conclusion: Future studies with a larger number of patients may help better investigate the factors affecting taste function in type 2 diabetics.

Keywords: Type 2 diabetes mellitus, sweet taste, sour taste, salty taste, bitter taste

INTRODUCTION

The prevalence of type 2 diabetes mellitus (T2DM) has increased rapidly worldwide over the past few decades, and is expected to rise by more than 50% by 2045 (1). T2DM is a chronic metabolic disease that requires continuous medical care in which the body cannot benefit adequately from carbohydrates, fats, and proteins due to insulin deficiency or impaired insulin action. Although T2DM is a polygenic illness, environmental and behavioural variables play a role in its incidence (2).

When the chemical concentration of a tastant exceeds a threshold level, taste receptors are activated, resulting in action potentials in fibers of taste nerve strong enough to produce taste perception (3). Previous studies (4,5) reported that activation of sensory receptors induces oral and gastrointestinal secretion, contributing to the metabolic and digestive process. Multiple factors affect the taste threshold, including genetics, age, body weight, consumption, smoking, acute and chronic diseases (6). Taste sensation and food preferences have been shown to be significant in dietary and food consumption. A

loss of taste sensation, which could lead to an increase in unhealthy eating habits, could have severe health consequences. It may increase the likelihood of metabolic disorders such as obesity, diabetes, and metabolic syndrome (7,8).

To date, there are very few reports that describe factors linked to taste function in type 2 diabetics. The results of these studies are contradictory in some aspects, suggesting the need for more evaluative studies. The aim of this current study was to determine the factors associated with taste function in type 2 diabetics.

MATERIAL AND METHOD

Study Population

The sample consisted of 61 individuals who had been diagnosed with type 2 diabetes for at least one year. Diabetic patients admitted to internal outpatient clinic. Participants who agreed to participate in this study were asked to sign an informed consent form in accordance with the Declaration of Helsinki. The study was carried out with

the permission of Gaziantep Islam Science and Technology University Non-interventional Clinical Researches Ethics Committee (Date: 27.09.2022, Decision No: 2022/148). Patients were subjected to preliminary interviews and their suitability for the study was evaluated. The inclusion criteria were age between 19 and 75 years, body mass index (BMI) <40 kg/m². Exclusion criteria were: smoking or history of smoking; chronic use of alcohol or substance abuse in the past 6 months; presence of comorbidity that affects taste (i.e., renal or liver diseases, presence or previous treatment with history of cancer, previous head and neck radiation, hypothyroidism, neurodegenerative diseases, depression, acute infections in the previous 2 weeks, respiratory diseases, periodontitis, anosmia and denture carriers), usage of antibiotics, antihistamines, antidepressants, anticonvulsants, antineoplastic drugs or environmental toxins; pregnancy and breastfeeding.

Data Collection

Face-to-face interviews were used to obtain data on demographic variables and diabetes information using a questionnaire form. Anthropometric measurements of the individuals (body weight, height) were taken. Blood samples were taken to test the fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c). Taste assessments were performed through taste strips.

Anthropometric Measurements

An trained dietitian took anthropometric measurements (weight, height) using standard measurements procedures (9). Body weight was determined using an electronic scale to the nearest 0.1 kilogram. Stadiometer was used to measure height to the nearest 0.1 cm. Body mass index (BMI) was calculated by dividing weight (kg) by the square of height (m²).

Laboratory Assays

FPG and HbA1c were measured in blood samples taken after 12 hours of fasting. FPG was measured by the glucose oxidase method. HbA1c levels were measured in the same laboratory by high-performance liquid chromatography.

Taste Test

Taste function tests was performed using the taste strips which are basically tastant impregnated filter paper strip (10). Each of the 16 taste stimuli was impregnated with one of these four tastes: sweet, sour, salty, and bitter. The following concentrations were used for taste stimuli: sweet: 0.4, 0.2, 0.1, 0.05 g/mL sucrose; salty: 0.25, 0.1, 0.04, 0.016 g/mL sodium chloride; bitter: 0.006, 0.0024, 0.0009, 0.0004 g/mL quinine hydrochloride; sour: 0.3, 0.165, 0.09, 0.05 g/mL citric acid. Tastants were solved in distilled water. During the test, participants washed their mouths with a sip of water before each taste strip. The strip was

placed in one third of the tongue. With their tongue still extended, the patients had to identify the taste from a list of four descriptors, sweet, sour, salty and bitter (multiple forced choice). The tastes were delivered with increasing concentrations in a random order. Each correct answer was given as 1 point (maximum 4 points for each taste quality score and 16 points for the overall test score). A taste score was calculated based on the number of accurately identified tastes. Taste strips provide various advantages, including a short testing period and good consistency of result (10).

Statistics

The data was analysed using SPSS version 22.0 (SPSS Inc. Chicago, IL, USA). Continuous variables were reported as mean (\bar{x}), with and standard deviation (SD), and categorical variables were expressed as number with and percentage. The normality of the variable distribution was checked with the Shapiro-Wilk test. Quantitative data was compared using the independent samples t-test. The spearman correlation coefficient was used to analyse the correlations among taste scores and variables. Multiple linear analysis was used to determine the factors related to overall taste scores. The value of $p < 0.05$ was set as statistically significant.

RESULTS

Table 1 describes the demographic characteristics and baseline measurements of the participants. The current study included 61 adults (33 men and 28 women) with a mean age of 52.39 ± 14.33 years (range from 20 to 74 years). The mean BMI of the participants was 25.38 ± 3.86 kg/m² and mean duration of type 2 diabetes was approximately 4 years. When it comes to biochemical parameters, the mean fasting blood glucose level was 171.64 ± 41.31 mg/dL and the mean HbA1c concentration was 7.59 ± 1.38%.

| | Total (n=61) $\bar{x} \pm SD$ | Men (n=33) $\bar{x} \pm SD$ | Women (n=28) $\bar{x} \pm SD$ | p |
|----------------------------|----------------------------------|--------------------------------|----------------------------------|--------|
| Age (years) | 52.39±14.33 | 49.52±14.18 | 55.79±14.00 | 0.089 |
| Weight (kg) | 71.56±12.25 | 78.43±9.48 | 63.47±10.06 | <0.001 |
| BMI (kg/m ²) | 25.38±3.86 | 26.50±3.52 | 24.05±3.88 | 0.012 |
| Duration of diabet (years) | 3.77±1.56 | 3.62±1.42 | 3.92±1.74 | 0.817 |
| FPG | 171.64±41.31 | 174.45±43.43 | 168.32±39.19 | 0.568 |
| HbA1c (%) | 7.59±1.38 | 7.26±1.34 | 7.98±1.36 | 0.043 |

BMI: Body mass index, FPG: Fasting plasma glucose, HbA1c: hemoglobin A1c

The mean taste strip scores of the participants for sweet, salty, bitter, sour and overall were 2.38 ± 0.88, 1.91 ± 0.92, 2.28 ± 0.76, 2.18 ± 1.01, 8.7 ± 1.81, respectively. Additionally, there were no statistically significant differences between taste scores and gender (all $p > 0.05$). **Table 2** displays the mean taste scores.

Table 2. Taste Scores of Participants

| | Total $\bar{x} \pm SD$ | Men $\bar{x} \pm SD$ | Women $\bar{x} \pm SD$ | P |
|--------------|---------------------------|-------------------------|---------------------------|-------|
| Taste scores | | | | |
| Sweet | 2.38±0.88 | 2.45±0.87 | 2.29±0.90 | 0.459 |
| Salty | 1.91±0.92 | 2.09±0.77 | 1.79±1.03 | 0.520 |
| Bitter | 2.28±0.76 | 2.24±0.71 | 2.32±0.82 | 0.775 |
| Sour | 2.18±1.01 | 2.33±1.08 | 2.00±0.90 | 0.201 |
| Overall | 8.70±1.81 | 9.12±1.88 | 8.21±1.62 | 0.068 |

The correlation between taste scores and investigated parameters are shown in **Table 3**. Age was significantly associated with taste score for salty ($r = -0.225$, $p = 0.041$) and sour ($r = -0.252$, $p = 0.040$). FPG and HbA1c were not associated with taste scores. Additionally, we also found that the duration of diabetes and BMI were not related to taste scores for any of the tastes.

Table 3. Correlation between taste scores and investigated parameters

| | | Sweet | Salty | Bitter | Sour |
|----------------------|---|--------|---------|--------|---------|
| Age | r | -0.174 | -0.225* | 0.096 | -0.252* |
| | p | 0.180 | 0.041 | 0.463 | 0.040 |
| BMI | r | 0.256 | 0.014 | -0.010 | 0.243 |
| | p | 0.066 | 0.916 | 0.940 | 0.059 |
| FBG | r | -0.019 | 0.082 | -0.118 | 0.209 |
| | p | 0.885 | 0.531 | 0.367 | 0.106 |
| HbA1c | r | -0.041 | -0.004 | -0.105 | -0.176 |
| | p | 0.751 | 0.978 | 0.419 | 0.175 |
| Duration of diabetes | r | 0.174 | 0.097 | 0.040 | 0.010 |
| | p | 0.179 | 0.457 | 0.758 | 0.938 |

BMI: Body mass index, FPG: Fasting plasma glucose, HbA1c: hemoglobin A1c

The multiple linear regression model was significant and could explain 8.2% of the variation in the overall taste score among the participants (**Table 4**). This analysis shows that only age had p-values smaller than 0.05, suggesting that age had a significant effect on the overall score of taste. Furthermore, the standardized β coefficients indicated that age was the independent variable with the highest explanatory power in the model (-0.280). Moreover, higher overall taste score was associated with lower age.

Table 4. Multiple linear regression model explaining variations in overall taste score

| | $\beta 1$ (%95 CI) | SE | $\beta 2$ | t | p | Zero | Partial |
|----------------------|--------------------------|-------|-----------|--------|-------|--------|---------|
| Constant | 8.478 (3.297 - 13.659) | 2.584 | | 3.281 | 0.002 | | |
| Age | -0.035 (-0.069 - -0.002) | 0.017 | -0.280 | -2.107 | 0.040 | -0.394 | -0.276 |
| Gender | -0.456 (-1.415 - 0.503) | 0.478 | -0.127 | -0.954 | 0.345 | -0.252 | -0.129 |
| BMI | 0.065 (-0.07 - 0.200) | 0.067 | 0.138 | 0.960 | 0.341 | 0.301 | 0.130 |
| FBG | 0.004 (-0.007 - 0.015) | 0.006 | 0.090 | 0.694 | 0.491 | 0.208 | 0.094 |
| HbA1c | -0.087 (-0.418 - 0.245) | 0.165 | -0.066 | -0.524 | 0.603 | -0.096 | -0.071 |
| Duration of diabetes | 0.166 (-0.118 - 0.451) | 0.142 | 0.144 | 1.173 | 0.246 | 0.135 | 0.158 |

F=2.658; $p=0.025$; Adj. $R^2=0.082$; $\beta 1$: unstandardized coefficient; $\beta 2$: standardized coefficient, BMI: Body mass index, FPG: Fasting plasma glucose, HbA1c: hemoglobin A1c

DISCUSSION

In the present investigation, the taste scores of 61 patients with T2DM were also examined taking into account gender, age, duration of diabetes, anthropometric measurements and biochemical parameters (FPG, HbA1c).

It has been extensively shown that the sense of taste plays a crucial role in the regulation of nutrient ingestion, the control of the digestive process, and the release of neuroendocrine hunger and satiety hormones. Although factors related to taste sensitivity have been studied in healthy people, patients with type 2 diabetes have reported less of these parameters. The ageing process can also lead to alterations in the sense of taste. It is generally assumed that a decrease in taste sensitivity occurs after the age of 60 years (11). In a study carried out by Pugnali et al. (12), it was shown that people with diabetes display a reduced overall taste discrimination, and the researchers also observed that the odds of success decreased by 6.5% for every additional 5 years of age. In this study, we found that age was negatively correlated with salty, sour and overall taste scores. Our findings are consistent with those of Pugnali et al. (12), who found that taste function in type decreases with age.

There is no obvious association between gender and taste sensitivity in the literature. Although many studies have reported that men were less sensitive compared to women in taste function in healthy people or cancer patients (13-15). The outcomes of studies on type 2 diabetes are contradictory. According to a study by Yu et al. (16), diabetic men are less sensitive to sweet taste than diabetic women. Some studies found that there was no significant effect of gender on differences in taste function in patients (12, 17, 18). In our study, we did not find significant differences in taste scores according to gender.

The current evidence for a relationship between BMI and taste in healthy adults is inconsistent, with some researches (19-21) finding no association, and others (22-24) suggesting a link between taste sensitivity and BMI. In a study of individuals with type 2 diabetes, it was found that there was no relationship between sucrose

supra-threshold and BMI (18). In this study, we also found that there was no association between taste scores and BMI.

Some researchers found a direct relationship between blood glucose concentration and taste (25, 26). However, according to other studies, there was no association between taste scores and HbA1c levels (12, 18, 25, 27, 28). In addition to this study, several studies (16, 18, 29, 30) revealed no association between taste and either plasma glucose or glycosylated haemoglobin concentration, confirming the findings of this study. Although the pathophysiology of taste change remains unclear in diabetic patients. In accordance with the literature (18, 28, 31, 32), although the pathogenesis of diabetic patients' taste changes is unknown, the present data demonstrate that taste sensation in type 2 diabetics is not correlated with disease duration. This may be related to additional benefit of antidiabetic drugs in reducing the progression of underlying disorders of altered taste sensitivity.

The exact underlying cause of diabetes-related taste impairment is uncertain. However, studies that examine taste function in T2DM have provided a variety of explanations for the decreased taste sensation in type 2 diabetics. First, taste impairment may be a degenerative complication of DM; due to neuropathy of the taste nerves. 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 the composition and structure (33). Second, peripheral neuropathy affecting taste nerves or microangiopathy affecting taste buds may be responsible for taste impairment, but this is unlikely in newly diagnosed diabetic patients with clinical signs of microvascular problems (34). Third, the altered taste in T2DM may be associated with a slower rate of receptor turnover (35). In addition, the possible involvement of reduced salivary flow and zinc deficiency in these individuals may be associated with reduced taste function (36). Further, an inherent or acquired defect of the taste receptor or an abnormality in the mechanism underlying the central appreciation of taste in the brain may represent additional involved mechanisms (29).

The limitations of the current study must be taken into account when interpreting its findings. In this case, the inherent limitations of the cross-sectional design cannot be overcome because causality cannot be established from an observational design. Also, the sample size is relatively small. Other limitations relate to medication use; it is essential to point out that the medications of

the participants were not documented in this study. Some studies (37-39) showed that diabetes medications (including metformin and losartan) have been linked to taste impairment. Despite limitations, the findings of this study are worthy; as it is one of the first studies to investigate effects of demographic, anthropometric, and clinical factors on taste alterations in type 2 diabetics.

CONCLUSION

The taste score for four basic taste modalities as well as the overall taste score were analysed in patients with Type 2 diabetes. It was discovered that the overall taste score of these individuals was not affected by any other confounding factors, with the exception of age. Future studies in a larger number of patients may help to better investigate the complex link between taste changes, diabetes, and related factors.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Gaziantep Islam Science and Technology University Non-interventional Clinical Researches Ethics Committee (Date: 27.09.2022, Decision No: 2022/148).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

REFERENCES

1. Perreault L, Skyler JS, Rosenstock J. Novel therapies with precision mechanisms for type 2 diabetes mellitus. *Nat Rev Endocrinol* 2021; 17: 364-77.
2. Unwin, N, Whiting, D, Guariguata, L. Diabetes Atlas. 5th ed. Brussels: International Diabetes Federation; 2012.
3. Gutierrez R, Simon SA. Chemosensory processing in the taste-reward pathway. *Flavour Fragr J* 2011; 26: 231-8.
4. Kitamura A, Torii K, Uneyama H, Nijima A. Role played by afferent signals from olfactory, gustatory and gastrointestinal sensors in regulation of autonomic nerve activity. *Biol Pharm Bull* 2010; 33: 1778-82.
5. Rolls ET. Smell, taste, texture, and temperature multimodal representations in the brain, and their relevance to the control of appetite. *Nutr Rev* 2004; 62: 193-204.
6. Bloomfield RS, Graham BG, Schiffman SS, Killenberg PG. Alterations of chemosensory function in end-stage liver disease. *Physiol Behav* 1999; 66: 203-7.

7. Barragán R, Coltell O, Portolés O, et al. Bitter, sweet, salty, sour and umami taste perception decreases with age: Sex-specific analysis, modulation by genetic variants and taste-preference associations in 18 to 80 year-old subjects. *Nutrients* 2018; 10: 1539.
8. Imoscoli A, Inelmen EM, Sergi G, Miotto F, Manzato E. Taste loss in the elderly: epidemiology, causes and consequences. *Aging Clin Exp Res* 2012; 24: 570-9.
9. Lohman TG, Roche AF, Martorell R. Anthropometric standardization reference manual. 1st ed. Champaign - IL: Human Kinetics Books; 1988. Anthropometric Standardization Reference Manual. Human Kinetics Books; 1998
10. Mueller C, Kallert S, Renner B, et al. Quantitative assessment of gustatory function in a clinical context using impregnated" taste strips". *Rhinology* 2003; 41: 2-6.
11. Mojet J, Christ-Hazelhof E, Heidema J. Taste perception with age: generic or specific losses in threshold sensitivity to the five basic tastes? *Chem Senses* 2001; 26: 845-60.
12. Pugnaloni S, Alia S, Mancini M, et al. A study on the relationship between type 2 diabetes and taste function in patients with good glycemic control. *Nutrients* 2020; 12: 1112.
13. Landis BN, Welge-Luessen A, Brämerson A, et al. "Taste Strips"—a rapid, lateralized, gustatory bedside identification test based on impregnated filter papers. *J Neurol* 2009; 256: 242-8.
14. Welge-Lüssen A, Dörig P, Wolfensberger M, Krone F, Hummel T. A study about the frequency of taste disorders. *J Neurol* 2011; 258: 386-92.
15. Vignini A, Borroni F, Sabbatinelli J, et al. General decrease of taste sensitivity is related to increase of BMI: A simple method to monitor eating behavior. *Dis Markers* 2019; 2019: 1-8.
16. Yu JH, Shin MS, Lee JR, et al. Decreased sucrose preference in patients with type 2 diabetes mellitus. *Diabetes Res Clin Pract* 2014; 104: 214-9.
17. 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.
18. Vidanage D, Prathapan S, Wasalathanthri S, Hettiarachchi P. Factors associated with sweet taste sensitivity in patients with type 2 diabetes mellitus (T2DM). *J Ruhunu Clin Soc* 2020; 25: 25-9.
19. Drewnowski A, Henderson SA, Cockcroft JE. Genetic sensitivity to 6-n-propylthiouracil has no influence on dietary patterns, body mass indexes, or plasma lipid profiles of women. *J Am Diet Assoc* 2007; 107: 1340-8.
20. Salbe AD, DelParigi A, Pratley RE, Drewnowski A, Tataranni PA. Taste preferences and body weight changes in an obesity-prone population. *Am J Clin Nutr* 2004; 79: 372-8.
21. Tucker RM, Kaiser KA, Parman MA, George BJ, Allison DB, Mattes RD. Comparisons of fatty acid taste detection thresholds in people who are lean vs. overweight or obese: a systematic review and meta-analysis. *PloS one* 2017; 12: e0169583.
22. Stewart JE, Feinle-Bisset C, Golding M, Delahunty C, Clifton PM, Keast RS. Oral sensitivity to fatty acids, food consumption and BMI in human subjects. *Br J Nutr* 2010; 104: 145-52.
23. Proserpio C, Laureati M, Bertoli S, Battezzati A, Pagliarini E. Determinants of obesity in Italian adults: the role of taste sensitivity, food liking, and food neophobia. *Chem Senses* 2016; 41: 169-76.
24. Hardikar S, Höchenberger R, Villringer A, Ohla K. Higher sensitivity to sweet and salty taste in obese compared to lean individuals. *Appetite* 2017; 111: 158-65.
25. Le Floch JP, Le Lièvre G, Sadoun J, Perlemuter L, Peynegre R, Hazard J. Taste impairment and related factors in type I diabetes mellitus. *Diabetes care*. 1989; 12: 173-8.
26. Bustos-Saldaña R, Alfaro-Rodríguez M, de la Luz Solís-Ruiz M, Trujillo-Hernández B, Pacheco-Carrasco M, Vázquez-Jiménez C. Taste sensitivity diminution in hyperglycemic type 2 diabetes patients. *Rev Med Inst Mex Seguro Soc* 2009; 47: 483-8.
27. Le Floch JP, Le Lièvre G, Labroue M, Paul M, Peynegre R, Perlemuter L. Smell dysfunction and related factors in diabetic patients. *Diabetes care* 1993; 16: 934-7.
28. Yazla S, Özmen S, Kırıyıcı S, Yıldız D, Haksever M, Gencay S. Evaluation of olfaction and taste function in type 2 diabetic patients with and without peripheral neuropathy. *Observational Study* 2018; 34: e2973.
29. Perros P, MacFarlane TW, Counsell C, Frier BM. Altered taste sensation in newly-diagnosed NIDDM. *Diabetes care* 1996; 19: 768-70.
30. Chochinov RH, Ulliyot GLE, Moorhouse JA. Sensory perception thresholds in patients with juvenile diabetes and their close relatives. *N Engl J Med* 1972; 286: 1233-7.
31. Naka A, Riedl M, Luger A, Hummel T, Mueller CA. Clinical significance of smell and taste disorders in patients with diabetes mellitus. *Eur Arch Otorhinolaryngol* 2010; 267: 547-50.
32. Weinstock RS, Wright HN, Smith DU. Olfactory dysfunction in diabetes mellitus. *Physiol Behav* 1993; 53: 17-21.
33. Latha G, Chandrashekar D, Puranik N. Altered taste threshold in chronic Type 2 diabetes mellitus. *Natl J Physiol Pharm Pharmacol* 2018; 8: 569-74.
34. Khobragade R, Wakode S, Kale A. Duration of Diabetes Mellitus and Taste Threshold. *Indian J Physiol Pharmacol* 2012; 56: 42-7.
35. Epstein F, Schiffman S. Taste and smell in disease. *N Engl J Med* 1983; 308: 1275-9.
36. Negrato CA, Tarzia O. Buccal alterations in diabetes mellitus. *Diabetol Metab Syndr* 2010; 2: 1-11.
37. Ohkoshi N, Shoji S. Reversible ageusia induced by losartan: a case report. *Eur J Neurol* 2002; 9: 315-21.
38. Schlienger R, Saxer M, Haefeli W. Reversible ageusia associated with losartan. *Lancet* 1996; 347: 471-2.
39. Lee AJ. Metformin in noninsulin-dependent diabetes mellitus. *Pharmacotherapy* 1996; 16: 327-51.