

Original Article

Determination of salivary urea and uric acid of patients with halitosis

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ABSTRACT

Background: Halitosis is the presence of unpleasant or foul smelling breath. The origin of halitosis may be related to both systemic and oral conditions, but a large percentage of cases, about 90%, is generally related to an oral cause. The aim of this study was to compare the concentration of urea and uric acid in patients with halitosis and people without halitosis.

Materials and Methods: In this case-control study, concentration of urea and uric acid was compared between two groups: (1) persons suffering halitosis (2) control group without halitosis. Each group includes fifty patients. Unstimulated saliva was collected in both groups. Then, concentration of urea, uric acid, and creatinine was determined. The results were statistically analyzed with SPSS software version 14 (SPSS Inc., Chicago, Illinois, USA) by *t*-test ($\alpha = 0.05$).

Results: Results showed that salivary urea and uric acid concentration in halitosis group were significantly greater than control group ($P < 0.05$). Salivary creatinine concentration in halitosis group was significantly lower compared to control group ($P < 0.05$). Salivary urea and uric acid concentration to creatinine ratios were higher in halitosis group than control group, and significant differences between them were existed ($P < 0.05$).

Conclusion: According to the results, urea and uric acid concentration show increase in patient suffering halitosis, and this increase may result in oral malodor.

Key Words: Halitosis, saliva, urea, uric acid

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INTRODUCTION

Halitosis is the unpleasant or foul smelling breath. The disease reported to be prevalent worldwide and causes many social problems for the patients. Halitosis may affect up to 30% of the population. In most cases, the etiology of the condition is from local oral causes.^[1] The origin of halitosis may be related to both systemic and oral conditions but a large percentage of cases, about 90%, is related to an oral cause^[2] According to Van den Velde breath analysis could potentially be used as a diagnosis tool

for detecting some systemic disease such as liver pathologies or chronic kidney failure.^[3] Halitosis, or bad breath, is caused by mainly volatile sulfur compounds (VSC) as a result of bacterial breakdown of protein and can be quantitatively and qualitatively measured in the expired oral breath.^[4] The methods of detecting or diagnosing halitosis are organoleptic or human sense of smell, sulfide monitoring, and gas chromatography. All of these methods have limitations and disadvantages. A more accurate,

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analytical system which will be able to precisely detect the volatile compounds in the expired air and correlate the results to a specific cause is not yet available.^[4] These VSCs are the predominant elements of oral malodor although some do believe that other odorous volatiles, such as certain amines and fatty acids, may play a role.^[5] The organoleptic diagnosis is the gold standard, and clinical management includes oral approaches, especially periodontal treatment and oral hygiene instructions, including the tongue. For the diagnosis of halitosis, we have self-assessment, organoleptic measurements, VSC monitoring, and Microbiologic tests.^[6] Mixed saliva contains numerous biological molecules which participate in the regulation of the functions of the major physiological systems or are products of their work. Therefore, salivary components reflect the status of body systems and can provide diagnostic information about their abnormalities.^[7,8] Saliva and its component are believed to have an important role in the alterations of mouth environment. The presence of nonprotein nitrogen compounds in saliva such as uric acid appeared to have important effects. Urea is the end product of amino acid metabolism in the blood which may be changed by several factors such as proteins, diet, and dehydration. There is a positive correlation between blood urea with saliva urea.^[9,10] Uric acid is the final metabolites of purines, for which a similar relationship has been reported in blood and saliva.

Tomás *et al.* showed salivary composition in patients with chronic renal failure is conditioned by the stage of renal failure. The relationship between these biochemical parameters and the oral health status has still not been definitively clarified.^[11]

Anuradha *et al.* showed alterations in salivary calcium, phosphorous, urea, sodium, and potassium levels were significantly higher in the chronic kidney disease patients when compared to healthy one, and the difference was insignificant in relation to bicarbonate level. The increased levels in dialysis patients correlated with renal disease severity.^[12]

The aim of this study was to compare the concentration of urea and uric acid in patients with halitosis and people without halitosis.

MATERIALS AND METHODS

In this case-control study, concentration of urea and uric acid were compared between two groups:

(1) persons suffering halitosis (2) control group without halitosis. Each group included fifty patients selected from patients referred to dental school of Khorasgan University. Age and sex were matched. Inclusion criteria: In test group, healthy controls whose chief complaint was halitosis.

Exclusion criteria: Those with the presence of active carious lesions, sign of periodontitis, faulty dental restoration, patients who suffer from xerostomia, cigarette smokers, any systemic disease like bronchial and lung infection, kidney failure, metabolic dysfunction and other disease that could affected conducting the study were excluded.

All patients were healthy and signed informed consent. Patients had no drug consumption or dietary uptake.

Saliva samplings were performed in both groups. Patients asked to rinse their mouth with water and spitting in test tube, then we stored 2 ml of saliva in sealed test tube in -20°C .

Urea measuring

For urea measurement, diacetyl monoxime colorimetric method has been applied. In this method, diacetyl monoxime in the presence of acid hydrolyzed and produce labile diacetyl which react with urea and create yellow color, then colorimeter in 520 nm wavelength was applied to measure urea.^[13]

Acid uric measurement

For uric acid measurement, phosphotungstate method was used. In this method, uric acid in the presence of phosphotungstic acid and sodium carbonate will create a blue complex which measure by colorimeter in 700 nm wavelengths.^[14,15]

Creatinine measurement

For creatinine measurement, Jaffe method was used. Creatinine creates orange complex with bicarbonate. (This color relate to creatine and other nonspecific material) with acidification, the color caused by exist of creatinine will be disappear. Different in color intensity in 520 nm has positive correlation with concentration of creatinine.^[16]

Statistical analysis

Data were analyzed with *t*-student test (confidence interval = 95%).

RESULTS

In fifty patients with halitosis and fifty patients without halitosis, saliva was measured by laboratory

techniques and as shown in Table 1; the mean urea concentration in saliva was 3.7 ± 1.89 mg/dl in halitosis group and 2.6 ± 1.84 mg/dl in control group. The differences between two groups were statistically significant ($P < 0.005$). Most of the patients with halitosis had urea concentration between 4 and 5 mg/dl; however, in most of patients in control group, urea concentration was between 1 and 2 mg/dl.

Uric acid concentration in saliva was measured in both groups. The mean concentration in halitosis group was 3.19 ± 1.12 mg/dl and 2.27 ± 1.18 mg/dl in control group. In most patients with halitosis, uric acid concentration was between 4 and 5 mg/dl and between 1 and 2 mg/dl in control group.

Saliva creatinine concentration was measured in both groups, and as shown in Table 1, the mean creatinine concentration was 0.67 ± 0.44 mg/dl in halitosis group and 0.98 ± 0.33 mg/dl in control group. The differences between the two groups were statistically significant ($P < 0.005$). In most of the patient with halitosis, creatinine concentration was below 0.6 mg/dl and beyond 0.6 mg/dl in control group.

Urea to creatinine concentration ratio was measured in all patients. This ratio is >3 in most patient suffering halitosis while it is <3 in most patients in control group. In addition, uric acid to creatinine concentration ratio was measured in both groups. The results show the most patient suffering halitosis, this ratio was >3 while it is <3 in control group.

DISCUSSION

Urea, uric acid, and creatinine secrete to saliva and it has been proved that changes in urea and uric acid are in concert with changes in blood components.^[10] Halitosis is a common complaint in patients and has social adverse effects, and it can guide us to their underlying disease.^[13]

Since high level of nitrogen compounds in saliva reflects their high concentration in blood plasma so, in some cases, noticing the etiology of halitosis may lead to the right diagnosis.

Table 1: Mean of salivary nitrogen components

Nitrogen components	Control group	Halitosis group
Urea	2.60 ± 1.84	$3.70 \pm 1.89^*$
Uric acid	2.27 ± 1.18	$3.19 \pm 1.12^*$
Creatinine	0.98 ± 0.33	$0.67 \pm 0.44^*$

*Differences between two groups are significant (Student' *t*-test) (CI=95%).
CI: Confidence interval

Results of our study show urea and uric acid in saliva are important factors in etiology of halitosis. Blood urea concentration is under the influence of diet, amount of proteins, and dehydration. Thyroid hormones and glucocorticoids have catabolic effect and may increase blood urea concentration while androgens and growth hormones with anabolic effect lead to a decrease in its concentration.^[14]

Urea could be excreted through saliva. Blood urea concentration and saliva urea concentration have a positive relation (yushihara). In our study, urea concentration in patient suffering halitosis increased for 20% compared to control patient.

Uric acid is one another nitrogen compound which increases in many situations such as, gout, pregnancy, leukemia, and polycythemia. Uric acid also could be found in saliva in concert with its blood concentration.^[17] In our study, the results show a 20% increase in uric acid concentration in halitosis group compared to control group.

Creatinine produced from keratin daily and its concentration depends on individual muscle mass. Any increase in concentration of creatinine shows kidney disease.

In our study, results showed a 20% decrease in creatinine concentration in patients suffering halitosis compared to control group.

The reason of this decrease in halitosis group is saliva buffering capacity. It means when urea and uric acid concentration increase in saliva due to hydrogen ion absorption by this compound creatinine concentration would decrease in saliva.^[18-20]

Dahlberg *et al.* demonstrated that parotid and serum ratio for urea were consistent, and saliva could be used to monitor the dialysis procedure.^[21] Peterson *et al.*^[22] and Obry *et al.* stated that salivary urea and uric acid are passively diffused from plasma and reflects the blood levels.^[23]

Epstein *et al.* stated that urea level was significantly high among dialyzed subjects, and the values in his study ranged from 7 ± 2 – 17 ± 7 mg% to 60 ± 36 – 93 ± 45 mg% for the control and study group, respectively. The salivary urea level of the control group in the present study was 31.9 ± 14.9 mg%.^[24]

Belazelkovska *et al.* reported that the concentration of salivary uric acid increase in patient with chronic renal disease along with the reduction of salivary

flow rate, so an increase the presence of uremic fetor may occur.^[25] Keles *et al.* and Martins *et al.* reported similar finding.^[26,27]

The range of salivary urea in halitosis patients in the present study was 3.70 mg% where as in Obry *et al.*, it ranged from 1.89 mg% to 8.14 mg%. This disparity could be due to a different method of analysis of saliva adopted by Obry *et al.*^[23]

The values for salivary urea in the present study were striking because the mean salivary urea for halitosis was about 2 times higher, respectively, when compared to the control subjects. This may signify that natural excretion occurs from salivary glands, thus accounting for high concentration of urea found in saliva.

Since the amount of creatinine production is consonant in 24 h, uric acid and urea-to-creatinine ratio are better to clarify the changes of this compound concentration in saliva. Both of these ratios are increased in halitosis group compared to control group.

CONCLUSION

Our findings clearly showed increased salivary uric acid, and urea concentration in patients suffering halitosis and these compounds are involved in etiology of halitosis. Therefore, halitosis and saliva analysis for its components may be very useful to diagnose underlying disease.

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Conflicts of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or nonfinancial in this article.

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