Relationship Between Halitosis and Periodontitis: a Pilot Study

Povezanost halitoze i parodontitisa: pilot-istraživanje

Introduction

Periodontitis is a chronic inflammatory disease of the tooth’s supportive tissues. The complex pathogenesis of the disease involves an inflammation triggered by the main causative factor, periodontal pathogenic bacteria (1). A variety of measures have been used in both clinical and research settings for diagnosis, evaluation of the treatment outcomes and long-term monitoring, needed due to the chronic nature of the disease, i.e. periodontal probing depth, gingival recession, clinical attachment level and indices of plaque and bleeding (2). Clinical parameters (indices) of bleeding in particular, have been employed to identify and assess active inflammatory sites (3).

In 2008, Nesse et al. introduced a new measure, PISA (Periodontal Inflammed Surface Area), that reflects the surface of the bleeding epithelium of the periodontal pocket (4). The measure was initially developed as a tool that quantifies the inflamed periodontal area and, as such, assesses the inflammatory burden of periodontitis. The authors highlighted the value of PISA in the definition of periodontitis as a risk factor for other systemic diseases. This relatively new, emerging measure was hitherto correlated to the classification of periodontitis (5,6) and HbA1c levels in healthy and diabetics.

Uvod

Parodontitis je kronična upalna bolest zubnih potpornih tkiva. Složena patogeneza bolesti uključuje upalu koju pokreće glavni uzročnik – parodontne patogene bakterije (1). U kliničkim i istraživačkim uvjetima primjenjuju se razni dijagnostički postupci za dijagnozu, procjenu ishoda liječenja i dugoročno praćenje potrebno zbog kronične prirode bolesti. To su dubina sondiranja parodonta, recesija gingive, razina kliničkog pričvrstka te indeksi plaka i krvenja (2). Klinički parametri (indeksi) krvenja koriste se za prepoznavanje i procjenu aktivnih upalnih mjesta (3). Nesse i suradnici predstavili su 2008. novi parametar – površinu parodonta zahvaćenu upalom – PISA-u (engl. Periodontal Inflamed Surface Area) koji se odnosi na krveću površinu epitelia parodontnog džepa (4). Taj je parametar na početku razvijen kao alat koji kvantificira upaljenu površinu parodonta i kao takav procjenjuje upalni teret (engl. inflammatory burden) parodontitisa. Autori su istaknuli vrijednost PISA-e kod parodontitisa kao čimbenik rizika za druge sistemске bolesti. Taj razmjerno novi parametar dosad je povezan s klasifikacijom parodontitisa (5, 6) i HbA1c kod zdravih pacijenata i dijabetičara (7,8) te je izračunat za pacijente koji boluju od kronične bolesti bubrega (9,10) i one s reumatoidnim artritisom (11).
ic patients (7,8) and calculated for chronic kidney disease (9,10) and rheumatoid arthritis patients (11).

Halitosis is defined as an unpleasant smell emanating from the oral cavity. Quirynen et al. reported on the etiology and characteristics of 2000 patients who visited a specialized, multidisciplinary halitosis clinic in Belgium (12). Almost 80% of halitosis cases were of intra-oral origin. Tongue coating was the most common cause, followed by gingivitis/periodontitis and a combination of the two, accounting, respectively, for 43%, 11% and 18% of the cases.

The olfactory malodourous compounds are primarily the endproducts of microbial degradation of both sulphur-containing (i.e. cysteine, cystine, methionine) and non-sulphur-containing amino acids (i.e. tryptophan, lysine, ornithine). These amino acids are mainly derived from proteins present in bacterial plaque, saliva, blood and tongue coating. Volatile compounds containing sulphur (i.e. volatile sulphur compounds - VSCs), hydrogen sulphide (H₂S), hydrogen mercaptan (CH₃SH) and dimethyl sulphide [(CH₃)₂S] are the major contributors to halitosis. Non-sulphur-containing volatile compounds, i.e. indole, skatole, amines and ammonia, contribute to halitosis to a lesser extent (13,14).

Halitosis is a common complaint in the population of patients affected by periodontitis. Anaerobic gram-negative bacteria of the red complex, Porphyromonas gingivalis, Tannerella forsythia and Treponema denticola, strongly relate to clinical measures of periodontal disease and are also associated with higher production of VSCs (15,16). However, the literature on the association between the depth of periodontal pockets and VSC production in patients with periodontitis reports conflicting data (17). Furthermore, there is a growing body of evidence that the activity of the disease, i.e. inflammation, expressed through measures of bleeding, is related to oral malodour (18–22). In patients with periodontitis, tongue coating can be another contributing factor to oral malodour since it has been reported that patients with periodontitis produce more tongue coating than healthy individuals (18).

Thus, this pilot study aims to evaluate the association between halitosis measures, clinical indicators of periodontitis and tongue coating. Furthermore, this study explores the correlation between halitosis parameters and a novel measure, periodontal inflamed surface area (PISA).

Material and methods

Study subjects

This pilot study is part of the doctoral dissertation study “Effect of probiotic Lactobacillus reuteri as an adjunct to nonsurgical treatment on halitosis of patients with periodontitis: a randomised placebo-controlled trial”, approved by the Ethics Committee of the School of Dental Medicine of the University of Zagreb (05-PA-15-11/2017). The present study used baseline clinical data obtained from 10 patients who participated in the study.

Patients that were seeking or were referred for periodontal care to the Department of Periodontology of the School of Dental Medicine of the University of Zagreb were screened for possible inclusion in the study. Furthermore, a simple di-

Halitosa se definira kao neugodan vonj koji se širi iz usne šupljine. Quirynen i suradnici izvijestili su o etiologiji i karakteristikama 2000 pacijenata koji su posjetili specijalizirani multidisciplinarni kliniku za halitozu u Belgiji (12). Gotovo 80% slučajeva halitozu bilo je intraoralnog podrijetla. Naslage na jeziku bile su najčešći uzrok, nakon čega slijedi gingivitis/parodontitisa i kombinacija gore navedenoga, odnosno prema učešću u 43%, 9% i 18% slučajeva. Spojevi neugodnog mirisa kod halitozu uglavnom su krajnji produkci i mikrobnog razgradnje aminokiselin i onih koji sadržavaju bumpor (tj. cistein, cistin, metionin) i aminokiseline koje ne sadržavaju bumpor (tj. triptofana, lizina ili ornitina). Te aminokiseline uglavnom potječu iz proteina u bakterijskom plaku, slini, krvi i jeziku. Hlapljiv spojevi koji sadržavaju bumpor (engl. volatile sulphur compounds – VSCs), suma rovdik (H₂S), metil-merkaptan (CH₃SH) i dimetilni sulfid [(CH₃)₂S] glavni su uzročnici halitozu. Hlapljivi spojevi koji ne sadržavaju bumpor, tj. indol, skatol, amini i amonijak, pridonose halitozi u manjoj mjeri (13, 14).

Pacijenti s dijagnozom parodontitisa učestalo se žale na halitozu. Anaerobne gram-negativne bakterije crvenoga kompleksa – Porphyromonas gingivalis, Tannerella forsythia i Treponema denticola – snažno su povezane s kliničkim vrijednostima parodontitisa te s većom produkcijom VSC-a (15, 16). No u literaturi postoje oprečni podaci o povezanosti dubine parodontnih džepova i stvaranja VSC-a kod pacijenata s parodontitismom (17). Nadalje, sve je više dokaza da je aktivnost bolesti, tj. upala izražena u vrijednostima krvenanja, povezana sa zahodom (18 – 22). Kod pojedinaca s parodontitismom naslage na jeziku mogu biti još jedan čimbenik koji pridonosi neugodnom zahodu, jer je zabilježeno da takvi pacijenti imaju više nasлага na jeziku nego zdrave osobe (18).

Dakle, ovim pilot-istraživanjem želi se procijeniti povezanost između mjera halitose, kliničkih pokazatelja parodontitisa i naslaga na jeziku. Cilj je također istražiti vezu između parametara halitose i površine parodonta zahvaćene upalom (PISA).
chotomous organoleptic assessment (halitosis present / not present) was employed as a preliminary screening method for halitosis. A thorough medical and dental history was then taken, following the recommendations from an international workshop consensus (25) to exclude extraoral halitosis, causative of systemic diseases and/or medications.

Inclusion criteria were: 1) Systemically healthy patients of both genders; 2) Non-smokers; 3) Presenting at least 20 teeth; 4) Untreated moderate to advanced generalised chronic periodontitis according to the 1999 Classification (23) / Generalised periodontitis stage II-IV according to the 2017 Classification (24); 4) Halitosis of intraoral origin, with a level of total sulphur compounds concentration - tVSC≥160 parts per billion (ppb) measured with a portable sulphide monitor (Halimeter®, Interscan Corporation Chatsworth, CA, USA).

Exclusion criteria were 1) Pregnant and lactating females; 2) Antibiotics received for dental or non-dental purposes within 6 months before the start of the study; 3) Presence of systemic diseases or the use of medication that may affect periodontal tissues, the parameter of bleeding that can be the cause of extra-oral malodour; 4) Acute oral or periodontal inflammation or infection (i.e. pericoronitis, necrotising periodontal diseases, etc.)

A comprehensive periodontal examination was performed by a single, calibrated periododontist (L.M.). The following parameters were measured and registered using a UNC-15 periodontal probe (Hu Friedy, Chicago, IL, USA): periodontal pocket depth (PPD), plaque (calculated as full-mouth plaque score – FMPS), bleeding on probing (calculated as full-mouth bleeding score – FMBS) and gingival recession (REC). A periodontal assessment of the parameters was done at 6 sites per tooth, excluding third molars due to the high prevalence of agenesis, absence due to extraction, malpositioning or infraocclusion, which may present difficulties in measuring periodontal parameters.

Halitosis assessment

Halitosis assessment was performed using an organoleptic method and a portable sulphide monitor, measuring tVSC, i.e. total concentration of the 3 sulphur compounds - hydrogen sulphide, methyl mercaptan and dimethyl sulphide (Halimeter®, Interscan Corporation Chatsworth, CA, USA). Both procedures were performed following recommendations from the literature (26) and the manufacturer’s instructions for the use of device (27). Patients were requested to refrain from eating spicy food, onion and garlic at least 24 hours before the assessment. Furthermore, they were asked not to use scented oral hygiene products on the morning of the assessment or infraocclusion, which may present difficulties in measuring periodontal parameters.

The organoleptic assessment and scoring were done by a single clinician (L.M.). The participant was asked to keep the mouth closed for 2 min and breathe through the nose. The examiner positioned approximately 5 – 10 cm from the participant’s mouth, scored the breath with the mouth open while the patient was slowly exhaling the breath. Malodour was given an organoleptic score (OLS) from 0 to 5 as follows: 0 – nema organoleptička procjena (halitoza prisutna / nije prisutna) / nema organoleptička procjena (halitoza prisutna / nije prisutna) / nema organoleptička procjena (halitoza prisutna / nije prisutna) / nema organoleptička procjena (halitoza prisutna / nije prisutna) / nema organoleptička procjena (halitoza prisutna / nije prisutna).

Kriteriji za isključenje bili su: 1) Trudnice i dojilje; 2) Antibiotički userti u stomatološke ili nestomatološke svrhe 6 mjeseci prije početka istraživanja; 3) Sustavne bolesti ili uporaba lijekova koji mogu utjecati na parodontna tkiva, parametar krvarenja ili ekstraoralni uzroci zadaha; 4) Akutna oralna ili parodontna upala ili infekcija (tj. perikoronitis, nekrotizirajuće parodontne bolesti itd.).

Sveobuhvatan parodontni pregled obavio je jedan klibirani parodontolog (L. M.). Sljedeći parametri izmjereni su i registrirani parodontnom sondom UNC-15 (Hu Friedy, Chicago, IL, SAD): dubina parodontnog dijela (PPD), plak (izračunato kao prisutnost plaka na razini cijelih usta – FMPS), krvarenje pri sondiranju (izračunato kao krvarenje na razini cijelih usta – FMBS) i recesija gingive (REC). Parodontna procjena parametara provedena je na šest mjesta po zubu, isključujući treće kutnjake zbog velike prevalencije njihove ageneze, odsutnosti zbog ekstrakcije i malpozicije ili intraokluzije, što može činiti poteškoće u mjerenju parodontnih parametara.

Procjena halitoze

Procjena halitoze provedena je organoleptičkom metodom i prijenosnim sulfitnim monitorom mjereći tVSC, tVSC, tVSC, tVSC. Ukupnu koncentraciju triju spojeva sa sumpornom - vodikov sodi, metil-merkaptana i dimetilnog sodi (Halimeter®, Interscan Corporation Chatsworth, CA, SAD). Oba postupka obavljena su prema preporukama iz literaturi (26) i proizvođača uređaja (27). Od pacijenata je zatraženo da se suzdžuje od konzumiranja začinjene hrane, luka i češnjaka zbog velike prevalencije njihove ageneze, odsutnosti zbog ekstrakcije i malpozicije ili intraokluzije, što može činiti poteškoće u mjerenju parodontnih parametara.

Kriteriji za uključenje bili su: 1) Tražnji liječenje za parodontalne bolesti; 2) Antibiotici uzeti u stomatološke ili nestomatološke svrhe 6 mjeseci prije početka istraživanja; 3) Sustavne bolesti ili uporaba lijekova koji mogu utjecati na parodontna tkiva, parametar krvarenja ili ekstraoralni uzroci zadaha; 4) Akutna oralna ili parodontna upala ili infekcija (tj. perikoronitis, nekrotizirajuće parodontne bolesti itd.).

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PISA calculation

PISA was calculated using an available calculator with an Excel spreadsheet, prepared by the authors Nesse et al. (4) and uploaded on the website www.parsprototo.info for research use. The calculation was done in 7 steps, previously reported in detail by the authors. In short: 1) Mean clinical attachment level (CAL) was calculated for each tooth after data input; 2) Calculated mean CAL was translated into attachment loss surface area (ALSA) for each tooth with an appropriate formula; 3) Mean recession was calculated for each tooth after data input; 4) Calculated mean recession was translated into recession surface area (RSA) for each tooth with an appropriate formula; 5) RSA was subtracted from ALSA for each tooth, calculating periodontal epithelial surface area (PESA); 6) PESA of each tooth was multiplied by the proportion of positive BOP sites of that tooth, rendering periodontal inflamed surface area (PISA); 7) Total PISA was calculated through the sum of PISAs of each individual tooth.

Data analysis

The normality of distribution was evaluated using the Shapiro-Wilk test and by inspecting normal Q-Q plots. A non-parametric correlation analysis (Spearman) was used to explore the relationship between variables PISA, FMBS, FMPS, PPD≥4mm, PPD≥6mm, tVSC, OLS, and TC. The statistical analysis was performed using SPSS (version 20, IBM, Armonk, NY, USA). Due to exploratory nature of this pilot study, the level of significance was set at $\alpha = 0.1$ (30).

Results

General results

A total of 10 participants, 5 male and 5 female, were included in this pilot study. The median age was 38.5 (range 0: no appreciable odour; 1: barely noticeable odour; 2: slight, but clearly noticeable odour; 3: moderate odour; 4: strong odour; and 5: extremely foul odour, as described by Rosenberg et al. (28).

The measurement of the tVSC (total volatile sulfur compounds) concentration, expressed as parts per billion, was obtained using the portable sulphide monitor. A disposable tube was inserted approximately 3 – 4 cm into the participant’s mouth, slightly opened, without touching any of the oral surfaces. 3 consecutive measurements were taken, and the mean of the measurements was recorded (Figure 1).

Tongue coating evaluation

The tongue coating (TC) assessment was done using the Winkel Tongue Coating Index (WTCI) (29). The dorsum of the tongue was divided into six areas, three in the anterior portion and three in the posterior portion, and each area was then assigned one of the three possible scores. No coating was scored as 0, light coating as 1 and heavy coating as 2, with a total tongue score ranging from 0 to 12.

Mjerenje koncentracije tVSC-a (ukupnih hlapljivih sum-pornih spojeva), izraženo u dijelovima na milijardu, učinjeno je s pomoću prijenosnog sulfidnog monitора. Jednokratna mjerna cjevica umetnuta je od 3 do 4 cm u sudionikova usta koja su bila minimalno otvorena, bez dodirivanja bilo koje površine usne šupljine. Učinjena su tri uzastopna mjerenja i zabilježena je srednja vrijednost mjerenja (slika 1.).

Procjena naslaga na jeziku

Procjena obloženosti, tj. naslaga na jeziku (TC) provedena je s pomoću Winkelova indeksa obloženosti jezika (WT CI) (29). Dorzum jezika podijeljen je na šest područja – tri u prednjem i tri u stražnjem dijelu, a svakom se području za tim dodijelio jedan od triju mogućih rezultata. Ako nema naslaga, ocjena je 0, mala količina naslaga znači ocjenu 1, a velika količina ocjenu 2, s ukupnim rezultatom u rasponu od 0 do 12.

Izračun PISA vrijednosti

PISA je izračunata korištenjem dostupnog kalkulatora u proračunskoj tablici Excel koju su pripremili autori Nesse i suradnici (4) i koja je postavljena na mrežnu stranicu www.parsprototo.info radi primjene u istraživanjima. Izračun se obavlja u sedam koraka, što su autori prethodno detaljno objasnili. Ukratko: 1) Prosječna razina kliničkoga pričvrstka (CAL) izračunava se za svaki Zub nakon unosa podataka; 2) Izračunata srednja vrijednost CAL-a pretvara se u površinu gubitka pričvrstka (ALSA) za svaki Zub s odgovarajućom formulom; 3) Prosječna recesija izračunavala se za svaki Zub nakon unosa podataka; 4) Izračunata srednja vrijednost recesije prevodi se u površinu recesije (RSA) za svaki Zub s odgovarajucom formulom; 5) RSA se oduzima od ALSA-e za svaki ZUB za razliku i priručnika parodontnog epitelja (PESA); 6) PESA svakog Zuba množi se s brojem pozitivnih BOP mjesta toga Zuba, što čini upaljenu parodontnu površinu (PISA); 7) Uukupna PISA izračunava se na temelju zbroja PISA-e svakoga Zuba.

Analiza podataka

Normalnost raspodjele procijenjena je Shapiro-Wilovim testom i ispitivanjem normalnih Q-Q ploha. Zbog utvrđenih odstupanja od normalnoga, podaciti su predstavljeni kao medijani i interkvarterni rasponi. Neparometrijska korelacijak analiza (Spearman) korištena je za istraživanje odnosa između varijabli PISA, FMBS, FMPS, PPD≥4 mm, PPD≥6 mm, tVSC, OLS and TC. Statistička analiza provedena je s pomoću SPSS-a (verzija 20, IBM, Armonk, NY, SAD). Zbog eksplo - ratorne prirode ovoga pilot-istraživanja razina značajnosti postavljena je na $\alpha = 0.1$ (30).

Rezultati

Općir rezultati

Ukupno 10 sudionika – 5 muškaraca i 5 žena – bilo je uključeno u ovu pilot-istraživanje. Srednja dob bila je 38,5
The median, minimum and maximum, and interquartile range of the measured parameters are listed in Table 1. The median PISA value was 1617.8. The halitosis measures median values, OLS and tVSC were 3.0 and 334.5, respectively. The median tongue coating value was 5.0.

**Correlations between different parameters**

In terms of the association between the clinical and halitosis measures, significant correlations were found between the OLS and FMPS ($r=0.614$, $p=0.059$), as well as between the OLS and TC ($r=0.554$, $p=0.097$) (Table 2). A significant correlation was found between OLS and tVSC values, $r=0.931$, $p<0.001$ (Figure 2).

In addition, the PISA values showed a positive correlation with FMBS and FMPS indices, $r=0.733$, $p=0.016$ and $r=0.839$; $p=0.002$, respectively.

### Table 1

| Parameter       | Median • Medijan | Minimum | Maximum • Maksimum | Interquartile range • Interkvartilni raspon |
|-----------------|------------------|---------|--------------------|---------------------------------------------|
| Age (y)         | 38.5             | 29.0    | 72.0               | 12.0                                        |
| PISA (mm²)      | 1617.8           | 1248.6  | 2950.7             | 934.4                                       |
| FMBS (%)        | 78.0             | 61.9    | 100.0              | 25.4                                        |
| FMPS (%)        | 82.9             | 75.0    | 100.0              | 17.6                                        |
| PPD≥4 mm (N)    | 57.0             | 41.0    | 111.0              | 53.0                                        |
| PPD≥6 mm (N)    | 14.5             | 0.0     | 63.0               | 17.0                                        |
| tVSC (ppb)      | 334.5            | 184.0   | 462.0              | 176.0                                       |
| OLS (N)         | 3.0              | 2.0     | 5.0                | 1.0                                         |
| TC (N)          | 5.0              | 1.0     | 10.0               | 4.0                                         |

PISA – periodontal inflamed surface area • površina parodontne upale; FMBS – full-mouth bleeding score • iznos krvarenja na razini cijelih usta; FMPS – full-mouth plaque score • iznos plaka na razini cijelih usta; PPD≥4mm – pocket probing depth ≥4 mm; PPD≥6mm – pocket probing depth ≥6 mm; tVSC – total volatile sulphur compounds, measured with Halimeter® • ukupni hlapljivi sumporni spojevi izmjereni instrumentom Halimeter®; OLS – organoleptic score • organoleptička ocjena; TC – tongue coating • obloženost (naslaga) jezika
Table 2

| PISA | FMBS | FMPS | PPD≥4mm | PPD≥6mm | rVSC | OLS | TC |
|------|------|------|---------|---------|------|-----|----|
|      | 0.733 (0.016) | 0.839 (0.002) | 0.572 (0.084) | 0.697 (0.025) | - | - | - |
| FMBS | - | - | - | - | - | - | - |
| FMPS | - | - | - | - | - | - | - |
| PPD≥4mm | - | - | - | - | - | - | - |
| PPD≥6mm | - | - | - | - | - | - | - |
| rVSC | - | - | - | - | 0.931 (0.000) | - | - |
| OLS | - | - | - | - | - | 0.554 (0.097) | - |
| TC | - | - | - | - | - | - | - |

Values • Vrijednosti: Spearman’s correlation coefficient – r (p-values) • Spearmanov koeficijent korelacije – r (p-vrijednosti)

PISA – periodontal inflamed surface area • površina parodontne upale; FMBS – full-mouth bleeding score • iznos krvarenja na razini cijelih usta; FMPS – full-mouth plaque score • iznos plaka na razini cijelih usta; PPD≥4mm – pocket probing depth ≥4 mm • dubina sondiranja parodontnog džepa ≥ 4 mm; PPD≥6mm – pocket probing depth ≥6 mm • dubina sondiranja parodontnog džepa ≥ 6 mm; rVSC – total volatile sulphur compounds, measured with Halimeter® • ukupni hlapljivi sumporni spojevi izmjereni instrumentom Halimeter®; OLS – organoleptic score • organoleptička ocjena; TC – tongue coating • obloženost (naslage) jezika

Discussion

The present pilot study explored the correlation between the parameters of halitosis and clinical indicators of periodontitis, tongue coating and, for the first time, the PISA.

Rizzo (31) and Tonzetich (32) were among the first to report a correlation between the production of sulfur compounds and periodontal disease, particularly the presence of periodontal pockets. While other research groups published similar findings, the correlation between the halitosis parameters and periodontal pocket depth was not always exclusive. A study by Liu et al., on a large population of 2000 participants, reported a significant correlation between the OLS and tVSC levels and pocket depth, however, tongue coating was highlighted as the most significant variable related to the oral malodour measures (19). Yaegaki & Sanada (18) showed the association between a higher concentration of methyl mercaptan in patients with pocket depths above 4 mm and bleeding on probing. The severity of periodontitis correlated with halitosis as reported by Söder et al. (33), as well as measures of oral hygiene, expressed through plaque and calculus indices. In our study, however, the number of pockets above 4 mm and 6 mm, respectively, showed no significant correlation with halitosis measures.

It is important to emphasize the fact that not all evidence supports the existence of correlation between the number of periodontal pockets and depth with halitosis measures, thus questioning the causative relationship between periodontitis and halitosis. Bosy et al. (34) found a correlation between tongue coating and floss odour after insertion in the interdental area with tVSC and OLS values. However, no significant difference in halitosis measures could be observed among patients with periodontitis and healthy groups of participants. In the present study, an association between OLS and FMPS was also observed. While the indices measuring plaque, i.e. oral hygiene, are not the same as ours and the abovementioned study, it has been suggested in the literature that poor oral hygiene could be a source of halitosis of patients with periodontitis irrespective of the presence of periodontal pockets (35).

Rasprava

Autori ovog pilot-projekta istraživali su korelaciju između parametara halitoze i kliničkih parametara parodontitisa, obloženosti jezika i, prvi put, PISA-e.

Rizzo (31) i Tonzetich (32) među prvima su izvijestili o povezanosti između stvaranja sumpornih spojeva i parodontne bolesti, odnosno prisutnosti parodontnih džepova. Iako su druge istraživačke skupine to potvrđivale, povezanost između parametara halitoze i dubine parodontnog džepa nije uvijek bila jedinstvena. Istraživanje Liu i suradnika, na većkoj populaciji od 2000 sudionika, pokazalo je da je riječ o njoj varijabli povezana s oralnim vrijednostima zahaza (19). Yaegaki i Sanada (18) istakli su povezanost veće koncentracije metil-merkaptana kod pacijenata s dubinom džepa iznad 4 mm i krvarenjem pri sondiranju. Kako su izvijestili Söder i suradnici (33), uznapredovalost parodontitisa koristila je s halitozem, ali i s vrijednostima oralne higijene izraženih kroz indeks plaka i kamenca. No u našem istraživanju broj džepova iznad 4 mm, odnosno 6 mm, nije pokazao značajnu korelaciju s vrijednostima halitoze.

Važno je istaknuti da svi dokazi ne podupiru povezanost broja i dubine parodontnih džepova s vrijednostima halitoze, čime se dovodi u pitanje uzročni odnos između parodontitisa i halitoze. Bosy i suradnici (34) pronašli su korelaciju između naslage na jeziku i mirisa zubnog konca nakon umetanja u međuzubno područje s vrijednostima tVSC-a i OLS-a. No nije se mogla uočiti značajna razlika u jačini halitoze između pacijenata s parodontitismem i zdravim sudionikom. U ovom istraživanju zapažena je i povezanost između OLS-a i FMPS-a. Iako indeksi kojima se mjeri plak, tj. oralna higijena, nisu jednaki u ovom i prije spomenutom istraživanju, u literaturi se sugerira da bi loša oralna higijena mogla biti izvor halitoze kod bolesnika s parodontitismom, bez obzira na parodontne džepove (35).
Calil et al. and De Bover & Loesche (36,37) reported an association between halitosis and tongue coating measures, yet not with periodontal disease measures.

As seen in the general population-based cross-sectional studies (12,19,20), tongue coating is suggested to be the primary cause of halitosis among periodontally healthy subjects. This is primarily attributed to the large surface of the tongue’s dorsum and its morphology (38), thus contributing to the accumulation of dead microbial and host cells, the source of halitosis. Furthermore, taking into account the evidence highlighted hitherto, it has been suggested that tongue coating is also an important contributing factor to halitosis in patients with periodontitis, since they produce more tongue coating than healthy individuals (39). They also harbour greater counts of the VSC-producing periodontal pathogen, Porphyromonas gingivalis, on the dorsum of the tongue (40).

Our study showed a correlation between tongue coating and OLS values, but not tVSC. While sulphide monitors such as Halimeter® and OralChroma™ are an objective measuring of tVSCs and previous studies confirmed their clinical value, they fail to capture the contributions of non-sulfur compounds to the overall halitosis (14,41,42). An organoleptic assessment is considered the gold standard for halitosis detection because the human nose can evaluate a greater variety of malodorous compounds/odourants (41). According to the manufacturer of the Halimeter, patients are diagnosed with halitosis when the level of VSCs exceeds 160 ppb, but as suggested by Vanderkerckhove et al. (41) this cut-off should be lowered in order to improve the sensitivity of the instrument with regard to organoleptic testing. The range of OLS and tVSC values in our study ranged from 2 - 5 and 184.0 - 462.0 ppb, respectively, and a strong correlation was found between the two halitosis variables (r = 0.931). This is considered an important finding, considering that this pilot study performed as a preliminary investigation for the upcoming comprehensive study "Effect of probiotic Lactobacillus reuteri as an adjunct to nonsurgical treatment on halitosis of patients with periodontitis: a randomised placebo-controlled trial", in which halitosis measurements will be done by OLS assessment, and Halimeter® as an adjunct.

As indicated before, bleeding expressed through various bleeding and inflammation indices was found to be correlated to halitosis in several published studies (18,19,21,43,44). Bleeding is a sign of inflammation of the connective tissue of the gingiva. Thus, a variety of bleeding indices are employed to assess the presence of inflammation. In particular, when bleeding is associated with pocket probing, it indicates a site with active periodontal disease (3,45). A possible explanation for the association of bleeding pockets and halitosis is the presence of periodontal pathogens, VSC-producing anaerobic bacteria at such sites (46). Indeed, as highlighted in a study by Torresyap et al., intra-pocket sulphide levels, measured with a specific Diamond Probe/Perio 2000 system, are higher in deeper pockets with higher counts of orange- and red-complex bacteria (47). Since PISA is a parameter that quantifies the surface of the bleeding epithelium of the pocket, one of the hypotheses of this study was that a correlation between this novel measure and halitosis might be observed.
However, the present study did not confirm this hypothesis since no significant observations with OLS or tVSC values were found. Nonetheless, the PISA values were positively correlated to values of FMPS and FMBS, as previously reported by Park et al. (5).

Leira et al. and Nesse et al. (4,6) correlated the PISA values and periodontal status, highlighting the increase in PISA values with disease severity, the former also suggesting a cut-off PISA value of ≥130.33 mm² as a predictor for the presence of periodontitis. In our study, the values of PISA ranged from 1248.6 to 2950.7 mm². These values correspond to the values calculated for severe periodontitis (6).

The intrinsic limitations of this pilot study are the small sample size and the absence of a control group. Due to the sample of n=10 representing a specific population of patients, i.e. only highly inflamed patients with a progressed periodontitis forms and identifiable intraoral halitosis, the analysis might not have captured the correlation between all of the parameters. A sequel study with a larger sample size will be performed, including a control group of patients with periodontitis and no halitosis.

**Conclusion**

This pilot study shows and further reiterates a complex interplay between different factors causative to halitosis in patients affected by periodontitis. OLS values correlated to measures of oral hygiene and tongue coating, however, no correlation to probing depth could be observed.

**Conflict of interest**

None declared

**Contributions:** L.M. – primary clinical investigator, data collection, concept and design, interpretation, visualisation, writing, approval of the article for publication; M.P. - concept and design, formal analysis, statistical analysis, interpretation, writing; J.P. – data collection, visualisation, writing; A.B. – interpretation, writing, critical review; D.P. – supervision, critical review and editing, approval of the article for publication; L.M. – clinical research operator, concept and design, interpretation, writing, critical review and editing.

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**Sazetak**

**Cilj istraživanja:** Halitozu ili zadan neugodan vonj koji se širi iz usne šupljine. Česta je pritužba među pacijentima s parodontitisom, no njihova povezanost nije u cijelosti razjašnjena. Cilj ovog istraživanja bio je procijeniti povezanost između parametara halitoe, kliničkih parametara parodontitisa i obloženosti jezika te novog parametra – površina parodonta zahvaćena upalom (engl. periodontal inflated surface area – PISA).

**Materijali i metode:** U ovo su istraživanje uključeni podatci 10 pacijenata s parodontitisom i halitozom. Halitozu je procijenjena organoleptičkom metodom i prijenosnim suflidnim monitorom kojim se mjere hlapljive sumporne spojeve. Prvenstveno je sveobuhvatni parodontitis klinički istraživač, recesija gingive, razine kliničkoga prićvrska, krvarenja pri sondiranju, plaka i naslaga na jeziku. PISA je izračunata koristeći se razinom kliničkoga prićvrska, recesije gingive i krvarenja pri sondiranju. **Rezultati:** Uočena je povezanost između organoleptičke ocjene halitoe i obloženosti jezika (r = 0.554) i plaka (r = 0.614). Nije zabilježena povezanost između parametara halitoe i dubine sondiranja ili PISA-e, Organoleptička ocjena halitoe i vrijednost hlapljivih sumpornih spojeva značajno su korelirali (r = 0.931).

**Zaključak:** Ovo pilot-istraživanje pokazuje i ponovno ističe složenu interakciju različitih čimbenika koji uzrokuju halitozu kod pojedinaca oboljelih od parodontitis. Vrijednosti OLS-a povezane su s vrijednostima oralne higijene i naslaga na jeziku, no nije uočena povezanost s dubinom sondiranja.

**Sukob interesa**

Autori nisu bili u sukobu interesa.

**Doprinos autora:** L. M. – primarni klinički istraživač, prikupljanje podataka, koncept i dizajn, interpretacija, vizualizacija, pisanje, odbivanje članka za objavljivanje; M. P. – koncept i dizajn, formalna analiza, statistička analiza, interpretacija, pisanje; J. P. – prikupljanje podataka, vizualizacija, pisanje; A. B. – interpretacija, pisanje, kritički osvrto; D. P. – nadzor, kritički pregled i uređivanje, odbivanje članka za objavljivanje; I. P. – operator kliničkog istraživanja, koncept i dizajn, interpretacija, pisanje, kritički pregled i uređivanje.

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**MeSH pojmovi:** oralna higijena; jezik

**Ključne riječi:** halitoz, parodontitis, jezik
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