Effects of Consuming Oral Hypoglycemic Agents on Salivary Parameters, Calcium Intake and Bleeding on Probing in Women with Type 2 Diabetes Mellitus

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Abstract

This study aimed to determine the value of salivary parameters (volume, pH, and calcium levels), calcium intake, and bleeding on probing (BOP) in women with type 2 diabetes mellitus (T2DM) who consume oral hypoglycemic agents (OHAs) and to compare them with women with T2DM who do not consume OHAs and healthy subjects.

This cross-sectional study includes 24 women with T2DM (12 who consumed OHAs and 12 who did not consume OHAs), and healthy subjects as controls (n=35). The sampling technique was non-random sampling. The salivary volume was measured using the spitting method. The pH paper test was used to determine the salivary pH score. Salivary calcium levels were determined using an atomic absorption spectrophotometer (AAS). The semi-food frequency questionnaire (FFQ) method was used to determine calcium intake. BOP was measured by the method described by Ainamo and Bay in 1975. The Kruskal–Wallis test was used to compare variables among study groups, followed by post hoc Dunn's test.

This study discovered significant differences in salivary parameters and BOP between subjects with T2DM (both consume and do not consume OHAs) and healthy subjects, but not between subjects who consume and do not consume OHAs. The difference in calcium intake between the three study groups is not statistically significant.

Women with T2DM have lower salivary volume, pH, and calcium levels, as well as a higher BOP than healthy subjects. These variations were discovered to be caused by the manifestation of the disease rather than OHAs consumption.

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Introduction

Oral health can be influenced by several factors such as salivary flow, composition, quality and pH.[1,2] Saliva is composed of organic and inorganic materials, one of which is the calcium ions. Calcium ions in saliva play an important role in the oral cavity, including maintaining alveolar bone and tooth stability, balancing body fluids, and activating salivary gland secretory cells.[3,4] According to research by Zaneta et al., low calcium levels can also cause increased bone resorption, including alveolar bone resorption.[5]

According to research by Hoseini et al, diabetes mellitus patients often experience more severe xerostomia which is associated with a decrease in salivary flow rate. This indicates that there is a dysfunction of the salivary glands. According to research by Fayhaa, oral hypoglycemic agents (OHAs) such as sulfonylureas and metformin can associated with dry mouth and salivary glands dysfunction or hypofunction. Salivary gland dysfunction causes a decrease in production and changes in the composition of saliva, including the content of calcium ions in it, causing a decrease in a person's quality of life, including decreased oral health.[6–8] Calcium intake from food can also

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affect the balance of calcium in the body, including in the salivary glands.[9–11] Decreased salivary calcium levels can lead to resorption of the alveolar bone, thereby increasing the incidence of bleeding on probing (BOP).[5,12] Based on the description above, it is necessary to determine the effect of consuming OHAs on salivary volume, pH, and calcium levels, as well as calcium intake, and BOP in women with type 2 diabetes mellitus (T2DM).

Materials and methods

This was a descriptive study using a cross-sectional approach. The minimum sample size was determined by the Lemeshow formula.[13] According to the formula, the minimum sample size is 21 people. To account for dropouts, 10% of the minimum sample size was added, resulting in a total of 24 samples.

Participants in this study included 24 women with T2DM (12 who consumed OHAs and 12 who did not consume OHAs) and 35 healthy subjects as controls. Women with T2DM aged 25 to 65 years, with diabetes mellitus for a maximum of 10 years, and willing to participate by signing an informed consent form were eligible to participate. Control subjects had to be healthy women between the ages of 18 and 40. Exclusion criteria included smoking, having a history of Bell's palsy, Sjogren syndrome, HIV, and TBC disease, experiencing acute toothache, and using orthodontics. The research sampling method used was non-random sampling.

In this study, the salivary parameters refer to volume, pH and calcium levels. The salivary volume in ml per 5 minutes was measured using the spitting method on unstimulated whole saliva. The pH paper test was used to determine the salivary pH score by observing the colour change. Salivary calcium levels were measured with atomic absorption spectrophotometry (SSA). Calcium intake was measured by using the semi-food frequency questionnaire (FFQ). BOP was measured by the method described by Ainamo and Bay in 1975. This research was conducted from October to November 2019 at six health centers in Bandung and Jatinangor, Indonesia.

Statistical Analysis

All data were processed using IBM Statistical Product and Service Solutions version 26.0 (IBM Corp, Armonk, NY). Age, height, weight, salivary calcium levels, calcium intake, BOP, salivary volume, and pH were all reported as means with standard deviations (SD). The calcium intake categories (adequate or inadequate) were presented as percentages. The Kruskal-Wallis test was used to compare salivary parameters, BOP and calcium intake among study groups. Significant results are defined as p-values < 0.05. Following the significant Kruskal-Wallis test, a post hoc Dunn's multiple comparisons test was performed to determine which groups differed from others. All analyses were displayed in tabular form.

Results

Table 1 shows that the age of most subjects with T2DM is in the age range 56-65 years, and most control subjects were in the age range of 17-35 years. The mean height of subjects with T2DM who consume OHAs and who do not consume OHAs was lower than that of control subjects. The average body weight of subjects with T2DM (who consume OHAs and do not consume OHAs) was lower than that of control subjects. The type of OHAs used by the subject is biguanides for 10 people and sulfonylureas for 2 people.

	Women with T2DM				Control (n=35)	
	Consume OHAs (n=12)		Do not consume OHAs (n=12)			
	Mean	SD	Mean	SD	Mean	SD
Age (years)	59.75	4.37	51.67	11.74	29.11	8.27
Height (cm)	152.1	4.99	149.18	4.30	152.71	11.03
Weight (kg)	54.3	9.85	54.8	8.53	55.28	10.4

Table 1. Physical characteristics of the study subjects.
*SD = Standard Deviation.

Table 2 compares salivary parameters and BOP between the three study groups using the Kruskal-Wallis test, revealing significant differences in all variables. The Dunn's multiple comparisons test, on the other hand, finds no significant difference between all salivary parameters and BOP between subjects with T2DM who consume OHAs and those who do not consume OHAs. The significant difference is found between the T2DM (both consume and do not consume OHAs) and control groups. The difference in calcium intake between the three study groups is not statistically significant, as shown in Table 3. In comparison to control

subjects, a higher proportion of T2DM subjects who consume OHAs and those who do not consume OHAs had inadequate calcium intake.

	Women with T2DM		Control (n=35)	Kruskal-Wallis test p-value
	Consume OHAs (n=12)	Do not consume OHAs (n=12)		
Calcium intake (mg)				0.460
Mean	454.41	371.90	541.85	
SD	414.82	272.00	456.04	
Min	138.08	48.98	100.07	
Max	1689.35	922.90	2124.00	
Category (%)				
Adequate	8.34	8.34	14.28	
Inadequate	91.66	91.66	85.72	

Table 3. Calcium intake of the study subjects.
SD = Standard Deviation.

Discussion

The mean salivary calcium levels in women with T2DM who consume OHAs (0.98 ± 0.52 mmol/L) and who do not consume OHAs (1.16 ± 0.77 mmol/L) was lower than normal salivary calcium levels (1.32 ± 0.24 mmol/L). The mean salivary calcium levels in control subjects (1.69 ± 0.81 mmol/L) were slightly higher than normal salivary calcium levels. The low salivary calcium levels in patients with T2DM are in accordance with a study conducted by Lopez et al (2009) which states that low salivary calcium levels may be related to absorption problems and changes in calcium excretion in the urine, which consequently can change calcium levels in saliva. Hyperglycemia can cause salivary gland dysfunction which affects salivary calcium levels.[14] Kuswandani (2016) stated that the salivary calcium levels are influenced by several factors such as the quality and quantity of saliva production and also the intake of foods containing calcium.[2,15] Ji-won (2019) postulated that drugs can cause disruption of the salivary glands. One of such drugs is metformin, which is an antidiabetic drug in the biguanide class excreted into saliva.[16,17] In this study, subjects who took oral OHAs had lower mean salivary calcium levels than those who did not, and 83.33% of subjects with T2DM consumed biguanide drugs.

The mean calcium intake in T2DM subjects who consume OHAs (454.41 ± 414.82 mg), subjects who do not consume OHAs (371.90 272.00 mg), and control subjects (541.85 ± 456.04 mg) was lower than the total calcium requirement, based on Regulation of the Minister of Health of the Republic of Indonesia No 75 of 2013 concerning the nutritional adequacy rate, which recommends a 80% intake of the total optimal calcium requirement of 1000 mg/day for people aged 18 years and above.[17] Both the T2DM and control groups had a higher proportion of subjects with inadequate calcium intake. Women with T2DM had a lower educational background than control subjects. Awareness about diabetes complications and consequent improvement in dietary knowledge, attitude, and practices lead to better control of the disease.[18] People with T2DM who live in rural areas do not really question what they eat and do not eat foods with balanced nutrition, which is further compounded by economic and environmental factors.[19]

The mean bleeding on probing (BOP) of subjects with T2DM who consume OHAs (6.03 ± 5 %) was lower than who do not consume OHAs (11.97 ± 8.36 %), and both were higher than control subjects (5.43 ± 4.52 %). Increased blood sugar levels in people with diabetes mellitus may cause damaged body immune function. This situation triggers the colonization of bacteria in the periodontal tissue.[15,19] Glucose levels in the crevicular fluid of gingiva and saliva are also higher in people with diabetes mellitus compared to healthy people, this results in an increase in the bacteria proliferation that will lead to gingival inflammation and the development of periodontal disease.[15,16]

Women with T2DM were mostly in the age range of 56-65 years, according research by Joseph et al., stating that increasing age can lead to glucose intolerance and the aging process results in a decrease ability of pancreatic beta cells to produce insulin. With increasing age, there will be a decrease in the body's function to metabolize glucose.[20]

The mean salivary volume of subjects with T2DM who do not consume OHAs (0.95 ± 0.33 ml/5 minutes) was lower than who consume OHAs (1.55 ± 1.47 ml/5 minutes), and both were lower than control subjects (2.27 ± 1.37 ml/5 minutes). These results may indicate a dysfunction of the salivary glands. Salivary gland dysfunction can affect the quality and quantity of saliva, including decreasing salivary pH, decreasing salivary volume, and causing xerostomia in T2DM patients.[6,7] As mentioned above that drugs can cause disruption of the salivary glands. One of such drugs is metformin,

which is an antidiabetic drug in the biguanide class excreted into saliva, which may contribute to salivary gland dysfunction.[16] The mean salivary pH of women with T2DM who consume and do not consume OHAs was lower than the normal pH range in this study, indicating that their salivary pH is acidic compared to normal salivary pH. Seethalakshmi (2016) states that normal pH ranges from 6.7-7.3 which means it is not acidic and non-alkaline, but a neutral pH. In patients with diabetes mellitus, in addition to an increase in blood glucose levels, there is also an increase in salivary glucose levels, which triggers a bacterial metabolic process which results in low or acidic salivary pH.[21]

The limitation of this study is that the we did not perform the intra-examiner calibration, but only did the inter-examiner calibration (between examiners). In this study, the resulting varied data may have occurred due to inaccurate examination methods or lack of consistency in the examination as we did not perform the intra-examiner calibration first. The subject's memory of the amount of food consumed also influenced the success of the semi-FFQ.

Despite the differences in salivary parameters and BOP between the three groups in this study, the significant difference was found between subjects with T2DM (both consume OHAs and do not consume OHAs) and healthy subjects. This finding is consistent with the findings of other studies.[16] This study suggests that changes in salivary parameters such as volume, pH, and calcium levels, as well as BOP, are influenced by the manifestation of the disease regardless of OHAs consumption.

Conclusions

Women with T2DM have lower salivary volume, pH, and calcium levels, as well as a higher BOP than healthy subjects. These variations were discovered to be caused by the manifestation of the disease rather than OHAs consumption. There is no difference regarding the calcium intake between groups in this study.

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Declaration of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

	Women with T2DM				Control (n=35)		Kruskal-Wallis test	Post hoc Dunn's multiple comparisons test		
	Consume OHAs (n=12)		Do not consume OHAs (n=12)					Consume OHAs-do not consume OHAs	Consume OHAs-control	Do not consume OHAs-control
	Mean	SD	Mean	SD	Mean	SD	p-value	p-value	p-value	p-value
Salivary volume (ml/5 minutes)	1.55	1.47	0.95	0.33	2.27	1.37	0.001*	0.28	0.000*	0.029*
Salivary pH	5.96	0.69	6	0.48	6.46	0.57	0.010*	0.71	0.009*	0.031*
Salivary calcium levels (mmol/L)	0.98	0.52	1.16	0.77	1.69	0.81	0.006*	0.71	0.006*	0.021*
BOP (%)	6.03	4.88	11.97	8.36	5.43	4.52	0.007*	0.61	0.002*	0.032*

Table 2. Salivary volume, pH, calcium levels, and bleeding on probing (BOP) of the study subjects.
*SD = Standard Deviation
*Statistically significant (p-value < 0.05)

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