Altered Taste Sensation in Newly-Diagnosed NIDDM

PETROS PERROS, MD
T. WALLACE MACFARLANE, DSC
CARL COUNSELL, MRCP
BRIAN M. FRIER, MD

OBJECTIVE — To assess gustatory appreciation in newly diagnosed NIDDM patients and to determine whether it altered with the improvement of glycemic control after treatment with diet and oral hypoglycemic drugs.

RESEARCH DESIGN AND METHODS — Assessments of taste, peripheral and autonomic neural function, diet, and oral microbiological flora were performed in 20 patients before and after treatment of hyperglycemia, 20 matched nondiabetic control subjects, and 11 patients with long duration of diabetes and advanced peripheral neuropathy.

RESULTS — Median total HbA_1 fell from 12.6 to 8.8% in new diabetic patients after 3–5 months of treatment. Electrical taste thresholds, detection threshold for glucose, and recognition threshold for glucose and salt were increased in newly-diagnosed NIDDM patients compared with the control subjects. The dose-response curve to glucose (using a visual analogue scale [VAS]) of newly-diagnosed NIDDM patients was significantly impaired and improved after treatment. By contrast, newly-diagnosed NIDDM patients had normal VAS taste responses to fructose, salt, and urea. Measurements of somatic and autonomic nerve function did not correlate with electrical or chemical taste function.

CONCLUSIONS — Newly-diagnosed NIDDM patients have a blunted taste response, which displays a degree of specificity to glucose, is partially reversed after correction of hyperglycemia, and is independent of somatic or autonomic nerve function. This taste abnormality may influence the premorbid choice of nutrients, with a preference for sweet-tasting foods, thereby exacerbating hyperglycemia.

A common observation in newly diagnosed untreated diabetic patients is their preference for sweet drinks to quench their thirst (1). A blunted taste sensation may influence the choice of nutrients, possibly with a preference for sweet-tasting foods. Taste sensation in diabetic patients has been reported to be impaired (2–4), but most studies have used electrogustometry as the principal tool of investigation, included both IDDM and NIDDM subjects, and were cross-sectional in design.

RESEARCH DESIGN AND METHODS

— A total of 20 newly diagnosed untreated NIDDM patients (group 1) and 20 nondiabetic control subjects (group 2) matched for age, sex, and BMI were studied. A group of 11 diabetic patients (5 IDDM, 6 NIDDM) with peripheral sensory neuropathy, neuropathic foot ulceration, and duration of diabetes >10 years were also studied (group 3). In group 2, 30% were smokers and 20% in group 1. Alcohol consumption was <100 g/week. The study was approved by the local medical ethics advisory committee, and informed consent was obtained from all subjects studied. Group 1 patients were assessed at the time of diagnosis and 3–5 months later. A diet low in refined carbohydrate was prescribed, and oral hypoglycemic agents commenced in patients who failed to respond to dietary treatment alone. The detection threshold (lowest concentration of a test substance perceived as tasting different from water) and recognition threshold (lowest concentration of a test substance recognized to have a specific taste) were determined using serial dilutions of glucose, fructose, sodium chloride, and urea. In addition, a visual analogue scale (VAS) was used to quantify taste perception. The test substances were of reagent grade (Sigma, Poole, U.K.), diluted in deionized water, and served at room temperature. Subjects were tested while in the fasting state. Taste was also assessed using an electrogustometer to define the electrical taste threshold. Nerve conduction studies (using a Medelec MS 91 apparatus) and autonomic function tests (5) were performed in most group 1 and 2 subjects. Microbiological samples were collected by an oral rinse technique (6). Venous plasma glucose concentration was measured by the glucose oxidase method, and total glycated hemoglobin was measured by high pressure liquid chromatography (nondiabetic range 5–8%).

Statistical analyses

Wilcoxon's signed-rank test, Spearman's correlation, and the Kruskal-Wallis statistic were used. Results are presented as the median.

RESULTS

— Patients in group 1 had elevated median venous plasma glucose concentrations (12.2 mmol/l) and total HbA_1 (12.6%), both of which fell after treatment to 7.4 mmol/l and 8.8%, respectively. Diet alone was effective in 25% of patients, the remainder required oral hypoglycemic agents.

Electrical taste threshold was increased in group 1 compared with group 2 (127 vs. 46.5 μA, $P < 0.05$) and was comparable to that of group 3 (149 μA). Detection thresholds for glucose (0.32 vs. 0.16 mol/l, $P < 0.05$) and recognition thresholds for glucose (0.46 vs. 0.32 mol/l, $P < 0.05$) and salt (0.079 vs. 0.040 mol/l, $P < 0.05$) were elevated in group 1

From the Department of Diabetes (P.P., B.M.F.), Royal Infirmary, Edinburgh; Department of Oral Microbiology (T.W.M.), Glasgow Dental Hospital and School, Glasgow; and the Department of Clinical Neurosciences (C.C.), Western General Hospital, Edinburgh, Scotland.

Address correspondence and reprint requests to P. Perros, MD, Department of Diabetes, Royal Infirmary, Edinburgh EH3 9YW, Scotland.

Received for publication 6 October 1995 and accepted in revised form 7 March 1996.

VAS, visual analogue scale.

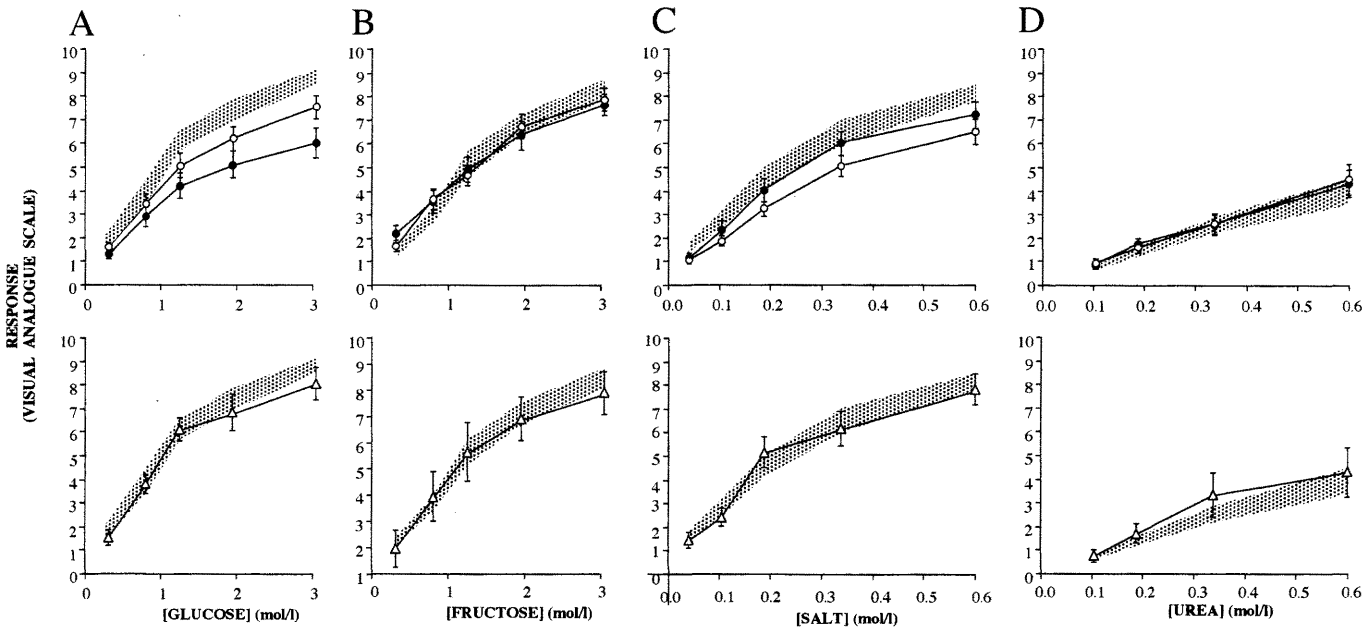

Figure 1—*Upper panels show VAS responses of group 1 before (●) and after (○) treatment for hyperglycemia to increasing concentrations of test substance. The lower panels (△) show the responses of group 3. The responses of group 2 are superimposed as a shaded area for comparison (± 1 SE above and below the mean). Response to glucose (A), response to fructose (B), response to salt (C), response to urea (D). Statistics: group 1 before treatment vs. group 2, P < 0.05; group 1 before treatment vs. group 1 after treatment, P < 0.05.*

compared with group 2. Group 3 had elevated detection thresholds for glucose (0.32 vs. 0.16 mol/l, $P < 0.05$) and recognition thresholds for glucose (0.60 vs. 0.32 mol/l, $P < 0.05$) and salt (0.079 vs. 0.040 mol/l, $P < 0.05$) compared with group 2. The VAS response of group 1 to glucose was significantly impaired compared with group 2 ($P < 0.05$) and improved after treatment ($P < 0.05$), although it remained significantly subnormal (Fig. 1, $P < 0.05$). By contrast, group 1 had normal VAS taste responses to fructose, salt, and urea, which remained so after glycemic control had been improved, with the exception of the response to salt, which deteriorated after treatment ($P < 0.05$). The VAS responses of group 3 were not significantly different from group 2.

Group 1 had slower nerve conduction velocities in the lower limbs than group 2 (common peroneal nerve motor velocity 41 [$n = 14$] vs. 52 m/s [$n = 7$], $P < 0.05$; sural nerve sensory velocity 39 [$n = 14$] vs. 44 m/s [$n = 7$], $P < 0.05$). Autonomic scores were similar between groups 1 and 2 and did not correlate with measurements of taste function either before or after treatment of hyperglycemia.

Clinical evidence of oral candidiasis was present in 25% of patients in group 1 and in none of the patients in group 2. The number of individuals who carried *Candida* was similar in both groups 1 and 2. Counts of bacteria and yeasts from oral rinses were similar between groups 1 and 2 and did not change significantly after treatment of hyperglycemia.

CONCLUSIONS— The present study has demonstrated that taste is impaired in patients with newly-diagnosed NIDDM. The gustatory defect appeared to be specific for glucose and improved after correction of hyperglycemia. Care was taken to match the experimental group closely with a nondiabetic control group. In addition to electrogustometry and assessment of the detection and recognition thresholds of chemical taste sensation (these being the methods used commonly to assess taste in previous studies), suprathreshold concentrations of chemical stimulants were used to study intermediate and maximal responses. Using a VAS, a pronounced gustatory defect for glucose was apparent in group 1 and improved after correction of hyperglycemia. All of the other taste modalities tested were normal with the exception of the chemical recognition threshold for salt, which was significantly elevated in group 1. It is possible that subtle defects in taste perception of other modalities may exist, which may have become apparent in a larger sample. However, a consistent abnormality was observed in chemical detection and recognition thresholds as well as the VAS response for glucose and strongly suggests that a relatively specific gustatory defect for glucose is present in untreated NIDDM patients. A novel finding of the present study was the partial reversibility of this gustatory abnormality after treatment of the diabetes. Previous studies in diabetic patients (7,8) have shown that taste impairment measured by electrogustometry correlates with the duration of diabetes and the presence of peripheral neuropathy. The present study confirmed elevated electrical and chemical thresholds for taste in neuropathic patients, but the VAS responses were preserved and were comparable to the group of nondiabetic control subjects, demonstrating a partial dissociation between electrical and chemical taste modalities.

The underlying cause of taste impairment in diabetes is unknown but could include an inherent or acquired defect of the taste receptor, peripheral neuropathy, or an abnormality of the mechanism underlying the central appreciation of taste within the brain. No correlation was found between any of the taste parameters measured and either the fasting plasma glucose or the glycated hemoglo-

bin concentration. A direct effect of blood glucose concentration on taste is therefore unlikely, which is consistent with previous reports (2,7). Peripheral neuropathy involving the taste nerves or microangiopathy involving the taste buds may be responsible for the taste impairment (8), but such a mechanism is unlikely in newly-diagnosed patients with NIDDM who have no clinical evidence of microvascular complications. An alternative hypothesis is that the glucose taste receptor may be inherently defective in NIDDM. A generalized defect in glucose sensing involving both the taste receptor and the pancreatic β-cell in NIDDM has been proposed (9,10), and the present study is consistent with this hypothesis, although the partial reversibility of this defect suggests that other factors may also contribute. A modulatory effect of the dietary intake of refined sugar on taste is a further possibility. Reduction of dietary refined carbohydrate was a fundamental part of the treatment prescribed in the newly-diagnosed NIDDM patients. However, no correlation was observed between any of the taste parameters measured and the amount of simple sugars consumed. An alteration in the oral flora might also have had an influence on taste perception, but no significant differences in the bacterial and fungal counts were demonstrated between the diabetic and nondiabetic subjects (a higher candidal count was present in diabetic patients compared with control subjects but did not reach statistical significance).

Smoking is a known factor that is associated with impaired taste function (11). Current smokers among the newly-diagnosed NIDDM patients performed worse on taste assessments than ex-smokers and current smokers, though these differences did not reach statistical significance. Smoking may have contributed to the impaired taste function of newly-diagnosed NIDDM patients described in this study; however, it is unlikely that this was a major influence because the taste defect identified in these patients was glucose-specific, and partial reversibility was demonstrated after treatment of hyperglycemia, while smoking habits remained unchanged.

A blunted taste for sweet foods may explain the craving for refined carbohydrate that is experienced by some untreated diabetic patients. This may result in the increased ingestion of sweet food and beverages and so worsen the hyperglycemia.

Acknowledgments— We wish to thank the Scottish Hospitals Endowments Research Trust for financial support.

We also wish to thank L. Clutton for dietetic assessments and D. Terrace, Medical Physics, Department of Medicine, Royal Infirmary of Edinburgh, for technical assistance.

References

1. Lean MEJ, Mann JI: Obesity, body fat distribution and diet in the aetiology of non-insulin dependent diabetes mellitus. In *Textbook of Diabetes*. Pickup JC, Williams G, Eds. Oxford, U.K., Blackwell Scientific Publications, 1992, p. 181–191
2. Chochinov RH, Ullyot LE, Moorhouse JA: Sensory perception thresholds in patients with juvenile diabetes and their close relatives. *N Engl J Med* 286:1233–1237, 1972
3. Le Mouel C, Oliva A, Giry P, Angot A, Renon P: Electrogustometric threshold in diabetes and chronic ethylism. *Ann Oto Laryngol* 94:715–724, 1977
4. Lawson WB, Zeidler A, Rubenstein A: Taste detection and preferences in diabetics and their relatives. *Psychosom Med* 41: 219–227, 1979
5. Wing DJ, Martyn CN, Young RJ: The value of cardiovascular autonomic function tests: 10 years experience in diabetes. *Diabetes Care* 8:491–498, 1985
6. Samaranayake LP, MacFarlane TW, Lamey PG, Ferguson MM: A comparison of oral rinse and imprint sampling techniques for the detection of yeast, coliform and Staphylococcus Aureus carriage in the oral cavity. *J Oral Pathol* 15:386–388, 1986
7. Le Floch JP, Le Lievre G, Verroust J, Philippon C, Peynegre R, Perlemuter L: Factors related to electric taste threshold in type 1 diabetic patients. *Diabetic Med* 7:526–531, 1990
8. Le Floch JP, Le Lievre G, Labroue M, Peynegre R, Perlemuter L: Early detection of diabetic patients at risk of developing degenerative complications using electric gustometry: a five-year follow-up study. *Eur J Med* 1:208–214, 1992
9. Robertson RP, Porte DJ: The glucose receptor: a defective mechanism in diabetes mellitus distinct from the beta adrenergic receptor. *J Clin Invest* 52:870–876, 1973
10. Niki A, Niki H: Is diabetes mellitus a disorder of the glucoreceptor? *Lancet* ii:658, 1975
11. Redington K: Taste differences between cigarette smokers and non-smokers. *Pharmacol Biochem Behav* 21:203–208, 1984