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PREGLEDNI RAD
REVIEW

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Kserostomija: novosti

Xerostomia: an Update

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Sažetak
Kserostomija može znatno utjecati na oralno zdravlje i kvalitetu života. Mnogobrojne nove terapije stalno se razvijaju i vrjednuju, ali općenito i dalje se teško liječe bolesti žlijezda slinovnica smještenih u podlozi. Važno je kod svih bolesnika s dugotrajnom kserostomijom obaviti pretrage koje će otkriti uzrok i bolesnicima omogućiti odgovarajuću profesionalnu oralnu njegu.

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Uvod

Kserostomija (suhoća usta) uobičajen je oralni simptom. Većina ljudi ima kratkotrajnu kserostomiju kada se budi iz sna ili su u stresu (na primjer tijekom ispita), a dugotrajna je također uobičajena, ali klinički uzrokuje veći problem (1). Ovaj članak sažima uzroke i liječenje kserostomije.

Klinička slika

Dugotrajna kserotomija je uobičajen problem. Ispitivanja u Sjedinjenim Američkim Državama i Velikoj Britaniji pokazala su da se 30% populacije žali na dugotrajnu suhoću usta. Kserostomija može imati različite kliničke simptome i znakove (Tablica 1.) koji mogu utjecati na kvalitetu života. Tako uzrokuje smetnje u govoru (dizartriju) i gutanju (dizfagiju), bol oralnih sluznica, smanjuje osjet okusa, a može se imati i neugodan zadah iz usta (halitosis) (1, 2).

Introduction

Xerostomia (oral dryness) is a common oral symptom. Most individuals have short-term xerostomia, for example upon wakening from sleep or when stressed (for example during examinations). Long-standing xerostomia is also common, but much more troublesome clinically (1). The present article summarises the cause and management of xerostomia.

Clinical features

Long-standing xerostomia is a common problem. Studies in the United States and United Kingdom have indicated that as many as 30% of the population may complain of long-standing oral dryness. Xerostomia gives rise to a variety of clinical symptoms and signs (Table 1) that can adversely affect quality of life. Oral dryness causes difficulty with speech (dysarthria), swallowing (dysphagia), re-

Tablica 1. Oralni problemi povezani s kserostomijom
Table 1 Oral problems of xerostomia

Suhoća sluznica • Mucosal dryness
Sklonost nastanku karijesa • Liability to dental decay
Sklonost upali gingive • Liability to gingival inflammation
Mogućnost nastanka gljivičnih infekcija • Possible fungal infection
Gubitak retencije proteza • Loss of denture retention
Infekcije žlijezda slinovnica • Salivary gland infection
Oralne manifestacije bolesti koja se nalazi u podlozi kserostomije • Oral manifestations of any associated disease

Dugotrajna kserostomija je predispozicija za mnogobrojne infekcije. Tako pojedinci mogu biti skloni infekciji kandidom, posebice akutnoj pseudomembranoznoj kandidijazi, palatitisu protetika (stanje se katkad naziva i kronična atrofična kandidijaza), medijanom romboidnom glositisu i angularnom heilitisu. Veća je i sklonost nastanka karijesa vrata i korijena zuba. Nema dokaza da dugotrajna kserostomija završava parodontitisom, ali ipak postoji sklonost prema akutnom i vjerojatno kroničnom gingivitisu. Smanjeno lučenje sline može završiti akutnim gnojnim sijaloadenitisom i uglavnom zahvaća parotidnu žlijezdu. Očituje se kao bolno povećanje parotida, a koža iznad žlijezde može biti osjetljiva i crvenkasta. Bolesnici se mogu žaliti na gorak okus (dizgeuzija) zbog toga što im izlazi gnoj iz izvodnog kanala parotide. Akutni gnojni sijaloadenitis rijetko može uzrokovati parotidni apsces. Kod bolesnika sa Sjögrenovim sindromom može potaknuti tumor limfnog tkiva povezan sa sluznicama (MALT, engl. mucosa-associated lymphoid tumour), a javlja se kod 2 do 4% bolesnika s dugotrajnom bolesti (3 - 5).

Etiologija

Mnogo je uzroka za dugotrajnu suhoću usta, kao što se vidi u Tablici 2., a najčešći je kserostomija uzrokovana lijekovima i Sjögrenovim sindromom. Mnogobrojni lijekovi mogu potaknuti kserostomiju i oni su navedeni u Tablici 3. Zanimljivo je istaknuti kako selektivni inhibitori ponovnog uzimanja serotonina (SSRI's. engl. selective serotonin reuptake inhibitors) imaju manje antikolinergičkih učinaka nego triciklički antidepresivi, iako kserostomija može biti posljedica u obama slučajevima. Čak i novi lijekovi, poput inhibitora proteaza koji se koriste u liječenju HIV-a, mogu rezultirati kserostomijom, kao i uobičajeni lijekovi poput inhibitora protonske pumpe (na primjer Omeprazol) (6, 7).

duced taste sensation, oral mucosal soreness and possibly oral malodour (halitosis) (1,2).

Long-standing xerostomia predisposes to a number of infections. Individuals with long-standing xerostomia are predisposed to candidal infection, in particular acute pseudomembranous candidosis (thrush), denture-associated stomatitis (sometimes termed chronic atrophic candidosis), median rhomboid glossitis and angular cheilitis. There is an increased predisposition to cervical and root caries. There is no evidence that long-standing xerostomia gives rise to periodontitis, however, it does predispose to acute and probably chronic gingivitis. Lack of salivary flow can give rise to acute suppurative sialadenitis, typically of the parotid gland. This manifests as a painful swelling of the parotid, the overlying skin can become tender and possibly red. Patients may also complain of a bitter taste (dysgeusia) as consequence of pus emanating from the parotid duct. Very rarely acute suppurative sialadenitis may give rise to parotid abscess. Patients with Sjogren's syndrome are at risk of mucosa-associated lymphoid tumour (MALT), this tumour arising in 2-4% of patients with long-standing disease (3-5).

Aetiology

There are many causes of long-standing oral dryness as summarised in Table 2. By far the most common causes are drug-induced xerostomia and Sjogren's syndrome. A wide variety of drugs can give rise to xerostomia as summarised in Table 3. It is interesting to note that while the Selective Serotonin Reuptake Inhibitor agents (SSRIs) give rise to less anti-cholinergic effects than tricyclic antidepressants, xerostomia can still be an adverse side effect of such drugs. Even new drugs such as protease inhibitors for the treatment of HIV disease can give rise to xerostomia, and common drugs such as proton pump inhibitors (e.g. omeprazole) have been suggested to give rise to long-standing oral dryness (6, 7).

Tablica 2. Etiologija kserostomije
Table 2 Aetiology of xerostomia

Uobičajeni uzroci • Common	Lijekovi • Drugs
	Zračenje glave i vrata • Radiotherapy to head and neck
	Sjögrenov sindrom • Sjogren's syndrome
	Psihogeni • Psychogenic
	Infekcija HCV-om • HCV disease
	Infekcija HIV-om • HIV disease
Rjeđi uzroci • Uncommon	reakcija odbacivanja nakon transplantacije koštane srži • Chronic graft-versus-host disease
	sarkoidoza • Sarcoidosis
	cistična fibroza • Cystic fibrosis
	dijabetes melitus • Diabetes mellitus
	amiloidoza • Amyloidosis
	hemokromatoza • Haemochromatosis
	Wegenerova bolest • Wegener's disease
	ageneza slinovnica • Salivary gland agenesis
	triple A sindrom • Triple A syndrome
	kolinergička dizautonomija • Cholinergic dysautonomia
	drugo • Others

Tablica 3. Lijekovima uzrokovana kserostomija
Table 3 Drug-induced xerostomia

Antikolinergici • Anti-cholinergic action	Atropin i analozi • Atropic and analogues
	Triciklički antidepresivi • Tricyclic antidepressants
	Inhibitori ponovnog uzimanja serotonina • Serotonin Re-uptake Inhibitors
	Antihistaminici • Antihistamines
	Antiemetici • Anti-emetics
	Antipsihotici • Anti-psychotics
Simpatomimetici • Sympathomimetic action	Dekongestivi • Decongestants
	Bronhodilatatori• Bronchodilators
	Supresori apetita • Appetite suppressants
	Amfetamini • Amphetamines
Drugi • Other drugs	Litij • Lithium
	Omeprazol i slični • Omeprazole and others
	Oksbutinin • Oxbutynin
	Dizopiramid • Disopyramide
	Dideooksinozin • Dideoxyinosine
	Didanozin • Didanosine
	Dijuretici • Diuretics
	Inhibitori proteaze • Protease inhibitors

Sjögrenov sindrom je druga najčešća bolest vezivnog tkiva nakon reumatoidnog artritisa. Tu bolest karakterizira suhoća očiju (keratoconjunctivitis sicca) i kserostomija.

Primarni Sjögrenov sindrom sastoji se od očnih i oralnih simptoma, iako se neki bolesnici mogu žaliti i na suhoću kože (kseroderma) te vagine. Sekundarni Sjögrenov sindrom sličan je primarnome, ali bolesnik ima i bolest vezivnog tkiva, najčešće reumatoidni artritis te sistemski lupus eritematodes, sklerodermu, primarnu bilijarnu cirozu, dermatomiozitis i miješane bolesti vezivnog tkiva. Ne zna se točna etiologija Sjögrenova sindroma, ali je poznato da je bolest imunološka te da T-stanice uništavaju žlijezde slinovnice i suzne žlijezde (8-11).

Zračenje glave i vrata može također uzrokovati kserostomiju – tada je stupanj kserostomije proporcionalan ukupnoj dozi zračenja i broju žlijezda slinovnica u području cijevi zračenja (12).

Kao što se vidi u Tablici 2., mnogobrojne različite bolesti mogu uzrokovati kserostomiju. Danas se zna da možda čak 80% bolesnika s infekcijom virusa hepatitisa C može imati simptome kserostomije. Virus hepatitisa C (HCV) izaziva HCV-sijaloadenitis koji karakterizira blago povećanje žlijezda slinovnica i kserostomiju. Točna etiologija toga po-

Sjogren's syndrome is the second most common connective tissue disease after rheumatoid arthritis. This disorder is characterised by dryness of the eyes (keratoconjunctivitis sicca) and xerostomia. Primary Sjogren's principally comprises these ocular and oral symptoms, however, some patients may also complain of long-standing lassitude dryness of the skin (xeroderma) and dryness of the vagina. Secondary Sjogren's is similar to primary Sjogren's syndrome, although patients also have a connective tissue disease – most commonly rheumatoid arthritis, although other associated disorders include systemic lupus erythematosus, scleroderma, primary biliary cirrhosis, dermatomyositis and mixed connective tissue disease. The precise aetiology of Sjogren's syndrome is unknown, however, certainly it is immunologically-driven giving rise to T cell-mediated destruction of the lacrimal and salivary glands (8-11).

Radiotherapy to the head and neck may also give rise to profound xerostomia, the degree of xerostomia being proportional to the total radiotherapy dosage and number of salivary glands that are in the field of the radiation beam (12).

As noted in Table 2, a variety of other disorders can give rise to xerostomia. Of note, it is now recog-

remećaja nije poznata. Mali broj bolesnika s HCV-sijaloadenitisom razvija non-Hodgkinov limfom jedne žlijezde slinovnice (13 -16). Infekcija virusom humane imunodeficijencije (HIV) može prouzročiti bolesti slinovnica, a očituje se u oteklinama i/ili kserostomiji. HIV-bolest žlijezda slinovnica prikazuje se kao sindrom difuzne infiltracijske limfocitoze (DILS) - vidi se infiltrat CD8 limfocita u plućima, suznim žlijezdama i žlijezdama slinovnicama. Drugi mogući uzrok za povećanje slinovnica kod HIV-a mogu biti non-Hodgkinov limfom, Kaposijev sarkom, akutni gnojni sijaloadenitis, povećanje limfnih čvorova i metastatsko širenje tumora u limfne čvorove. Kao što je već istaknuto, inhibitori proteaze mogu također biti uzročnici kserostomije (17,18).

Dijagnoza

Dijagnoza kserostomije je jednostavna i temelji se na mjerenju ukupne količine izlučene sline. Ako bolesnik ima manje od 1,5 ml sline tijekom 15 minuta bez stimulacije, postavlja mu se dijagnoza kserostomije. Naravno, kako bi se ustanovio točan uzrok, može se obaviti niz pretraga - neke su nabrojene u Tablici 4. (19 -22).

Liječenje

Liječenje dugotrajne kserostomije i dalje ne zadovoljava. Može se smanjiti stupanj kserostomije uzrokovane zamjenom lijeka, ali općenito nije moguće vratiti funkciju žlijezda slinovnica nakon zra-

nised that perhaps as many as 80% of patients with hepatitis C infection may have symptoms of xerostomia. The hepatitis C virus (HCV) gives rise to HCV sialadenitis, this being characterised by mild salivary gland enlargement and xerostomia. The precise aetiology of this disorder is unclear. Small numbers of patients with HCV sialadenitis have developed non-Hodgkin's lymphoma of one of the salivary glands (13-16).

Human Immunodeficiency Virus (HIV) infection can give rise to salivary gland disease, this manifesting as swelling and/or xerostomia. HIV salivary gland disease is typically a feature of diffuse infiltrative lymphocytosis syndrome (DILS), this being characterised by an infiltrate of CD8 lymphocytes of the lungs, lacrimal glands and salivary glands. Other causes of salivary gland enlargement in HIV disease include non-Hodgkin's lymphoma, Kaposi's sarcoma, acute suppurative sialadenitis, lymph node enlargement and metastatic spread of tumours into the lymph nodes. As noted above, protease inhibitors may also give rise to xerostomia (17, 18).

Diagnosis

The diagnosis of xerostomia is very straightforward, this simply involving the measurement of resting whole saliva production. If a patient produces less than 1.5ml of whole saliva over a 15 minute period, without stimulation, this is considered to represent xerostomia. Of course a variety of other investigative methods are required to establish the precise cause of the xerostomia, some of these are summarised in Table 4 (19-22).

Treatment

The treatment of long-standing xerostomia remains very unsatisfactory. It may be possible to lessen any drug-induced xerostomia by altering the drug therapy, but in general it is impossible to re-

Tablica 4. Pretrage kod bolesnika s kserostomijom
Table 4 Investigation methods for xerostomia

Sijalometrija • Sialometry
Sijalografija • Sialography
Ultrazvuk • Ultrasound
Ultrazvukom vođena punkcija malim ili srednje velikim iglama • Ultrasound-guided fine-needle or medium-needle biopsy
Kompjutorizirana tomografija (+/- sijalografija) • CT (+/- sialography)
Magnetska rezonanca (+/- sijalografija) • MRI (+/- sialography)
Scintigrafija tehnecij pertehnetatom • 99mTc-pertechnetate scintigraphy
Biopsija labijalnih slinovnica • Labial gland biopsy
Serologija • Serology

čenja ili imunoloških procesa (na primjer Sjögrenov sindrom).

Suhoća usta

Glavni načini da se olakšaju simptomi suhoće su izbjegavanje sredstava koja ju potiču (na primjer alkohol i duhan) i/ili propisivanje preparata za zamjenu sline ili onih za stimulaciju sekrecije sline (sijalogoga).

Mogu se koristiti i razni nesintetički preparati za zamjenu sline, kao na primjer mali gutljaji vode ili sokova bez šećera, iako oni mogu oštetiti zube. U svakom slučaju bolesnicima treba preporučiti da ne piju napitke sa sukrozom. Postoji mnogo sintetičkih preparata za zamjenu sline, a uglavnom se temelje na karboksimetilcelulozi (Tablica 5.). Njihov učinak znatno varira od bolesnika do bolesnika i ni jedan nije mnogo bolji od drugoga. Nedavno je predložen kao učinkovit Salinum, derivat lanenog ulja. U jednom je istraživanju 75% bolesnika sa Sjögrenovim sindromom izvijestilo da su im se poboljšali klinički simptomi kserostomije nakon što su redovito rabili taj preparat (23-25).

verse any salivary gland destruction caused by radiotherapy or immunologically-mediated processes (e.g. Sjogren's syndrome).

Oral dryness

The principle methods of resolving oral dryness include the avoidance or drying agents (e.g. alcohol and tobacco) and/or the prescribing of salivary substitutes or salivary stimulants (sialogogues).

A variety of non-synthetic salivary substitutes can be used, for example sipping water or sugar free juices, although the latter can give rise to dental erosion. Certainly patients should be advised not to drink sucrose-containing drinks. A variety of synthetic salivary substitutes are available, these often being based on carboxymethylcellulose (Table 5). The benefits of such agents vary considerably between patients, no one agent being significantly more effective than another. Recently Salinum, a derivate of linseed oil, has been suggested to be an effective means of lessening oral dryness. In one study, 75% of the above group of patients with primary Sjogren's syndrome reported an improvement in clinical symptoms of xerostomia following regular use of this agent. (23-25).

Tablica 5. Liječenje suhoće oralnih sluznica
Table 5 Management of oral mucosal dryness

Izbjegavanje sredstava koja suše sluznicu • Avoid drying agents	Duhan • Tobacco
	Alkohol • Alcohol
Zamjena sline (umjetna slina) • Salivary substitutes	Saliva Orthana • Saliva Orthana
	Glandosane • Glandosane
	Luborant • Luborant
	Oral Balance • Oral Balance
	BioXtra • BioXtra
	Salinum • Salinum
Stimulacija sline • Salivary stimulants	Pilokarpin • Pilocarpine (Salagen)
	Cevimelin • Cevimeline
	Drugi • Others
Druge metode • Other methods	Akupunktura • Acupuncture
	Neurofiziološka stimulacija • Neurophysiological stimulation

Velik broj sijalogoga naveden je kao djelotvoran u liječenju dugotrajne kserosotmije, a većina je usmjerena poboljšanju kolinergične stimulacije žlijezda slinovnica. Pilokarpin je predložen zato što smanjuje kserostomiju povezanu sa Sjögrenovim sindromom ili zračenjem. On potiče kolinergične muskarinske receptore u žlijezdama slinovnicama i može kod nekih bolesnika povećati količinu izlučene sline. Kao posljedica toga muskarinskog djelo-

A variety of sialogogues have been suggested to be of value in the treatment of long-standing oral dryness, these principally being directed towards enhancing the cholinergic stimulation of the salivary glands. Pilocarpine in particular has been proposed as an effective means of reducing xerostomia associated with radiotherapy or Sjogren's syndrome. Pilocarpine stimulates cholinergic muscarinic receptors within salivary glands and can produce an

vanja, Pilokarpin je kontraindiciran kod bolesnika s astmom ili na terapiji beta blokatorima ili ako imaju anomalije srca s aritmijama. Bolesnici koji uzimaju taj lijek mogu se žaliti na abdominalne grčeve i gastrointestinalne tegobe te pojačano znojenje. Cevimelin je nedavno predložen kao učinkovito kolinergičko sredstvo za liječenje dugotrajne kserostomije, posebice zato što ima manje popratne pojave na kardiovaskularni sustav u odnosu prema Pilokarpinu. Preparat se trenutačno u Europi ne može nabaviti, iako istraživanja u Sjedinjenim Američkim Državama i Japanu pokazuju da je djelotvoran (26 -28).

Velik broj drugih sijalogoga može biti u interakciji s kolinergičkim mehanizmima te postoji malo dokaza o tome da su oni učinkoviti u liječenju dugotrajne kserostomije.

improvement in salivary flow rates in some, but not all, patients. As a consequence of its muscarinic action, pilocarpine is contraindicated in patients who have asthma or individuals receiving beta blockers or have cardiac arrhythmia anomalies. Patients receiving pilocarpine can report abdominal cramps and gastrointestinal upset and enhanced sweating. Cevimeline has recently been proposed as a useful cholinergic agent for the treatment of long-standing xerostomia. In particular cevimeline may give rise to less cardiac side effects than pilocarpine. While there are data from the United States and Japan to suggest that cevimeline may be an effective means of lessening xerostomia, this agent is not currently available within Europe (26-28).

A variety of other sialogogues that interfere in cholinergic pathways have been suggested, but there is little evidence to indicate that these are of notable benefit in the management of long-standing xerostomia.

Karijes

Kao što je već istaknuto, bolesnici s dugotrajnom kserostomijom podložni su karijesu zubnog vrata i korijena te gingivitisu. Visoko koncentrirani fluoridni gelovi koji se danas nalaze na tržištu, smanjuju rizik od tih komplikacija. Osnovno je ipak da svi dobiju upute o oralnoj higijeni, kako bi se osiguralo učinkovito čišćenje zuba. Ti bolesnici također moraju redovito dolaziti na preglede, kako bi se kontroliralo čišćenje zuba. U tome mogu pomoći mnogobrojna interdentalna sredstva za čišćenje, kao na primjer električne naprave poput Oral B Hummingbirda. Treba imati na umu i da bolesnici s bolestima vezivnog tkiva mogu imati poteškoće s interdentalnim čišćenjem zuba zbog manualne ograničenosti (29).

Dental decay

As noted previously, patients with long-standing xerostomia are liable to cervical and root caries, and gingivitis. High concentration fluoride gels are now available which may lessen the risk of such disease. It is essential, however, that all patients receive oral hygiene instruction to ensure tooth cleaning is effective, and should have regular professional recalls to ensure that such tooth cleaning is maintained. A variety of interdental cleaning agents may aid tooth cleaning, for example electric flossing devices such as the Oral B Hummingbird, however, it must be remembered that patients with connective tissue disease may have difficulties with interdental cleaning as a consequence of compromised manual dexterity (29).

Oralna infekcija kandidom

Kandidijaza se u kserostomiji može smanjiti liječenjem dugotrajne suhoće sluznice. Rijetko je bolna i malo je vjerojatno da uzrokuje sistemske bolesti, pa liječenje nije uvijek potrebno. Korisna topikalna sredstva za liječenje oralne kanidijaze su Nistatin (10 mg 4x na dan), Amfotericin B (100, 000 IU 4x na dan) i Mikonazol gel (stavlja se na bazu proteze ili u kut usana, ako postoji angularni heilitis) (1, 30, 31).

Akutni gnojni sijaloadenitis općenito je miješana infekcija, a nastaje iz flore usne šupljine. Učinkovito liječenje temelji se na primjeni Amoksicilina (250 mg 4x na dan) ili Fukloksacilina (250 mg 3x

Oral candidal infection

Oral candidal infection in xerostomia can be lessened by managing the associated long-standing oral dryness. Oral candidal infection is rarely painful and is unlikely to give rise to systemic disease, therefore treatment may not always be warranted. Useful topical agents for the treatment of oral candidal infection include nystatin (e.g. 10mg 4x daily), amphotericin B (e.g. 100,000 IU 4x daily) and miconazole gel (e.g. placed on the fitting surface of a denture, or at the corners of the mouth if there is evidence of angular cheilitis) (1, 30, 31).

Acute suppurative sialadenitis is generally a mixed infection derived from the oral microflora,

na dan). Rijetko postoji opravdan razlog za mikrobiološku analizu gnoja. Kirurška drenaža potrebna je samo ako je moguć parotidni apsces (1).

Neugodan zadah iz usta

Neugodan zadah iz usta može se smanjiti učinkovitim čišćenjem zuba i kontrolom suhoće oralne sluznice. Ako se redovito koriste, kombinirani preparati na bazi ulja i vode, kao što je Dentyl pH, mogu smanjiti neugodan zadah. Čišćenje jezika (kako bi se smanjila populacija anaeroba na dorzumu) ima ograničen učinak, ali kako ne šteti može biti korisno kod nekih bolesnika (1).

Kserostomija uzrokovana zračenjem

Mnogobrojni različiti postupci predloženi su kako bi se smanjila mogućnost od kserostomije kao posljedice zračenja. To uključuje konfokalno zračenje koje omogućuje precizno ciljanje polja zračenja, a da znatno ne uništava tkiva žlijezda slinovnica, te uporabu zaštite od zračenja – na primjer Amifostin. Ubuduće bi zaštita od zračenja mogla uključivati i Tempol (32-34).

Sjögrenov sindrom

Raspon preparata koristi se kako bi smanjile štetne posljedice imunološki posredovane destrukcije slinovnica u Sjögrenovu sindromu. Prijašnja liječenja, koja su se temeljila na imunološkom posredovanju, uključivala su sistemske kortikosteroide (na primjer Prednizolon) te Azatiprin, Metotreksat i Ciklofosfamid. Nedavno je predložen Talidomid i nekoliko specifično biološki aktivnih lijekova, poput Infliksimaba, Adalimumaba, Etanercepta i Rituksimaba. Do danas nije dokazana klinička učinkovitost ni jednoga od navedenih. Jedini pozitivan nalaz je dokaz da MALT povezan sa Sjögrenovim sindromom može regredirati nakon primjene Rituksimaba (35 -37).

Terapija genima

Ako se imunološki posredovano liječenje pokaže djelotvornim u liječenju Sjögrenova sindroma, vrlo je vjerojatno da će ga biti potrebno primjenjivati nekoliko mjeseci, ako ne i nekoliko godina, pa će se možda pojaviti i neželjene popratne pojave. Zato

the bacteria derived from the mouth. Effective therapies may include amoxicillin (250mg 4x daily) or flucloxacillin (250mg 3x daily). There is rarely any justification for the microbiological analysis of pus. Surgical drainage is only warranted if there is likelihood of a parotid abscess (1).

Oral malodour

Oral malodour may be lessened by effective tooth cleaning and control of any oral mucosal dryness. Oil-water preparations such as Dentyl pH may lessen oral malodour if used regularly. Tongue cleaning (to lessen the anaerobic population of the dorsum) would seem to have a limited benefit, but as it is unlikely to cause harm, some patients may still find benefit in this practice (1).

Radiotherapy-associated xerostomia

A variety of methods have been recently proposed to lessen the severity of the likelihood of radiotherapy-induced xerostomia, these include confocal radiotherapy, which allows precise radiation targeting without causing significant salivary gland destruction, and the implementation radioprotectants such as amifostine. Future radioprotectants may include Tempol (32-34).

Sjogren's syndrome

A spectrum of agents has been used to reverse or reduce the immunologically-mediated salivary gland destruction of Sjogren's syndrome. Previous suggested immunologically mediated therapies have included systemic corticosteroids (e.g. prednisolone) and corticosteroid sparing agents such as azathioprine, methotrexate and cyclophosphamide. Recently thalidomide and a variety of specific biologically active agents such as infliximab, adalimumab, etanercept and rituximab have been proposed. To date none of these agents have proven to be of any clinical benefit. The only perhaps fortuitous finding has been that MALT associated lymphoid tumour associated with Sjogren's syndrome may regress with rituximab (35-37).

Gene therapy

If immunologically-mediated therapy is proven to be effective for the treatment of Sjogren's syndrome, it is likely to require administration over many months, if not years, and has the potential to give rise to adverse side effects. Thus it has been suggested

se sugerira da terapija genima može biti učinkovitija u liječenju bolesti poput Sjögrenova sindroma. Ti su postupci još u početnim stadijima razvoja, a temelje se na postavu slabo virulentnih virusa opremljenih genima koji kodiraju važne proteine za funkciju žlijezda slinovnica u tkivo slinovnica (putem izvodnog kanala velikih slinovnica). Optimistični dokazi ispituju se na životinjama koje imaju kserostomiju uzrokovanu zračenjem. Adenovirus transficiran s ljudskim genom akvaporinom-1 pojačava salivarnu funkciju i ne dovodi do znatnijih imunih odgovora domaćina. Zanimljivo je da je taj prijenos gena unutar slinovnica ustanovljen i kao sredstvo prijenosa gena koji nemaju veze sa slinovnicama, kao što su na primjer ljudski hormoni rasta i inzulin – oni se javljaju u povećanoj količini u sistemskoj cirkulaciji (38).

that gene therapy may be a more effective means of managing disorders such as Sjogren's syndrome. These methods, which are still in the early stages of development, entail the placement of a low pathogenic virus equipped with a gene coding for an important protein of salivary gland function into the salivary tissue (via the duct of a major gland). The most promising data has come from studies on animals with radiotherapy-induced xerostomia. Adenovirus transfected with the human acquaporin-1 gene has been found to enhance salivary gland function, and not give rise to any significant host immune response. Interestingly, this intra-salivary gene transfer method has also been found to be a means of transferring non-salivary genes such as those for human growth hormone and insulin such that increased levels of the hormones appear in systemic circulation (38).

Abstract
Xerostomia can have a significant adverse effect upon oral health and quality of life. A variety of new therapies are continuously being developed and assessed, but in general the treatment of the underlying salivary gland disease remains difficult. It is important, however, that all patients with long-standing xerostomia are appropriately investigated to establish the underlying aetiology, and to receive professional oral health care.

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