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Comparative study of the concentration of salivary and blood glucose in type 2 diabetic patients

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Abstract: The objective of the present study was to comparatively evaluate the concentrations of blood and salivary glucose as well as salivary flow and xerostomia in type 2 diabetic and non-diabetic patients. The mean salivary glucose level in diabetic patients was 14.03 ± 16.76 mg/dl and 6.35 ± 6.02 mg/dl (*P* = 0.036) in the control group. The mean capillary blood glucose level in diabetic patients was 213 ± 88 mg/dl, while that in non-diabetic patients was 99 ± 14 mg/dl (*P* = 0.000). The mean value for resting salivary flow was 0.21 ± 0.16 ml/min in diabetic patients and 0.33 ± 0.20 ml/min in the control group (*P* = 0.002). The stimulated salivary flow was lower in the group of diabetic patients, with a mean of 0.63 ± 0.43 ml/min, whereas the control group showed a mean of 1.20 ± 0.70 ml/min (*P* = 0.000). Of the diabetic patients, 45% exhibited hyposalivation, in contrast to 2.5% of the non-diabetic patients (*P* = 0.000). Xerostomia was reported in 12.5% of diabetic patients and 5% of non-diabetic patients (*P* = 0.23). We can conclude that salivary glucose concentration was significantly higher in the experimental group and that there was no correlation between salivary and blood glucose concentrations in diabetic patients. The total salivary flow was significantly reduced in diabetic patients and there was no significant difference as to the presence of xerostomia in both groups. (J Oral Sci 52, 293-298, 2010)

Keywords: salivary glucose; type 2 diabetes mellitus; xerostomia.

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Introduction

Diabetes mellitus (DM) is an endocrine disease characterized by a deficit in the production of insulin with consequent alteration of the process of assimilation, metabolism and balance of blood glucose concentration. It is classified, according to its etiology, as type 1 or 2 (1,2). Type 1 results in the destruction of the beta cells of the pancreas causing absolute deficiency of insulin, while type 2 results from cellular dysfunction in resistance to insulin by peripheral tissues (1,3,4).

Saliva is an organic fluid that can indicate local and systemic alterations, such that the components of saliva can be related to the hormonal, immunologic, neurologic, nutritional and metabolic state of the individual (5).

Glucose is a small molecule capable of moving easily through the membranes of blood vessels, passing from the blood plasma to the gingival fluid, via the gingival sulcus, reaching the saliva (6). The increase in blood glucose in the diabetic patient could cause higher levels of salivary glucose with the consequent loss of homeostasis and greater susceptibility to diseases in the oral cavity. The literature, however, shows controversial findings with

regard to the comparative values of blood and salivary glucose. There are reports affirming that individuals with elevated levels of blood glucose show oral alterations such as greater incidence of caries (7-9), periodontal disease (9), and candidosis (10).

The present research was proposed to conduct a comparative analysis of the concentrations of salivary glucose and capillary blood glucose, salivary flow and xerostomia in type 2 diabetic patients and non-diabetic patients. Considering the worldwide increase in the incidence of diabetes mellitus, research directed towards the measurement of glucose by simple and non-invasive methods, such as collecting saliva, may be useful in the diagnosis of diabetes, thereby improving the quality of life of these individuals. Furthermore, there is a lack of consensus among authors who have evaluated salivary flow and composition in diabetic individuals and a scarcity of studies regarding this subject.

Materials and Methods

The present study was submitted for evaluation to the Research Ethics Committee of the Centro de Ciências da Saúde da Universidade Federal da Paraíba, being approved under review number 55/06/07.

A total of 80 adults, of both sexes, seen in the Endocrinology Service of the Center for Specialized Medical Care (CAME) and in the Stomatology Clinic of the School of Dentistry of the Universidade Federal of Paraíba (UFPB), both located in the municipality of João Pessoa, Paraíba were selected. The sample was divided into two groups: experimental, including 40 adults with type 2 diabetes, and control, consisting of 40 non-diabetic adults, similar in sex ratio and age.

To be included in the experimental group, the patients needed to be diabetic, and in the control group, nondiabetic. Excluded from the study were those who smoked, those suffering from alcoholism, pregnant women, edentulous individuals, those who had prior surgery of the salivary glands, those being treated with radiotherapy of the head and neck region, and those with Sjogren syndrome, rheumatoid arthritis or lupus erythematosus.

To determine the resting and stimulated salivary flow, saliva was collected in the morning, between 08:00 and 11:00, with the patient not having eaten or exercised any oral hygiene 90 min before the procedure. Hyposalivation was diagnosed as when the values obtained for resting salivary flow (RSF) and stimulated salivary flow (SSF) were equal to or less than 0.1 ml/min and 0.5 ml/min, respectively, in accordance with Sreebny and Valdini (11). The rates for total resting salivary flow were determined according to the technique of salivary expectoration proposed by Navazenh et al. (12) and Fox et al. (13). The collected saliva was stored frozen until use in the glucose assay (12,13).

Salivary glucose level was determined in saliva samples that were thawed and centrifuged. A pipette was used to transfer 10 µl of the supernatant into previously numbered Eppendorf tubes. Next, 1 ml of enzyme reagent was added to each tube containing saliva. Three standard solutions were prepared, mixing them with the enzyme reagent of the glucose test kit (Glucose Liquicolor, in Vitro Diagnostica, Itabira, MG, Brazil), along with a blank solution composed of only enzyme reagent. The standard solution was used to calculate the level of salivary glucose. The purpose of the blank solution was to zero the spectrophotometer. After preparation of the tubes, they were mixed for a few seconds with a vibrator, in order to homogenize the saliva and enzyme reagent. After mixing well, the samples, standards and blank were incubated in a warm-water bath at 37°C for 5 min.

The salivary glucose assay mixtures were transferred to 1.5-ml cuvettes, and the absorbance was read with a spectrophotometer, at a wavelength of 500 nm. After each reading, the sample was discarded and the cuvette was rinsed thrice with distilled water and wiped dry with fine lens paper.

The subjective experience of dry mouth was diagnosed using the question: "Does your mouth feel dry frequently?" (13).

Peripheral glycemia was determined at random. The pulp of the index finger of the patient was cleaned with cotton soaked in 70% alcohol, and a disposable sterile needle was then used to puncture the skin and obtain a drop of blood with slight finger pressure. The blood was collected on a glucose test strip (One touch ultra, Johnson & Johnson, São Paulo, SP, Brazil), which was inserted in the respective glucosemeter. The reading of the blood glucose level determined by the glucosemeter was expressed in mg/dl, and the values were recorded on specific patient charts. Peripheral blood glucose levels were considered normal between 70 and 140 mg/dl, for random monitoring. A schematic of the study design is shown in Fig. 1.

The information was organized and analyzed in an electronic databank, in the Statistical Package for the Social Sciences (SPSS) version 12.0 for Windows. Due to the characteristics of the study, the data were evaluated by statistical techniques for descriptive analysis, and the Mann-Whitney and Spearman correlation tests were applied, with the level of significance set at 5%.

Results

As shown in Table 1, in both experimental and control

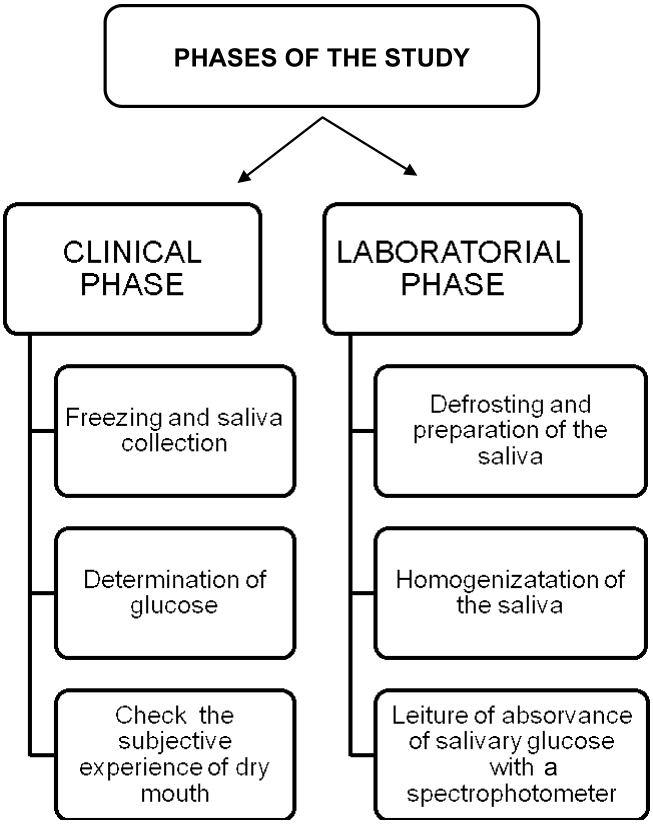

Fig. 1 A schematic of the study design.

Table 1 Distribution of the groups studied according to sex and age of the patients

	Experimental group	Control group
Male	20	20
Female	20	20
Age	57.7 ± 8.9	50.2 ± 12.3

Table 2 General characteristics of the groups studied

	Experimental group	Control group	*P* value
Salivary glucose (mg/dl)	14.03 ± 16.76	6.35 ± 6.02	0.036*
Capillary blood glucose (mg/dl)	213 ± 88	99 ± 14	0.000*
Salivary flow/resting (ml/min)	0.21 ± 0.16	0.33 ± 0.20	0.002*
Salivary flow/stimulated (ml/min)	0.63 ± 0.43	1.20 ± 0.70	0.000*
Hyposalivation	18 (45%)	1 (2.5%)	0.000*
Xerostomia	5 (12.5%)	2 (5%)	0.23

* Statistically significant difference

groups, 50% of patients were females and 50% males. The mean age of the experimental group was 57.7 ± 8.9 years, and the mean age of the control group was 50.2 ± 12.3.

As shown in Table 2, the mean salivary glucose concentration for the experimental group was 14.03 ± 16.76 mg/dl and in the control group, 6.35 ± 6.02 mg/dl,

a statistically significant difference ($P = 0.036$). In relation to blood glucose, the experimental group exhibited a mean of 213 ± 88 mg/dl, while the mean of the control group was 99 ± 14 mg/dl; also a statistically significant difference ($P = 0.000$). No statistically significant association was found between the salivary and capillary blood glucose in both experimental and control groups. The mean resting salivary flow was 0.21 ± 0.16 ml/min in the experimental group and 0.33 ± 0.20 ml/min in the control group; a statistically significant difference ($P = 0.002$). Mean stimulated salivary flow was 0.63 ± 0.43 ml/min in the experimental group and 1.20 ± 0.70 ml/min in the control group; also a statistically significant difference ($P = 0.000$). It was also observed that 45% of patients in the experimental group and, one individual, or 2.5% of the non-diabetic group showed hyposalivation, a difference that was statistically significant ($P = 0.000$). With regard to xerostomia, 12.5% of patients in the experimental group and 5% of the non-diabetic individuals reported the symptom of dry mouth, without any statistically significant difference ($P = 0.23$).

Discussion

The use of saliva as a diagnostic resource has recently prompted studies aimed at determining characteristics of normality. There is a possibility of saliva substituting for blood in some laboratory tests, for example, in determining glycemia in the monitoring of diabetes mellitus, thereby being a non-invasive procedure and allowing multiple sampling (14-16). As glucose concentration is elevated in diabetics, it is important to compare the levels of salivary and blood glucose in diabetic patients and non-diabetic individuals.

In the present study, we found that the concentration of salivary glucose in diabetic patients was significantly higher than in non-diabetic individuals. This result is in agreement with that obtained by Aydin (14), Ben-Ayred et al. (17) and Carda et al. (18), who similarly evaluated salivary glucose levels in type 2 diabetic patients and non-diabetics. However, there is divergence with respect to absolute values determined for salivary glucose concentration. It is believed that such differences can be due to differences in methods utilized to determine glucose and in saliva collection.

The correlation between the level of capillary blood glycemia and concentration of salivary glucose was not observed in the present study. This finding corroborates those of Ben-Aryeh et al. (17), Carda et al. (18) Forbat et al. (19) and Kjellman (20). However, it differs from the results of Karjalainen et al. (10) and Reuterving et al. (21) in studies conducted in diabetic children from whom saliva was stimulated from the parotid glands, showing a correlation between salivary glucose concentration and glycemia. Kjellman (20) affirmed the existence of a significant correlation between the concentration of glucose in gingival fluid and glycemia in diabetic patients. The disparities shown here are evidence that the monitoring of glycemia in saliva of diabetic patients is not a viable option.

Karjalainen et al. (10), Carda et al. (18), Reuterving et al. (21) and Bernardi et al. (22) demonstrated that the level of salivary glucose is augmented only when the concentration of glucose in blood is elevated. Carda et al. (18) observed that only diabetic individuals with fasting glycemia of 180 mg/dl and glycosylated hemoglobin higher than 8%, showed elevated salivary glucose, compared to those patients with poor metabolic control. In the present study, glycosylated hemoglobin was not determined.

In the literature, there is considerable disagreement regarding the effect of diabetes mellitus in relation to salivary flow rates. However, various explanations are cited for the possible reduction of salivary flow in diabetic individuals. Carda et al. (18) affirmed that the decrease in salivary flow in diabetic patients is caused by the increase in diuresis which, in turn, is related to a marked reduction in extracellular fluid directly affecting salivary production. Multiple physiologic factors can contribute to the compromise of salivary function in diabetic adults with poor metabolic control. As a result of metabolic dysregulation, diabetes mellitus often causes hormonal, microvascular and neuronal alterations which compromise the functionality of various organs (3). Microvascular alterations are capable of compromising the ability of salivary glands to respond to neural or hormonal stimulation. Besides, as salivary secretion is controlled by the autonomic nervous system, it is possible that neuropathy can interfere with the ability of an individual to respond to stimulation of the salivary glands, altering salivary flow and composition (23).

In the present work, total salivary flow, resting and stimulated, was significantly lower in the diabetic group compared to the control group. These results corroborate those of Lin et al. (24), Mata et al. (15) and Chavez et al. (3), but diverge from those reported by Aydin (14), Dodds and Dodds (4), Meurman et al. (25) and Soares et al. (26).

The divergence among the results of studies evaluating total salivary flow in diabetics can be explained by differences in the methods employed in collection of saliva, by the variation in age of the subjects studied, and also the different level of metabolic control in diabetic patients (24). In addition, diabetic patients frequently make use of medications capable of interfering in the stimulation of salivary gland secretion (26). In the present

study, we did not determine the influence of medication use on salivary secretion in diabetic patients.

In the present work, diabetic patients were found to show a statistically greater percentage of hyposalivation compared to non-diabetic patients. This finding confirms the marked reduction in salivary flow in these diabetic individuals, of around 45 to 50%, and reflects the presence of salivary gland dysfunction (14).

With respect to the presence of xerostomia, no statistically significant difference was observed between the diabetics and control subjects. The percentage of xerostomia found in the sample of the present study was similar to that observed by Meurman et al. (25). However, it was much lower that that determined by Ben-Aryeh et al. (17) and Carda et al. (18). In the evaluation of these differences, the presence of xerostomia could be influenced by characteristics such as age and psychological condition of the group studied, as well as a collateral effect related to the use of drugs and controlled medications (27).

As the number of diabetes mellitus patients has been increasing recently compared to metabolic syndrome, a simple and non-invasive screening examination should be used universally and the present study contributes to broadening the understanding of the field of blood glucose monitoring. When an easier method than self monitoring of blood glucose is evaluated as reasonable, the diabetes mellitus patients will be free from some burden. Thus, a saliva glucose method and/or modality would be helpful. The relationship between period, glycated hemoglobin (HbA1c), xerostomia subjective complaint and salivary glucose concentrations should be evaluated in further studies.

Based on the results obtained in the present study, it can be concluded that: 1) diabetes influences the concentration of salivary glucose; 2) salivary glucose is not directly influenced by glycemia, and thus cannot be used to monitor glycemic control in diabetics; 3) diabetes causes hyposalivation; 4) The relationship between period, glycated hemoglobin, xerostomia subjective complaint and salivary glucose concentrations should be evaluated in further studies.

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References

1. Motta M, Bennati E, Ferlito L, Passamonte M, Malaguarnera M (2007) Value and significance of new diagnostic criteria of diabetes mellitus in older. Arch Gerontol Geriatr 45, 103-108.
2. Soares MS, Batista-Filho MM, Pimentel MJ, Passos IA, Chimenos-Küstner E (2009) Determination of salivary glucose in healthy adults. Med Oral Patol Oral Cir Bucal 14, e 510-513.
3. Chavez EM, Taylor GW, Borrell LN, Ship JA (2000) Salivary function and glycemic control in older persons with diabetes. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 89, 305-311.
4. Dodds MW, Dodds AP (1997) Effects of glycemic control on saliva flow rates and protein composition in non-insulin-dependent diabetes mellitus. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 83, 465-470.
5. Carlson GW (2000) The salivary glands. Embryology, anatomy, and surgical applications. Surg Clin North Am 80, 261-273.
6. Belazi MA, Galli-Tsinopoulou A, Drakoulakos D, Fleva A, Papanayiotou PH (1998) Salivary alterations in insulin-dependent diabetes mellitus. Int J Paediatr Dent 8, 29-33.
7. Jones RB, McCallum RM, Kay EJ, Kirkin V, McDonald P (1992) Oral health and oral health behaviour in a population of diabetic outpatient clinic attenders. Community Dent Oral Epidemiol 20, 204-207.
8. Pohjamo L, Knuuttila M, Tervonen T, Haukipuro K (1988) Caries prevalence related to control of diabetes. Proc Finn Dent Soc 84, 247-252.
9. Twetman S, Johansson I, Birkhed D, Nederfors T (2002) Caries incidence in young type 1 diabetes mellitus patients in relation to metabolic control and caries-associated risk factors. Caries Res 36, 31-35.
10. Karjalainen KM, Knuuttila ML, Käär ML (1996) Salivary factors in children and adolescents with insulin-dependent diabetes mellitus. Pediatr Dent 18, 306-311.
11. Sreebny LM, Valdini A (1988) Xerostomia. Part I: relationship to other oral symptoms and salivary glan hypofunction. Oral Surg Oral Med Oral Pathol 66, 451-458.
12. Navazesh M, Brightman VJ, Pogoda JM (1996) Relationship of medical status, medications, and salivary flow rates in adults of different ages. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 81, 172-176.
13. Fox PC, Busch KA, Baum BJ (1987) Subjective reports of xerostomia and objective measures of

salivary gland performance. J Am Dent Assoc 115, 581-584.
14. Aydin S (2007) A comparison of ghrelin, glucose, alpha-amylase and protein levels in saliva from diabetics. J Biochem Mol Biol 40, 29-35.
15. Mata AD, Marques D, Rocha S, Francisco H, Santos C, Mesquita MF, Singh J (2004) Effects of diabetes mellitus on salivary secretion and its composition in the human. Mol Cell Biochem 261, 137-142.
16. Di Gioia ML, Leggio A, Le Pera A, Liguori A, Napoli A, Siciliano C, Sindona G (2004) Quantitative analysis of human salivary glucose by gas chromatography-mass spectrometry. J Chromatogr B Analyt Technol Biomed Life Sci 801, 355-358.
17. Ben-Aryeh H, Serouya R, Kanter Y, Szargel R, Laufer D (1988) Salivary composition in diabetic patients. J Diabetic Complications 2, 96-99.
18. Carda C, Mosquera-Lloreda N, Salom L, Gomez de Ferraris ME, Peydró A (2006) Structural and functional salivary disorders in type 2 diabetic patients. Med Oral Patol Oral Cir Bucal 11, E309-314.
19. Forbat LN, Collins RE, Maskell GK, Sönksen PH (1981) Glucose concentrations in parotid fluid and venous blood of patients attending a diabetic clinic. J R Soc Med 74, 725-728.
20. Kjellman O (1970) Secretion rate and buffering action of whole mixed saliva in subjects with insulin-treated diabetes mellitus. Odontol Revy 21, 159-168.
21. Reuterving CO, Reuterving G, Hägg E, Ericson T (1987) Salivary flow rates and salivary glucose concentration in patients with diabetes mellitus influence of severity of diabetes. Diabete Metab 13, 457-462.
22. Bernardi MJ, Reis A, Loguercio AD, Kehrig R, Leite MF, Nicolau J (2007) Study of the buffering capacity, pH and salivary flow rate in type 2 well-controlled and poorly controlled diabetic patients. Oral Health Prev Dent 5, 73-78.
23. Dodds MW, Yeh CK, Johnson DA (2000) A Salivary alterations in type 2 (non-insulin-dependent) diabetes mellitus and hypertension. Community Dent Oral Epidemiol 28, 373-381.
24. Lin CC, Sun SS, Kao A, Lee CC (2002) Impaired salivary function in patients with noninsulin-dependent diabetes mellitus with xerostomia. J Diabetes Complications 16, 176-179.
25. Meurman JH, Collin HL, Niskanen L, Töyry J, Alakuijala P (1998) Saliva in non-insulin-dependent diabetic patients subjects: the role of the autonomic nervous system. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 86, 69-76.
26. Soares MSM, Passos IA, Maia RMF, Costa LM, Veloso DJ (2004) Salivary flow and consumer of drugs in elderly diabetic patients. Arquivos em Odontologia 40, 101-110. (in Portuguese)
27. Sreebny LM, Yu A, Green A, Valdini A (1992) Xerostomia in diabetes mellitus. Diabetes Care 15, 900-904.