

Salivary Analytes in Patients with Oral Squamous Cell Carcinoma

Petra Nola Fuchs², Dunja Rogić³, Danica Vidović-Juras¹, Mato Sušić², Aleksandar Milenović⁴, Vlaho Brailo¹ and Vanja Vučićević Boras¹

¹ University of Zagreb, School of Dentistry, Department of Oral Medicine, Zagreb, Croatia

² University of Zagreb, School of Dentistry, Department of Oral Surgery, Zagreb, Croatia

³ University of Zagreb, Zagreb University Hospital Center, Laboratory for Enzymatic Analysis, Zagreb, Croatia

⁴ University of Zagreb, Dubrava University Hospital, Clinic for Maxillofacial Surgery, Zagreb, Croatia

ABSTRACT

Literature data indicates that measurement of certain salivary constituents might serve as a useful diagnostic/prognostic tool in the patients with oral squamous cell carcinoma (OSCC). In 24 patients with OSCC (60±2.5yrs) and in 24 controls (24±3.7yrs) we have determined levels of salivary magnesium, calcium, copper, chloride, phosphate, potassium, sodium, total proteins and amylase. Sodium, potassium and chloride were determined by indirect potentiometry whereas copper, magnesium and phosphate were determined by atomic absorption spectrophotometry. Total proteins were determined by pyrogallol colorimetric method. Amylase levels were determined by continued colorimetric method. Statistical analysis was performed by use of χ^2 test and Spearman's correlation test. The results of this study indicate that the concentrations of sodium and chloride were significantly elevated in patients with OSCC when compared to the controls. However, level of total protein was significantly decreased when compared to the healthy controls. Furthermore, there was a negative correlation between alcohol consumption and total protein concentration in patients with oral carcinoma. We might conclude that in patients with OSCC increased salivary sodium and chloride might reflect their overall dehydration status due to alcohol consumption rather than consequence of OSCC itself.

Key words: oral squamous cell carcinoma, saliva

Introduction

Classically, oral squamous cell carcinoma (OSCC) is confirmed by histopathological finding. Certain salivary variables have been investigated in order to diagnose OSCC more easily, however the results of the studies are inconclusive. Saliva is a complex fluid which is easy to collect and non-invasive and therefore might serve as a useful diagnostic tool in certain oral diseases as well as in OSCC. Although, it is well known that changes in the serum electrolytes might reflect systemic diseases, the role of salivary electrolytes in certain conditions has not yet been studied comprehensively¹. Altered concentrations of various salivary electrolytes and ions may compromise various salivary functions related to re-mineralization,

maintaining buffering capacity, taste functions while reduced amylase activity may impair digestive ability of the saliva. Changes in the salivary electrolytes have been reported as a consequence of increasing age, periodontal and dental status, smoking, etc. Sevon et al.² suggested that concentration of salivary calcium may be associated with both dental and periodontal health. High salivary calcium concentrations seem to be associated with more sound, intact teeth than the average. At the same time, high salivary calcium seems to accelerate the calcification rate of dental plaque and to be associated with a higher prevalence of gingivitis and adult periodontitis. Apart from calcium there is little information about the

association between salivary electrolytes and oral health. Comprehensive salivary analysis revealed an overall altered salivary composition in oral squamous cell carcinoma patients, indicating a compromised oral environment in these patients and suggesting salivary analysis as a new diagnostic tool for oral cancer³. It is well known that alcohol and cigarette consumption are still two major causes in the development of oral squamous cell carcinoma. It is also known that persons with alcohol addiction experience increased, reduced or no effect on the parotid salivary flow rate⁴⁻⁶. Enberg et al.⁷ reported that sodium, calcium, amylase and total protein levels were significantly decreased in alcoholics after acute alcohol intake when compared to the healthy controls. Laine et al.⁸ reported that smoking was associated with high salivary calcium, magnesium and potassium levels in the older age group of their participants. Therefore the aim of this study was to evaluate salivary analytes in patients with OSCC in order to determine whether these salivary analytes might be useful as a diagnostic tool.

Materials and Methods

Prior to this investigation all the participants signed informed consent according to the Helsinki II. There were 24 patients (60±2.5yrs) with pathohistologically confirmed diagnosis of oral squamous cell carcinoma (OSCC) (Table 1). Control group consisted of 24 participants who were dental students, (24±3.7yrs). Every participant underwent clinical examinations which included: salivary flow rate (unstimulated whole saliva), Community Periodontal Index Treatment Needs (CPITN)⁹, cigarette and alcohol consumption per day. In every patient with OSCC, duration of the disease itself, size of the lesion, localisation of the lesion and TNM staging was recorded (Table 2). Sodium, potassium and chloride were determined by indirect potentiometry on the automatic biochemical analyser Olympus AU2700. Copper, magnesium and phosphate were determined by atomic absorption spectrophotometry. Total proteins were determined by pyrogallol colorimetric method. Amylase levels were determined by IFCC (continued colorimetric method). The laboratory itself is accredited according to the usual standards¹⁰. Statistical analysis was performed with statistical soft-

ware SPSS v.11 (SPSS Inc., Chicago, IL, USA). Statistical analysis was performed by use of descriptive statistics i.e. χ^2 -test and Spearman's correlation analysis. P values lower than 0.05 were considered as significant.

Results

Patients with oral carcinoma were significantly older than healthy controls (Table 1).

Patients with oral carcinoma had significantly elevated levels of sodium and chloride in the saliva when

TABLE 1
DEMOGRAPHIC CHARACTERISTICS OF THE PARTICIPANTS

	Oral cancer	Controls	p
Age (median±SE)	60±2.5	24±3.7	0.0001*
Sex N (%)			
female	4 (16.7)	15 (62.5)	0.001*
male	20 (83.3)	9 (37.5)	
Smoking			
yes	21 (12.5)	9 (37.5)	0.0009*
no	3 (87.5)	15 (62.5)	
Cigarettes per day (median±SE)	20±4	13.3±5	0.0001*

*Significant difference (p<0.05)

TABLE 2
CLINICAL CHARACTERISTICS OF ORAL CANCER

Duration in months (median±SE)	3±2.45
Size in mm ² (median±SE)	600±119.26
Localization N (%)	
tongue	4 (16.7)
sublingual area	61 (66.6)
soft palate	4 (16.7)
Stage N (%)	
1	2 (8.3)
2	2 (8.3)
3	8 (33.4)
4	12 (50)

TABLE 3
CORRELATION OF SALIVARY ANALYTES AND CLINICAL PARAMETERS IN PATIENTS WITH ORAL SQUAMOUS CELL CARCINOMA

	Phosphate	Na ⁺	K ⁺	Cl ⁻	Cu	Mg	Amylase	Protein
Age	0.149	-0.187	0.183	-0.272	0.030	-0.132	0.147	-0.150
Duration	0.105	0.159	0.155	0.092	-0.206	-0.011	0.093	-0.116
Size	0.025	0.397	0.203	0.069	0.058	0.019	0.192	0.074
CPITN	0.01	-0.011	-0.196	-0.072	-0.014	0.202	0.088	0.168
Salivary flow rate	0.045	0.172	-0.024	0.090	0.226	0.083	-0.258	-0.034
No. of cigarettes/day	0.52	-0.056	-0.063	0.039	0.124	-0.183	0.140	-0.053
Alcohol units/day	-0.077	0.096	-0.075	0.063	-0.025	-0.105	0.252	-0.627*

*Significant correlation (p<0.05)

compared to the healthy controls. However, level of total protein was significantly decreased when compared to the healthy controls (Table 3).

There was also negative correlation between alcohol consumption and total protein concentration in patients with oral carcinoma (Table 3).

There were no correlations between investigated salivary analytes and age of the patients with OSCC, lesion surface, duration of oral lesion, community periodontal index (CPITN), salivary flow rate, number of smoked cigarettes and alcohol units which were consumed per day (Table 3).

Discussion

Alcohol abusers represent one of the major social problems together with their impact on personal, family, professional and social life. It is well known that abusers come from dysfunctional families¹¹. Apart from that they are prone to various pathological systemic conditions, OSCC has been recognized as one of the most serious consequences in alcohol abusers especially if they smoke as well. Schpitzer et al.³ reported that concentrations of sodium, calcium, phosphate and magnesium were significantly higher in 25 patients with OSCC when compared to the 25 healthy controls whereas potassium concentrations were significantly lower in controls when compared to the OSCC patients. This is partially in concordance with our results as we also found increased levels of sodium and chloride in patients with OSCC when compared to the controls.

Zuabi et al.¹² found that the subjects with periodontal disease had elevated concentrations of sodium, calcium and magnesium, however within this group smokers with periodontal disease had reduced sodium, calcium, and magnesium. This is in contrast with our finding as our patients with OSCC were all smokers but had elevated levels of sodium and chloride when compared to the controls. Dental status has not been evaluated comprehensively in this study, however, in the previous study (article under review) we found that patients with OSCC didn't have dental status significantly different from the control group although control group in that study consisted of alcohol abusers so their dental status might be worse than average. It is well known that certain groups

of patients have increased needs for dental treatment due to their systemic conditions¹³. Sevon et al.² found clear increase in salivary calcium and phosphate together with increasing age, a finding which we couldn't confirm as there were no significant differences between our two study groups regarding calcium and phosphate and age range between our two groups was significantly different. Mandel¹⁴ reported elevated sodium levels in diabetes mellitus patients. On the contrary Marder et al.¹⁵ could not confirm that finding. Ben Aryeh¹⁶ noted an elevation in salivary sodium in digitalized patients in the unstimulated whole saliva. However, we must conclude that neither of our patients was diabetic, nor was anyone taking digitalis so increased levels of sodium and chloride in our study are probably due to some other cause. We might hypothesize that elevated sodium and chloride which are usually seen in sera of dehydrated patients are not so much connected to the oral carcinoma itself but a more related to the dehydration status of oral carcinoma patients who were all alcoholic. It is well known that alcohol has a diuretic effect due to its effect on the kidneys in terms of reduced reabsorption of the water. Also it is quite possible that these patients prefer to drink alcohol in comparison to the other beverages. Further study where salivary analytes of patients with oral carcinoma are compared to the alcoholics without oral carcinoma would perhaps clarify this assumption. Salivary level of total protein was significantly decreased in patients with oral carcinoma when compared to the healthy controls which is in concordance with Enberg et al.⁷ and there was also negative correlation between alcohol consumption and total protein concentration in patients with oral carcinoma. Both findings are quite logical as these patients are usually not eating enough, i.e. they are protein deprived in comparison to the healthy controls. Previously our colleagues¹⁷ reported that salivary calcium was elevated in HIV positive patients receiving highly antiretroviral therapy as a consequence of drug intake as there were no differences between HIV positive patients and controls regarding salivary sodium, calcium, magnesium and zinc. Finally, we could not confirm finding of Enberg et al.⁷ as well as Abelson et al.¹⁸, Dutta et al.⁴, Scott et al.⁵ that alcohol consumption lead to the changes in salivary flow rate as there were no differences between our patients with OSCC and controls regarding the salivary flow rate.

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V. Vučićević Boras

University of Zagreb, School of Dentistry, Gundulićeva 5, 10000 Zagreb, Croatia
email: boras@sfzg.hr

SALIVARNI ANALITI U OSOBA S ORALNIM PLANOCELULARNIM KARCINOMOM

SAŽETAK

Podatci iz literature pokazuju kako mjerenje određenih salivarnih sastojaka može biti koristan dijagnostički/prog-
nostički biljeg u oboljelih od oralnog planocelularnog karcinoma (OPCK). U 24 bolesnika s OPCK (60±2,5 godina sta-
rosti) i u 24 kontrolna ispitanika (24±3,7 godina starosti) su se određivali salivarni magnezij, kalcij, bakar, kloridi,
fosfati, kalij i natrij kao i ukupni proteini i amilaza. Natrij, kalij i kloridi su određeni indirektnom potencijometrijom dok
su bakar, magnezij i fosfati određeni atomskom apsorpcijskom spektrofotometrijom. Ukupni proteini su određeni kolo-
rimetrijskom metodom uz pomoć pirogalola, a amilaza sa kontinuiranom kolorimetrijskom metodom. Statistička ana-
liza je napravljena uz pomoć χ^2 testa te Spearmanovog testa korelacija. Rezultati ovog istraživanja pokazuju kako je
koncentracija salivarnog natrija i klorida bila znakovito povišena u bolesnika s OPCK u usporedbi s kontrolnom sku-
pinom. Ukupni proteini sline ispitne skupine su bili sniženi u odnosu na kontrolnu skupinu. Postojala je negativna
korelacija između konzumiranja alkohola i ukupnih proteina u bolesnika s OPCK. Vjerojatno povišena koncentracija
natrija i klorida nije u vezi sa lezijama OPCK već je možda posljedica dehidracije koja nastaje uslijed konzumiranja
alkohola.