

Effects of Oral Hypoglycemic Drugs on Flow Rate and Protein Composition of Saliva in Patients with Diabetes Mellitus

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الخلاصة

الهدف من الدراسة: معرفة تأثير كل من مرض السكر والأدوية المستخدمة في علاجه (عقار الميتفورمين) على نسبة جريان اللعاب والمستوى الكلي للبروتينات في اللعاب عند المرضى المصابين ببدء السكر ومقارنتهم بالأشخاص الأصحاء وتحديد صحة الفم لدى هؤلاء المرضى. **المواد والطرائق:** أجريت هذه الدراسة على ٤٥ شخص (٢٧ ذكور، ١٨ إناث)، ١٥ منهم كانوا أشخاصاً أصحاء وتم اعتبارهم مجموعة أولى (مجموعة سيطرة) المجموعة الثانية والتي تتكون من ١٥ مريض مصاب ببدء السكر ولم يتلقى أي نوع من العلاجات أما المجموعة الثالثة فتتكون ١٥ مريض مصاب ببدء السكري ويتعالج بعقار الميتفورمين فقط. تم اختيار المرضى من قسم جراحة الوجه والفكين /كلية طب الأسنان/ جامعة الموصل. تم جمع عينة اللعاب وقياس نسبة الجريان ومستوى البروتين لكل شخص كما تم تحديد صحة الفم لكل منهم حسب مؤشر صحة الفم المبسط (Green and Vermillion). **النتائج:** عند إجراء التحليل الإحصائي بطريقة One way analysis of variance تم ملاحظة وجود فروق معنوية بين مجاميع الدراسة كافة، لكل من نسبة جريان اللعاب ومستوى البروتين فيه، كما أظهرت نتائج الإحصاء حسب Duncan's multiple analysis range test أنه لا يوجد فروقات معنوية لكل من نسبة جريان اللعاب ومستوى البروتين فيه بين المجموعتين الأولى والثالثة، بينما نجد فروقات معنوية بين المجموعتين الأولى والثانية وكذلك بين المجموعة الثانية والثالثة. أما بالنسبة إلى نتائج قياس صحة الفم، لم يكن هناك أي فرق معنوي بين المجموعتين الأولى والثالثة، بينما وجد هذا الفرق المعنوي بين المجموعتين الأولى والثانية وكذلك بين المجموعة الثانية والثالثة. **الإستنتاج:** إن مرض السكري يمكن أن يحدث تغييراً في معدل جريان اللعاب ومستوى البروتين، والذي بدوره يمكن أن يؤثر على صحة الفم عند مرضى السكري بينما لا تحدث الأدوية والعقاقير القوية المستعملة لعلاج السكري مثل هذا التأثير.

ABSTRACT

Aims: To study the effects of both diabetes mellitus and oral hypoglycemic drugs (metformin) on salivary flow rate and total protein levels of saliva and to compare them with control healthy subjects and to determine their effects on oral health of these patients. **Materials and Methods:** This study was carried out on 45 individuals (27 males and 18 females); 15 individuals of them were healthy subjects and considered as control group. The second group which comprised 15 patients with diabetes mellitus and received no any treatment (uncontrolled). The third group, diabetic patients were treated with metformin only. Subjects were selected from the out patients attending Oral Surgery Department, College of Dentistry-University of Mosul. The samples of saliva were collected and salivary flow rates and total protein was determined for each individual, then its relation to oral health was measured according to Simplified Oral Hygiene Index by Greene and Vermillion. **Results:** One way analysis of variance was performed and showed that there were significant differences among all study groups for both salivary flow rate and total salivary protein concentration. The results of Duncan's Multiple analysis range test showed that there were no significant differences in salivary flow rates and total salivary protein concentrations between first and third groups while significant differences were seen between first and second and between second and third groups. For oral health scores, there was no significant differences between first and third groups while significant differences were observed between first and second and between second and third groups. **Conclusions:** Changes in salivary flow rates and salivary protein concentrations can result from diabetes mellitus which can affect oral health of these patients, while oral hypoglycemic drugs had no such effects.

Key Words: Diabetes Mellitus, salivary flow rate, salivary proteins, oral hypoglycemic drugs.

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INTRODUCTION

Diabetes mellitus is a wide spread complex disease with high morbidity and

health care costs⁽¹⁾. It is a metabolic disease characterized by hyperglycemia due to defects in insulin production, insulin

action, or both ⁽²⁾. It can be treated by oral hypoglycemic drugs such as sulfonylureas and metformin ⁽³⁾. Both diabetes mellitus and drugs used in the treatment of this disease can affect the mouth and salivary glands ⁽⁴⁾.

The oral complications of uncontrolled diabetes mellitus are devastating. These may include xerostomia, salivary gland dysfunction, gingivitis and periodontal disease and this is related to several pathological events associated with diabetes ⁽⁵⁾. Several classes of drugs were associated with dry mouth and salivary gland dysfunction or hypofunction which may influence concentrations of salivary proteins leading to changes of oral health status among individuals using these drugs ^(6, 7, 8). Since saliva is a diagnostic medium that can be easily collected with minimal invasion ⁽⁹⁾, this study was conducted to investigate the effects of both Diabetes Mellitus and antidiabetic drugs on salivary flow rate and total protein concentrations of saliva compared to control healthy subjects and to determine their effects on oral health of these patients.

MATERIALS AND METHODS

Forty – five individuals have participated in this study, their age ranged between 35 - 65 years with mean age of 50 ± 1 years. Fifteen of them were healthy individuals and considered as control group, while the other 15 individuals were suffering from diabetes mellitus and received no any treatment (uncontrolled). The third group was diabetic patients treated with metformin only with dose ranged 500 - 1000 mg\ day. The duration of disease for both second and third groups ranged between 3-11 years (mean 7 ± 1 year). All these individuals were selected from out - patient clinic at Oral Surgery Department, College of Dentistry, University of Mosul. A questionnaire was conducted to subjects and those who reported to have diabetes were requested to present their medical records and/or prescriptions which confirmed their diabetes status. Subjects were seated on a chair under quit standardized condition ^(10, 11). The samples of stimulated saliva were collected from 45 individuals using spitting method .The time of collection was 5 continuous minutes (without swallowing), it was per-

formed at the same time of day (2 hr after having breakfast) to avoid circadian variations ^(12, 13), each subject was asked to wash his\her mouth three times with distilled water and to take drops of a sugar free lemon juice before spitting. Saliva volume was measured, placed in a test tube then closed with a plastic stopper and stored in deep freeze until the time of experiment ⁽¹⁴⁾. Total protein for each sample of saliva was determined using Biuret method by mixing of 0.2 ml of saliva with 2.8 ml of distilled water and then adding 5 ml of Biuret reagent which was prepared by dissolving 9 gm of sodium potassium tartrate in 500 ml of 0.2 N-sodium hydroxide , adding 3 gm of copper sulfate and dissolved by stirring , then 5gm of potassium iodide was added to make the volume 4 L with 0.2 N – sodium hydroxide ⁽¹²⁻¹⁵⁾. Ultraviolet visible spectrophotometer (CECIL, CEIO021, England) at wave length of 540 nm was used to determine the total protein in saliva sample. For investigation of salivary flow rates, all subjects were told not to eat, drink or smoke for 1 hr before each sampling. The saliva samples were always collected in restful and quiet circumstances, unstimulated whole saliva was collected for 5 min by the subjects leaning forward and letting the saliva drain into a graded sampling tube, the flow rates were evaluated visually from graded test tubes as ml \min ⁽¹⁶⁾.

On other hand, oral hygiene for each individual was evaluated by Simplified Oral Hygiene Index according to Greene and Vermillion .It consist of two components, a Simplified - Debris Index and a Simplified - Calculus Index, each component was assessed on a scale of 0 - 3. Only mouth mirror and sickle type dental explorer were used for the examinations. The criteria for scoring the debris and calculus components of the Simplified Oral Hygiene Index are as follows: Oral – Debris Index [DI-S]:

0 = no debris or stain present.

1 = soft debris covering not more than one third of the surface or the presence of extrinsic stains without other debris regardless of surface area covered.

2 = soft debris covering more than one third but not more than two thirds of the exposed tooth surface.

3 = soft debris covering more than two thirds of the exposed tooth surfaces. Calculus Index [CI-S]:

0 = no calculus present.

1 = supragingival calculus not more than one third of the exposed tooth surface.

2 = supragingival calculus covering more than one third but not more than two thirds of the exposed tooth surface, or the presence of individual flecks of subgingival calculus around the cervical portion of the tooth; or both.

3 = supragingival calculus covering more than two thirds of the exposed tooth surface or a continuous heavy band of subgingival calculus around the cervical portion of the tooth or both. The Simplified Oral Hygiene Index score per person is the total of the debris and calculus scores per person⁽¹⁷⁾. Statistical analysis of data was carried out using ANOVA test to examine the differences among 3 groups.

RESULTS

One way analysis of variance was performed to test the differences in salivary protein concentrations among the first group (control), second group (uncontrolled diabetic patients) and third group (diabetic patients treated by oral hypoglycemic drugs). It was found that there were significant differences among them for both total salivary protein concentrations ($p < 0.04$) and salivary flow rates ($p < 0.000$). The results of Duncan's multiple analysis range test demonstrated that there were no significant differences in salivary protein concentrations and flow rates between the first and third groups, significant differences were observed between first and second and between second and third groups ($p < 0.040$, $p < 0.000$ respectively) as shown in Table 1 and Table 2.

Table (1): Analysis of variance of salivary protein concentrations in all study groups

	1st group (normal)	2nd group (uncontrolled)	3rd group (controlled)	P-value	F-value
Salivary protein concentrations (mg/ml) (mean ± SD)	0.46 ± 0.12	0.59 ± 0.45	0.30 ± 0.24	0.040*	3.480
Duncan's grouping	A	B	A		

SD = standard deviation; *Significant difference at $p \leq 0.05$; ** Different letters mean a significant difference exists.

Table (2): Analysis of variance of salivary flow rates in all study groups

	1st group (normal)	2nd group (uncontrolled)	3rd group (controlled)	P-value	F-value
Salivary flow rate (ml/min) (mean ± SD)	4.00 ± 1.31	1.80 ± 0.77	3.87 ± 0.83	0.000*	22.750
Duncan's grouping	B	A	B		

SD = standard deviation; *Significant difference at $p \leq 0.05$; ** Different letters mean a significant difference exists.

For oral health scores, also it was found that there is no significant differences between first and third groups, while

significant differences were observed between second and third groups ($p < 0.007$), as shown in Table 3.

Table (3): Analysis of variance of oral health scores in all study groups

	1st group (normal)	2nd group (uncontrolled)	3rd group (controlled)	P-value	F-value
Oral health scores (mean ± SD)	5.8 ± 10.7	4.21 ± 0.935	3.87 ± 0.834	0.007*	5.724
Duncan's grouping	A	B	A		

SD = standard deviation; * Significant difference at $p \leq 0.05$; ** Different letters mean a significant difference exists.

DISSCUSION

Dentists play a major role as part of an allied health team in providing oral care to patients with diabetes mellitus which is a complex and pernicious syndrome that is characterized by high blood glucose and abnormalities in carbohydrates, lipids and proteins metabolism⁽⁵⁾. Diabetes mellitus can cause alterations in salivary parameters of patients like total salivary proteins and salivary flow rates⁽¹⁸⁻²⁰⁾ which can cause disorders of hard and soft tissues of the mouth leading to gingival lesions and bad oral health⁽¹⁵⁾. In this study ,results obtained from uncontrolled diabetic patients were showed that salivary protein values were higher than that of normal healthy subjects and controlled diabetic patients probably due to greater microorganism activity, or they could perhaps be proteins of periodontal tissues origin, or it can be due to modifications in biochemical composition of salivary gland caused by diabetes mellitus⁽²¹⁾. This was in agreement with other studies which reflect high level of proteins in saliva of uncontrolled diabetic patients^(2,15, 22, 23).

This quantitative variations in salivary protein concentrations will affect oral health prevalence since that these proteins influence plaque formation and oral infections^(20, 24, 25). An increased salivary protein concentration reflects a raised oral inflammation, so periodontal status was bad in patients with uncontrolled diabetes mellitus^(2, 26, and 27).

Dry mouth (xerostomia) is a common complaint among diabetic patients^(28, 29, and 30). Results of this study showed that there was decrease in salivary flow rates of uncontrolled diabetic patients compared to normal healthy subjects and controlled diabetic patients and this was in agreement with other studies^(15, 18, 19, 22, 23, and 31). Dry mouth complaint in diabetic patients may be due to polyuria or underlying metabolic or endocrine problems can alter the normal environment of the oral cavity make it more susceptible to periodontal diseases and deterioration of the oral health^(5,32-34). Results of this study regarding increased salivary protein concentrations and decreased salivary flow rate were in disagreement with other studies^(35, 36) which showed that poorly controlled diabetes mellitus had no influence on saliva.

In this study, the pattern of increased protein concentrations, decreased flow rate and state of oral health were similar in both first and third study groups and differ from second one suggesting that disease specific mechanisms may be responsible and indicated that oral hypoglycemic drugs had no effects on these parameters and this in agreement with studies^(21, 23, 37) and disagreement with other.⁽³⁸⁾ In general, adults with well controlled diabetes mellitus had no more significant risk of experiencing oral disease progression than those do without diabetes , and hence, can be treated similarly, whereas similar dental diseases in poorly controlled patients may need an immediate dental treatment to decrease the risk of progression.

CONCLUSIONS

Prolonged and severe hyperglycemia is associated with alterations in saliva which can cause oral complications. Thus management plane is needed. Although saliva is diagnostic medium that can be easily collected with minimal invasion; it had been neglected in the past. Saliva nowadays is being used more often to study diseases and drug effects aided by current technological developments.

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