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Razine folata u sindromu pekućeg jezika

Folate Levels in Burning Tongue

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Sažetak
Zapaženo je da su u sindrom pekućeg jezika uključene određene hematološke abnormalnosti. Svrha istraživanja bila je usporediti razine folata pacijenata s pekućim jezikom i ispitanika iz zdrave kontrolne skupine. Sudjelovalo je 29 pacijenata i 21 zdrav dobrovoljan sudionik. Ispitane su kompletne krvne slike, tipizirani su hemoglobin, serumski folati, folati iz crvenih krvnih stanica te razine serumskog vitamina B12. Svi su također morali reći uzimaju li kakve lijekove i imaju li sustavne bolesti. Rezultati su pokazali da je 13 od 29 pacijenata (44,83 %) imalo nisku razinu folata u crvenim krvnim stanicama, a kod zdravih ispitanika bila je normalna. Pacijenti s niskim razinama folata definirani su nazivom folatna deficijencija (n=6), folatima deficijentna eritropoeza (n=2), te folatna deplecija (n=5). Zabilježena je znatna razlika u razinama folata između dviju promatranih skupina (p=0,000). Zanimljivo je to što su se kod 11 od 29 pacijenata iz skupine s niskim razinama folata u crvenim krvnim stanicama pojavili različiti oblici zahvaćenosti jezika, poput linguae geographicae, fissuratae, atrophice, obloženog jezika te upale foliatnih papila. U samo dvama slučajevima pekućeg jezika s normalnim kliničkim izgledom, pronađene su niske razine folata u crvenim krvnim stanicama. Štoviše, nije bilo velike razlike između skupine na lijekovima i one bez lijekova (p=0,534). Ovo je istraživanje upozorilo na povezanost razina folata u crvenim krvnim stanicama i pekućeg jezika, no nikakva povezanost nije zabilježena između razina folata i bilo kojeg sustavnog stanja te uzimanja propisanih lijekova.

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Ključne riječi
pekući jezik; sustavno stanje; lijekovi; folna kiselina

Uvod

Zna se da klinički izgled jezika omogućuje uvid u čovjekovo opće zdravstveno stanje. Pekući jezik je česta tegoba, ali njegovo je liječenje složeno i dosta teško. Pacijenti s pekućim jezikom mogu imati normalan ili različit klinički izgled jezika, poput linguae geographicae i atrophicae. To stanje može biti udruženo s određenim čimbenicima i lijekovima te hematološkom poremećajima. (1, 2). Uočena je i uključenost određenih krvnih diskrazija, kao razine folata te vitamina B12 kod glositisa, stomatitisa i rekurentnog aftoznog stomatitisa (2-4). U ranijim je istraživanjima upozoreno na niske serumske razine vitamina B12 (5) i folata u crve-

Introduction

It has been known that the tongue can provide some clinical clues of general health. Burning tongue is the common condition affected patients which is difficult to treat. Patients with burning tongue may present with normal or various appearances such as geographic and atrophic tongue. The condition may be associated with some factors such as medications and hematological disorders (1,2). It can be recognized that some blood abnormalities such as folate and vitamin B_{12} levels are involved in glossitis, stomatitis and recurrent aphthous stomatitis (2-4). Previous study reported that patients with glossitis or stomatitis had low serum vitamin B_{12} (5) and red cell folate levels (6).

nim krvnim stanicama (6) kod pacijenata s glositisom ili stomatitisom.

Ova je studija pokazala kako određene sustavne bolesti i lijekovi remete metabolizam folata. Tako su lijekovi, poput antacida i estrogena, prouzročili niske razine folata u crvenim krvnim stanicama u usporedbi sa sudionicima iz kontrolne skupine (6). Ipak, teško je tvrditi jesu li oralne lezije rezultat hematoloških poteškoća. Još nije razjašnjeno je li ukupna krvna slika potrebna kod svakog slučaja (7). Svrha je ovog istraživanja usporediti razine folata između pacijenata s pekućim jezikom i zdrave kontrolne skupine. Zatim, proučavali su se i različiti oblici kliničkog izgleda jezika, poput normalnog, obloženog, atrofičnog, geografskog, fisuriranog te upale lisnatih papila. Kod pacijenata s pekućim jezikom ispitan je i odnos između sustavnih stanja i propisanih lijekova. Rezultati bi mogli pomoći u liječenju i održavanju postignutih rezultata.

Materijali i metode

U istraživanje je bilo uključeno 29 pacijenata sa simptomima pekućeg jezika (20 žena i 9 muškaraca), a obavljeno je u Klinici za oralnu medicinu Stomatološkoga fakulteta Sveučilišta u Chulalongkornu. Analizirani su trajanje simptoma, manifestacije na jeziku, uzimanje lijekova te sustavne bolesti. Svi su ispitanici kao razlog dolaska naveli simptome pekućeg ili bolnog jezika. Iz ispitivanja su isključeni slučajevi vezani za kandidijazu, zbog studija u kojima je već proučena povezanost sindroma pekućih usta i infekcija kandidom (8-10). Manifestacije na jeziku dijagnosticirane su oralnim pregledima te su razvrstane u sljedeće kriterije (11, 12):

- obložen jezik: potpuna ili bijela obloženost dorzuma jezika, pa izgleda poput gustoga bijelog krzna;
- fisurirani jezik: kratka ili duga duboka centralna brazda na dorzumu jezika s višestrukim nepravilnim bočnim brazdama;
- lingua geographica: crvene i bijele mrlje na dorzumu jezika - crvena su područja na mjestima gdje manjkaju papile, pa su atrofična, a bijela su područja populirana ili normalnim ili hiperplastičnim papilama;
- atrofičan jezik: jezik nema uobičajen hrapav izgled stvoren papilama;
- papilitis lisnatih papila: upalu folijatnih papila karakteriziraju otekline i bol.

Istaknimo da je 21 zdrav, dobrovoljan sudionik (15 žena i 6 muškaraca) s normalnim kliničkim izgledom jezika i bez drugih simptoma, bio uključen u kontrolnu

Recent study showed that some systemic diseases and medications may interfere with folate metabolism. Those drugs such as antacid and estrogen caused significant low red cell folate levels when compared with the control group (6). However, it is difficult to establish whether the oral lesions are directly due to the underlying diseases or are the reflection of hematological deficiencies. It is still questionable whether a complete blood testing would be essential in each case (7). The purpose of this study was to compare the folate levels between patients with burning tongue and healthy control group. Moreover, various tongue appearances such as normal, coated, atrophic, geographic, fissured tongues and foliate papillitis were also studied. The relationships between systemic conditions and prescribed medications in patients with burning tongue were investigated. The results of this study may be useful for treatment and management in the patients with burning tongue.

Material and methods

Twenty-nine patients with burning tongue symptoms (20 females, 9 males) referred to the Oral Medicine clinic, Faculty of Dentistry, Chulalongkorn University were enrolled in this study. The duration of symptoms, manifestations of the tongue, medications taking and systemic conditions were recorded. All of their complaints included burning sensation or soreness on the tongues. Candida infection was excluded as earlier studies reported the association between burning mouth syndrome and candida infection (8-10). The manifestations of the tongue were diagnosed by oral examinations as the following criteria (11,12).

- Coated tongue: complete or partial white coating of the dorsum of the tongue giving the appearance of thick white fur
- Fissured tongue: short or long deep central groove on the dorsum of the tongue with multiple irregular side grooves
- Geographic tongue: red and white patches on the dorsum of the tongue. The red patches lack of papillae and are atrophic while the white areas have either normal or hyperplastic papillae
- Atrophic tongue: the tongue lacks of normal rough appearance created by the papillae
- Foliate papillitis: an inflammation of the foliate papillae characterized by swelling and pain

Additionally, 21 healthy volunteers (15 females, 6 males) who had normal tongues upon oral examination and no other symptoms were included as the control group. The age in patients with burning

skupinu. Dob pacijenata s pekućim jezikom kretala se između 28 i 79 godina (prosjek±SD = 52,83±11,02), a dob pripadnika kontrolne skupine bila je od 21 do 60 godina (prosjek±SD = 33,71±10,77). Trajanje simptoma variralo je 0,5 do 120 mjeseci (prosjek±SD = 21,90±32,40). Svi su pacijenti i zdravi ispitanici dali pristanak za sudjelovanje u istraživanju.

Laboratorijske pretrage

Ukupna krvna slika, tipizacija hemoglobina, razine serumskih folata, folata u crvenim krvnim stanicama te serumske razine vitamina B12, ispitane su prema navedenom opisu (6). Anemija je definirana kao hematokrit niži od 39% kod muških ispitanika i 36% kod ženskih. Makrocitoza je definirana kao prosjek corpuscular volume (MCV) iznad 100 fL, normocitoza kod MCV-a od 80-96 fL, a mikrocitoza kod vrijednosti niže od 80 fL (13). Razina folata u crvenim krvnim stanicama manja od 100 ng/mL smatrala se folatnom deficijencijom, razina od 100 do 120 ng/mL kao deficijentni eritropoezam, a razina od 120 do 160 ng/mL definirana je kao folatna deplecija. Serumska razina vitamina B12 niža od 150 pg/mL smatrala se niskom (14).

Statistika

Za usporedbu skupina koristili su se hi-kvadrat i Studentov t-test. Statistički znatnom smatrala se p-vrijednost manja od 0,05.

Rezultati

Prosjeci i rasponi serumskog folata, folata iz crvenih krvnih stanica i razina vitamina B12 među ispitanicima, prikazana je u Tablici 1. Prosječna razina folata iz crvenih krvnih stanica kod pacijenata s pekućim jezikom bila je niža nego u kontrolnoj skupini (p = 0,045). Niska je razina folata iz crvenih krvnih stanica ustanovljena kod 13 od 29 pacijenata s pekućim jezikom (44,83%). Definirani su kao folatno deficijentni (n=6), deficijentne folatne eritropoeze (n=2) te folatno depletni (n=5) (Tablica 2.). U kontrolnoj skupini kod svih je pronađena normalna razina folata iz crvenih krvnih stanica. Zabilježena je i znatna razlika u razini folata iz crvenih krvnih stanica između pacijenata s pekućim jezikom i onih u kontrolnoj skupini (p=0,000). Tri su pacijenta s pekućim jezikom i dva zdrava ispitanika imala nisku razinu serumskih folata. Nije bilo veće razlike u prosječnim serumskim razinama folata između dviju promatranih skupina (p=0,145). No, razine serumskog vitamina B12 bile su u obje skupine u

tongue ranged between 28 to 79 years (mean±SD = 52.83±11.02) and between 21 to 60 years (mean±SD = 33.71±10.77) in the control group. The duration of symptoms varied from 0.5 to 120 months (mean±SD = 21.90±32.40). Informed consents were obtained from all patients and the healthy controls before participating in this study.

Laboratory investigations

Complete blood count, hemoglobin typing, serum folate, red cell folate and serum vitamin B_{12} levels were investigated as previously described (6). Anemia was defined as a hematocrit of less than 39% for males and less than 36% for females. The macrocyte was defined as a mean corpuscular volume (MCV) above 100 fl, normocyte as MCV 80-96 fl and microcyte as MCV less than 80 fl (13). A red cell folate level below 100 ng/ml was defined as folate deficiency, 100–120 ng/ml as folate deficient erythropoiesis and 120-160 ng/ml as folate depletion. A serum vitamin B_{12} level less than 150 pg/ml was defined as low (14).

Statistics

The Chi-square and Student's t - test were used to compare between the groups. A p-value of less than 0.05 was considered statistically significant.

Results

The means and ranges of serum folate, red cell folate and vitamin B_{12} levels among the subjects are shown in Table 1. The mean red cell folate level in patients with burning tongue was lower than the control subjects (p = 0.045). Low red cell folate levels were determined in 13 out of 29 patients with burning tongues (44.83%). They were defined as having folate deficiency (n = 6), folate deficient erythropoiesis (n = 2) and folate depletion (n = 5) (Table 2). In the control group, all of the subjects showed normal red cell folate levels. Furthermore, there was a significant difference in red cell folate levels between patients with burning tongues and the control subjects (p =0.000).Three patients with burning tongue and 2 healthy subjects had low serum folate levels. There was no significant difference in the mean serum folate levels between two groups (p=0.145). Whereas, serum vitamin B_{12} levels were within normal ranges in both groups. One of the patients revealed Hb E trait and another was

Tablica 1. Prosjeci i rasponi serumskih folata, folata iz crvenih krvnih stanica i serumskih vitamina B12 kod pacijenata s pekućim jezikom u usporedbi s kontrolnom skupinom
Table 1 The means and ranges of serum folate, red cell folate and serum vitamin B12 levels in patients with burning tongue compared with the control group

Skupina • Group	Broj • Number	Serum folate (ng/ml) Prosjek±SD (raspon) • Mean+SD (range)	Red cell folate (ng/ml) Prosjek±SD (raspon) • Mean+SD (range)	Vitamin B_{12} (pg/ml) Prosjek±SD (raspon) • Mean+SD (range)
Pekući jezik • Burning tongue	29	18,12 ± 14.96 (3,6 - 62,17)	234,90 ± 191,78 (31 - 867)	593,68 ± 352,32 (222 - 1806)
Kontrolna skupina • Control	21	12,82 ± 7,85 (3,22 - 32,49)	319,29 ± 92,68 (202 - 629)	502,33 ± 147,73 (321 - 997)

Normalni rasponi u tajlandskoj kontrolnoj skupini bili su za serumske folate 5-24 ng/ml, za folate iz crvenih krvnih stanica 221-1,113 ng/ml, a za serumski vitamin B_{12} 211-911 pg/ml (vrijednosti iz Odjela za tropske radioizotope Fakulteta za tropsku medicinu Sveučilišta Mahidola u Bangkoku, Tajland).• The normal ranges in the Thai control group were serum folate 5-24 ng/ml, red cell folate 221-1,113 ng/ml and serum vitamin B12 211-911 pg/ml (Value from Department of Tropical Radioisotopes, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand).

Tablica 2. Folatni je status određen razinama folata iz crvenih krvnih stanica kod pacijenata s pekućim jezikom koji su uzimali lijekove ili nisu, te onima iz kontrolne skupine.
Table 2 The folate status determined by red cell folate levels among patient with burning tongue who received medication or no medication and the control

Skupina • Group	Broj • Number	Folatna deficiencija • Folate deficiency <100 ng/ml	Folatno deficijentna eritropoeza • Folate deficient erythropoiesis 100-120 ng/ml	Folatna Deplecija • Folate depletion 120-160 ng/ml	Normalna • Normal > 160 ng/ml
Pekući jezik • Burning tongue	29	6	2	5	16
S lijekovima • with medication	13	1	2	2	8
Bez lijekova • without medication	16	5	0	3	8
Kontrolna skupina • Control	21	-	-	-	21

Tablica 3. Folatni status određen je razinom folata u crvenim krvnim stanicama između pacijenata s pekućim jezikom te sudionika u kontrolnoj skupini
Table 3 The folate status determined by red cell folate levels among patients with burning tongue and control

Pekući jezik • Burning tongue (n=29)	Pridružena stanja i bolesti[a] (Broj slučajeva) • Associated conditions[a] (number of cases)		Niska razina folata iz crvenih krvnih stanica • Low red cell folate	Normalno • Normal
	Sustavna stanja i bolesti • Systemic conditions	Lijekovi • Medication		
Sa sustavnim bolestima • with systemic conditions (17)	Menopauza • Menopause (4) Psihogeno • Psychogenic (4) Hipertenzija • Hypertension (3) Diabetes mellitus (3) Hiperlipidemija • Hyperlipidemia (3) Astma • Asthma (2) Peptički vrijed • Peptic ulceration (3) Migrene • Migraine (1) Anemija • Anemia (1) Hb E svojstvo • Hb E trait (1) Reumatoidni artritis • Rheumatoid arthritis (1)	Antidepresivi & Anksiolitici • Antidepressant & Antianxiety (4) Estrogen • Estrogen (3) Hypoglicemija • Hypoglycemic (3) Antihipertenzivi • Antihypertensive (1) Hipolipidemija • Hypolipidemia (1) NES protuupalni lijekovi • NSAIDs (1) Drugi i herbalni • Others and herbal (3)	5	12
Bez sustavnih stanja • Without systemic condition (12)	-	-	8	4

[a] Neki su pacijenti imali više od jednog sustavnog stanja i pritom su uzimali više od jednog lijeka, no neki nisu primali nikakve lijekove za svoje sustavne bolesti. • Some patients had more than one systemic condition and were taking more than one medication , however some patients did not receive any medications for their systemic diseases.

Tablica 4. Kliničke slike pacijenata s pekućim jezikom i razine folata iz crvenih krvnih stanica
Table 4 Clinical appearances in patients with burning tongue and red cell folate levels

Kl. sl. jezika • Tongue appearances	Broj pacijenata • No.of patients	Broj pacijenata s niskim razinama folata iz crvenih krvnih stanica • No.of patients with low red cell folate
Atrofični • Atrophic	9	2
Obloženi • Coated	3	2
Fisurirani • Fissured	3	1
Fisurirani i atrofični • Fissured with atrophic	3	2
Geografski • Geographic	2	2
Fisurirani i geografski • Fissured with geographic	1	1
Folijatni papilitis • Foliate papillitis	2	1
Normalan jezik • Normal tongue	6	2

granicama normale. Kod jednog je pacijenta uočena Hb E karakteristika, a kod drugoga se sumnja na alfa-talasemiju. Kod svih ostalih hemoglobinsko je tipiziranje prošlo bez osobitosti.

S obzirom na propisane lijekove, pet od trinaest pacijenata (38,46%) uzimalo je lijekove, poput antidepresanata i anksiolitika (n=1), estrogen (n=2), hipoglikemični lijek (n=2), NES protuupalne lijekove i biljne preparate (n=1), a kod svih je ustanovljena niska razina folata iz crvenih krvnih stanica. Uzimali su jedan ili više lijekova u sklopu terapije svojih sustavnih bolesti. No, osam od šesnaest pacijenata (50%) koji nisu primali nikakve lijekove, također su imali niske razine folata iz crvenih krvnih stanica (Tablica 2.). Štoviše, nije zabilježena nikakva veza između razine folata iz crvenih krvnih stanica i propisanih lijekova (p=0,534).

Sustavna su stanja ustanovljena kod 17 od 29 pacijenata s pekućim jezikom (58,62%), poput menopauze (n=4), psihogena (n=4), hipertenzije (n=3), diabetesa mellitusa (n=3) i hiperlipidemija (n=3) (Tablica 3.). Pet od 17 pacijenata (29,41%) koji su bolovali od jedne ili više sustavnih bolesti, imali su nisku razinu folata iz crvenih krvnih stanica, kao i 8 od 12 pacijenata (66,67%) bez sustavnih bolesti. Nije bilo znatne razlike u razinama folata između pacijenata sa sustavnim bolestima i onih koji od njih ne boluju (p=0,361).

Zanimljivo je da su 2 od 6 pacijenata s normalnim kliničkim izgledom jezika, ali i osjećajem pekućeg jezika, također imali niske razine folata iz crvenih krvnih stanica (33,33%), a 11 od 23 pacijenta (47,83%) kod kojih je izgled jezika bio različit od normalnoga, poput atrofičnog, fisuriranog, obloženog, geografskog te folijatnog papilitisa, imali su niske razine folata iz crvenih krvnih stanica (Tablica 4.).

suspected of being alpha-thalassemia. The rest had normal hemoglobin typing.

Regarding to prescribed medications, 5 out of 13 patients (38.46%) who had been taking medications including antidepressant and antianxiety agents (n = 1), estrogen (n = 2), hypoglycemic drug (n = 2), NSAIDs and herb (n = 1) showed low red cell folate levels. They had been taking one or more medications for their systemic conditions. Whereas 8 out of 16 patients (50%) who did not receive any medications also had low red cell folate levels (Table 2). Moreover, no association was observed between red cell folate levels and prescribed medications (p=0.534)**.**

Systemic conditions were found in 17 out of 29 patients with burning tongue (58.62%) such as menopause (n = 4), psychogenic (n = 4), hypertension (n = 3), diabetes mellitus (n = 3) and hyperlipidemia (n = 3) (Table 3). Five out of 17 patients (29.41%) who had one or more systemic conditions had low red cell folate levels while 8 out of 12 patients (66.67%) who had no systemic conditions showed low red cell folate levels. There was no difference in folate levels between patients with systemic conditions and no systemic condition (p=0.361)

Interestingly, 2 out of 6 patients who had normal tongues with burning sensation also showed low red cell folate levels (33.33%) whereas 11 out of 23 patients (47.83%) who had one or more various tongue appearances such as atrophic, fissured, coated, geographic and foliate papillitis revealed low red cell folate levels (Table 4).

Rasprava

Različiti klinički izgledi jezika kod pacijenata s osjećajem pečenja mogu dati uvid u nekoliko stanja, poput niskih razina folata iz crvenih krvnih stanica. Vjerojatno je da je izgled jezika često posljedica statusa malnutricije. Iako je glosodinija vezana za nutricijske deficijencije rijetka, različiti oblici nepravilne prehrane ipak ju mogu uzrokovati zajedno s pridruženim znakovima upale (15). Atrofija papila, koja se dovodila u vezu sa specifičnim prehrambenim deficijencijama te promjene, povlačila se nakon primjene specifične terapije (2-4). U našem je istraživanju uočeno da je 13 od 29 pacijenata (44,83%) s pekućim jezikom imalo niske razine folata iz crvenih krvnih stanica, što je slično rezultatima iz ranijih studija (6, 7). Opisana su 23 slučaja različitih kliničkih izgleda jezika, a uključivali su atrofiju, fisuriranost, geografski jezik, obložen jezik i folijatni papilitis. Samo su dva od šest slučajeva pekućeg jezika imala normalan izgled jezika, a istodobno i niske razine folata iz crvenih krvnih stanica.

Zanimljivo je još da su kod svih pacijenata s geografskim jezikom te kod 4 od 7 slučajeva s isključivo fisuriranim jezikom, fisuriranim jezikom uz geografski jezik ili fisuriranim jezikom s atrofijom, pronađene niske razine folata iz crvenih krvnih stanica. Ipak, fisurirani je jezik fiziološka pojava u starijoj populaciji te je istodobno i najčešći razvojni defekt (11). Jedno je istraživanje pokazalo da pacijenti s fisuriranim jezikom imaju prosječne razine folata nešto manje od prosjeka kontrolne skupine (16). Kod pacijenata starije dobi s pekućim jezikom te geografskim ili fisusiranim, preporučujemo kompletan pregled krvne slike, uključujući i pretrage razina folata kako bi se omogućilo pravilno liječenje.

S obzirom na propisane lijekove, u ranijim se radovima isticalo da je oralni estrogen uzrok niskih razina folata iz crvenih krvnih stanica (6, 17). Dva su od tri ispitanika obuhvaćenih našim radom, uzimali estrogen te imali niske razine folata iz crvenih krvnih stanica. Taj je preparat poznat po tome što je folatni antagonist te može biti interferirajući čimbenik u metabolizmu folata. No, nakon što se prestane uzimati oralni estrogen te počne liječenje folnom kiselinom u dozi od 5mg/dn tijekom jednog mjeseca, atrofični se jezik može vratiti u normalno stanje.

U našem su ispitivanju četiri pacijenta uzimala triciklične antidepresive ili anksiolitike. Ti lijekovi mogu inducirati kserostomiju, a ona može prouzročiti i druge komplikacije poput osjećaja pečenja, gljivične infekcije i zubnog karijesa (18, 19). No, simptom pečenja u ustima čest je kod psihijatrijskih

Discussion

Various tongue appearances with burning sensation can provide some clinical clues to several conditions such as red cell folate levels. It is likely that the tongue appearances in many cases may be a result of the malnutritional status. Although glossodynia related to nutritional deficiency is uncommon but various types of nutritional deficiencies can produce glossodynia and associated signs of inflammation (15). The atrophy of the papillae has previously been related to specific nutritional deficiencies and the changes have reverted upon a specific treatment (2-4). In our study, we found 13 out of 29 patients (44.83%) with burning tongue who had low red cell folate levels which was similar to the results of the previous studies (6,7). There were 23 cases with various tongue appearances such as atrophic, fissured, geographic, coated and foliate papillitis. Only 2 out of 6 cases of burning tongues but normal appearance also showed low red cell folate levels.

Interestingly, all of the patients with geographic tongue and 4 out of 7 cases of patients with fissured tongue alone, fissured with geographic tongue or fissured with atrophic tongue showed low red cell folate levels. However, fissured tongue is a normal condition in old age patients and it is the most common developmental defect (11). One study has shown that patients with fissured tongue had the mean levels of folate slightly lower than the controls (16). In old age patients with burning sensation and geographic or fissured tongues, we recommend a full investigation of blood examination including folate levels for proper treatment. Moreover, reassurance in those patients will help them to understand about various tongue appearances in case of normal blood examination.

Regarding to prescribed medications, previous studies reported that oral estrogen had been implicated as a cause of low red cell folate levels (6,17). Two out of three cases in our study who had taken estrogen showed low red cell folate levels. This medication has been known that it is a folate antagonist and it can be an interfering factor in folate metabolism. However, after stopping to use the oral estrogen and treatment with folic acid 5 mg twice daily for one month, the atrophic tongue can return to normal condition.

In our study, four patients with burning tongue had taken tricyclic antidepressant or antianxiety agents. These medications can induce xerostomia which may lead to other complications such as burning sensation, fungal infection and dental car-

pacijenata te može ili ne mora ovisiti o uzimanju lijekova. Činjenica jest da je osjećaj pečenja u usnoj šupljini višestruke etiologije s lokalnim, sustavnim i psihološkim čimbenicima (20, 21). Ova je studija pokazala da je jezik najčešća lokacija sindroma pekućih usta (49%) te da ne pokazuje nikakav napredak nakon liječenja i dugotrajnog praćenja (22). Zatim, potpuna je remisija zabilježena samo kod 3,7% pacijenata. Dakle, liječenje i vođenje pacijenata s pekućim jezikom te ukupno poboljšanje čini se teškim zadatkom, a spontana remisija simptoma može se dogoditi samo kod ponekoga pacijenta. Kako pokazuje naše iskustvo, dodaci folata mogu djelomice poboljšati simptome kod pacijenata s niskim razinama folata. No, potpora je isto tako važna kako bi se poboljšala kvaliteta života tih pacijenata.

U ovom je ispitivanju zabilježena veza između *Helicobacter pylori kod* gastričnih bolesti i osjećaja pečenja, halitoze te lingvalne hiperplazije (23). No, u samo jednom je slučaju od tri promatrana s peptičkim vrijedom, pronađena niska razina folata iz crvenih krvnih stanica. Iako je patofiziološki mehanizam *H. pylori* ostaje i dalje predmet proturječja, slučajeve s peptičkim vrijedom, pekućim jezikom ili halitozom trebalo bi posebno obraditi i pozorno pratiti.

Naše je ispitivanje upozorilo na vezu između razina folata u crvenim krvnim stanicama i pekućega jezika. Iznenađuje to što nije dokazan nikakav odnos između sustavnih bolesti ili uzimanja propisanih lijekova i pekućeg jezika. Moguće je da smo analizirali mali uzorak te da broj uključenih u ispitivanje nije bio reprezentativan, kad je riječ o skupini oboljelih od sustavnih bolesti. Dodajmo da je većina pacijenata imala više od jednog sustavnog stanja i uzimala više od jednog lijeka, pa je zato iz dostupnih podataka teško razlučiti jesu li sustavno stanje i uzimanje propisanih lijekova uključeni u osjećaj pekućeg jezika. Zato smo preporučili pacijentima s pekućim jezikom i različitim kliničkim izgledima jezika, da obave pretrage ukupne krvne slike, uključujući i razine folata. Daljnje istraživanje na većem uzorku trebalo bi obaviti u nekoj budućoj studiji, kako bi se razjasnio odnos razina folata i pekućeg jezika.

Zaključak

Ovo je ispitivanje pokazalo veliku povezanost između razina folata iz crvenih krvnih stanica i pekućeg jezika, no ne i povezanost između razina folata i bilo koje sustavne bolesti, ili uzimanja propisanih lijekova.

ies (18,19). However, burning mouth in psychiatric patients is a common complaint that may or may not associate with their medication taking. In fact, burning sensation in the oral cavity has a multifactorial etiology with local, systemic and psychological factors (20,21). Recent study showed that the tongue was the most common site of burning mouth syndrome (49%) and showed no improvement after treatment and long-term follow-up (22). Furthermore, complete remission was seen in only 3.7% of patients in that study. Thus, treatment and management in such patients with burning tongue seem to be difficult to achieve complete improvement and spontaneous remission of the symptoms may occur in only a small number of patients. From our experiences, folate supplement for the patients with low folate levels can improve partial symptoms in some cases. However, reassurance is also important to improve quality of life in these patients.

A recent study reported that *Helicobacter pylori* in gastric diseases is associated with burning sensation, halitosis and lingual hyperplasia (23). However, only one out of three cases with peptic ulceration in the present study showed low red cell folate level. Although, the pathophysiologic mechanism of *H. pylori* remains controversial, the cases of peptic ulceration and burning tongue or halitosis should be received special attention and close follow-up.

Our study showed an association between red cell folate level and burning tongue. Surprisingly, we did not find any relationship between systemic condition or prescribed medication and burning tongue. It was possible that we studied in a small population and the number of our patients including in this study might not represent systemic condition group. In addition, most of the patients had more than one systemic condition and had taken more than one medication so it was difficult to establish from the present data whether systemic condition and prescribed medication are involved in burning tongue. Therefore, we recommend that patients with burning and various tongue appearances should be investigated for complete blood examination including folate levels. Further investigation with large samples is still needed in prospective study to clarify the relationship between folate level and burning tongue.

Conclusion

Our present study showed a significant association between red cell folate level and burning tongue but no association between folate level and any systemic condition or prescribed medication.

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Abstract

It can be recognized that some hematological abnormalities are involved in burning tongues. The aim of this study was to compare folate levels between patients with burning tongue and healthy control group. Twenty-nine patients with tongue symptoms were enrolled in this study. They were compared with 21 healthy volunteers. Complete blood counts, hemoglobin typing, serum and red cell folate, and serum vitamin B12 levels were investigated. Medication taking and systemic diseases in all subjects were recorded. The results showed that 13 out of 29 patients (44.83%) had low red cell folate levels, whereas all healthy subjects had normal red cell folate levels. Patients with low red cell folate levels were defined as folate deficiency (n=6), folate deficient erythropoiesis (n=2) and folate depletion (n=5). There was a significant difference in red cell folate levels between two groups (p=0.000). Interestingly, 11 out of 29 patients with low red cell folate levels showed various tongue appearances such as geographic, fissured, coated, atrophic and foliate papillitis. Only 2 cases of burning tongue with normal appearance revealed low red cell folate levels. Moreover, there was no significant difference in red cell folate levels between medication and non medication taking patients (p=0.534). This study showed an association between red cell folate level and burning tongue but no association was observed between folate levels and any attendant systemic condition or prescribed medication.

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Burning mouth syndrome, Folic acid, Systemic condition, Medication

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