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Stimulated and Unstimulated Saliva Glucose and Flow Rate in Children with Type 1 Diabetes Mellitus

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ABSTRACT

Background and Objective: The level of fasting blood sugar (FBS) must be regularly monitored in diabetic patients. Unlike blood, saliva sampling is a noninvasive technique, saliva glucose was evaluated in controlled and uncontrolled type 1 diabetes mellitus (T_1DM) children in this study.

Methods: In this cross-sectional study, 40 uncontrolled T_1DM and 40 controlled T_1DM children were enrolled. The FBS and stimulated and unstimulated saliva glucose was assayed by the GOD-POP method and analyzed by an unpaired Student's t-test.

Findings: Serum and stimulated saliva glucose levels were higher in the uncontrolled T_1DM than that in the controlled T_1DM. However, there was no significant difference in unstimulated saliva between the two groups. Serum glucose had a positive correlation with unstimulated ($r=0.403$; $p<0.001$) and stimulated ($r=0.232$; $p=0.005$) salivary glucose levels. The stimulated and unstimulated salivary flow rate was significantly lower in uncontrolled T_1DM.

Conclusion: Stimulated salivary glucose level similar to serum was higher in uncontrolled T_1DM than in controlled T_1DM children. Therefore, it may be suitable as an alternative for serum glucose to monitor T_1DM patients.

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Introduction

Diabetes is a type of metabolic disorder [1]. Type 1 diabetes mellitus (T_1DM) is called insulin-dependent diabetes mellitus [2]. The average annual incidence of T_1DM is increasing. The disease begins most often between the ages of 7 and 15 years, although it can occur at any age. No preventative factors for T_1DM are known yet. The annual incidence of T_1DM in Iran is estimated at 3.7 cases per 100,000 people [3]. Important complications of diabetes that can be mentioned are neuropathy, nephropathy, ocular and coronary heart disease [4].

To minimize the risk of an illness, the level of glucose in diabetic patients must be monitored regularly; taking blood samples from the patient is one of the most common methods for controlling the level of blood sugar, which is a stressful and invasive technique. On the other hand, some patients have hemorrhagic and coagulation complications that can make it difficult to get blood from them [5, 6]. In recent years, researchers introduced oral fluids as a tool for assessing health and disease status [7-9]. Diagnosis of the disease through saliva analysis can be especially important for children and the elderly, as saliva collection is less difficult than blood sample collection [6]. Studies have shown that serum glucose level in patients with uncontrolled diabetic children is significantly higher than that in controlled diabetic children [10, 11]. It has been shown that the level of glucose in the saliva of children with diabetes is greater than in healthy children [12-14]. The aim of this study was to obtain a correlation between blood glucose and saliva glucose in children with uncontrolled and children with controlled T_1DM to assess whether saliva glucose may indicate the severity of the disease to help for follow up of T_1DM.

Methods

Study design and subjects

In a cross/sectional study 40 uncontrolled T_1DM [glycated hemoglobin (HbA1c) values between 7.5 and 11.0% or fasting blood sugar greater than 200 mg/dl], and 40 controlled T_1DM children, who were conducted to the children's hospital medical center of Tehran University of Medical Sciences, were enrolled. Patients were free from any other systemic illness, did not have any other obvious oral lesion, and were not previously treated for any salivary gland disorder.

After giving explanations on the implementation of the plan, written consent was obtained from the parents. Demographic characteristics and medical history of patients were recorded.

Data collection

Saliva and blood were taken between 8-11 am in a fasting state. Blood samples (2.5cc) were taken by laboratory experts and poured into 2 tubes for measuring blood glucose and the percentage of HbA1c. Unstimulated saliva samples of patients were collected by spitting method in a microtube. For stimulated saliva samples, patients were requested to chew a piece of sugar-free chewing gum for 2 minutes and swallow saliva. After 2 minutes, drain the saliva into another microtube. The flow rate was calculated as saliva volume (ml) divided into the duration of saliva sampling (minute). Serum and saliva samples were frozen at -20°C to measure glucose by the Enzymatic colorimetric GOD-PAP method and HbA1c by the immunoturbidimetric method using a photometer and attributed kits (Pars Azmun, Karaj, Iran), according to the manufacturer's instruction.

Statistical Analysis

Mean ± standard error mean (SEM) has been used to show the results of the research on quantitative variables with normal distribution. Statistical analysis was performed by unpaired Student's t-test. Pearson correlation analysis was used to evaluate the correlation between serum and salivary glucose. In all analyses, the significance of the results is P-value < 0.05.

Results

There was no significant difference in sex between uncontrolled (15 boys, 25 girls) and controlled (12 boys, 28 girls) T_1DM children and

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also in age between controlled (9.3±2.0) and uncontrolled (10.0±2.4) T_1DM children (P >0.05).

The mean serum glucose and HbA1c levels were higher in the uncontrolled T_1DM than that in the controlled T_1DM (table1). Mean stimulated salivary glucose level was lower in the controlled T_1DM than that in the uncontrolled T_1DM (Table1). However, there was no significant difference between the two groups in mean unstimulated salivary glucose levels (Table1). The present study revealed positive correlations between serum glucose level and unstimulated salivary glucose level (r=0.403; p<0.001) and also between serum glucose level and stimulated salivary glucose level (r=0.232; p=0.005). A significantly positive correlation was observed between serum glucose level and serum HbA1c level (r=0.609; p<0.001).

Stimulated and unstimulated salivary Flow rate levels were greater in controlled T_1DM compared to uncontrolled T_1DM (table1).

Table 1. Serum and saliva levels of glucose, HbA1c; and saliva flow rate in uncontrolled and controlled type 1 diabetes mellitus (T_1DM)

Variables	Uncontrolled T_1DM	Controlled T_1DM	P value
Fasting blood sugar (FBS) (mg/dL)	265.6±15.9	186.4±14.8	0.0001*
Unstimulated saliva glucose (mg/dL)	8.9±3.7	8.4±2.2	0.319
Stimulated saliva glucose (mg/dL)	9.2±2.3	2.5±0.4	0.0001*
Blood HbA1c (%)	11.2±0.6	7.1±0.2	0.0001*
Unstimulated saliva flow rate (ml/min)	0.15±0.02	0.18±0.01	0.040*
Stimulated saliva flow rate (ml/min)	0.19±0.01	0.22±0.01	0.045*

Data are expressed as mean ± standard error of the mean (SEM); P < 0.05

Discussion

Current study showed that stimulated salivary glucose level similar to serum was higher in uncontrolled T1DM than controlled T1DM children. Many studies conducted on diabetic people are mostly related to adults; however, there are few reports about children [10, 12-14]. In the current study, we studied two groups of controlled and uncontrolled T_1DM. The results showed that saliva and serum levels of glucose were higher in uncontrolled T1MD children, which is in agreement with the results of Panchbhai et al. [11] and Harrison et al. [10].

In the ongoing study, there was a great correlation between serum glucose and salivary glucose. This correlation was found in the study of Satish et al., also in the study of Panchbhai et al., and other previous studies [5, 11, 14-18]. In the study of Gupta et al., which evaluated the relationship between glucose and saliva in diabetic patients in 2015, this correlation was not present [6]. The probability of not having a relationship in this study may be due to the use of a blood glucometer for measuring blood and it has a low accuracy than our measurement method. Also, a study by Aydin S, showed that salivary glucose was measured by glucose oxidase in 40 diabetic patients and 20 healthy patients and found no significant association between salivary glucose and blood glucose [19]. This may have been due to the low sensitivity of the glucose test kit. The study of Abikshyeet et al. reported a very significant relationship between HbA1c levels and salivary glucose, which was similar to the current study results [20]. Moreover, similar results were obtained in studies conducted by Satish et al. and Mahdavi et al [5, 17]. In one study conducted by Sashikumar et al., the correlation between HbA1c levels and salivary glucose was not present [21].

Stimulated and unstimulated salivary flow rate levels were greater in controlled T_1DM compared to uncontrolled T_1DM. Several studies have shown a significant reduction in salivary flow rate in diabetic people [22- 24]. The decreased salivary flow or dry mouth that occurs in diabetes can be due to several reasons, can be the penetration of fat cells into the salivary glands, physical changes in mucous cells after dehydration due to polyuria, microvascular disease, local inflammation, and irritation in the oral cavity, infections, metabolic disorders, neuropathy affecting the salivary glands, medication for diabetes or concomitant medications [11]. Therefore, polyuria causes dehydration and consequently reduces the flow rate of saliva. Harrison et al. found that the stimulated salivary flow rate of uncontrolled

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diabetic children was significantly lower than controlled diabetic and non-diabetic children [10]. However, there was no significant relationship between controlled and uncontrolled diabetic patients in the study of Panchbhai et al. [11].

Limitations of the study

One of the limitations for this study may be the sample size, so a larger sample size may be needed to determine the cut-off point.

Conclusion

Stimulated salivary glucose level similar to serum was higher in uncontrolled T_1DM than in controlled T_1DM children. Therefore, it may be helpful to diagnose and monitor T_1DM patients.

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Ethical approval

The Ethics Committee of Tehran University of Medical Sciences approved the study (No: IR.TUMS.REC.1395.2595).

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Conflict of interest

The authors declare that there is no conflict of interest.

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