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Managing the care of patients with Sjögren syndrome and dry mouth

Comorbidities, medication use and dental care considerations

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Autoimmune diseases are characterized by the abnormal production of antibodies and T-cell activation directed against various tissues. The misdirection of the immune system in autoimmunity leads to inflammation of the affected tissues and tissue damage. Although Sjögren syndrome (SS) is the second most common autoimmune disorder and has had a variable reported prevalence of 0.06 percent for primary SS¹ and up to 4.8 percent for primary and secondary SS combined,^{2,3} it is perhaps the most concerning autoimmune disorder for oral health care professionals.

SS is characterized by diminished salivary and lacrimal gland function and may be associated with other autoimmune diseases such as arthritis and with skin and mucosal tissue damage.⁴ Microbial shifts in the oral cavity may result in increased cariogenic flora and fungal infection. Dental demineralization and damage can occur owing to limited buffering capacity of saliva, lack of dental remineralization and rampant caries. Mucosal health and wound healing may be affected by loss of mucin and a reduction in mucosal epithelial growth factors and salivary antibodies, resulting in mucosal atrophy, fragility and delayed repair. Quality of life often is diminished as the loss of mucosal wetting and of hydration, diluting and lubrication functions leads not only to poor oral function but also to additional systemic concerns. Changes in taste, chewing, speaking, food bolus formation and swallowing, as well as trauma to oral tissues, often are experienced. Patients with dental prostheses

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ABSTRACT

Background. As North Americans live longer, have more chronic conditions and take more medications, adverse oral events are likely to increase and aggravate the symptoms of Sjögren syndrome (SS).

Methods. A total of 151 adults who self-reported having SS and who had a mean (standard deviation [SD]) age of 65.8 (11.5) years completed a survey that included questions about basic demographic information, current medical conditions, medications used (prescription and over the counter [OTC]) and the use of oral products to manage SS symptoms. Owing to the self-reporting process in our survey, the term “SS” in our study population represented a mixture of people with SS and people with dry mouth symptoms.

Results. The mean (SD) number of daily medications recorded as prescription, OTC and oral care products were 4.9 (3.5), 4.5 (2.8) and 4.6 (1.4), respectively. Participants with four or more comorbid medical conditions ($n = 74$; 49.0 percent) had significant differences ($P < .05$) in oral symptoms compared with those who had fewer than four ($n = 75$; 49.7 percent). Participants who were taking fewer than four prescription and OTC medications daily ($n = 61$; 40.4 percent) has significant differences ($P < .05$) in voice hoarseness compared with those taking four or more prescription and OTC medications daily ($n = 54$; 35.8 percent).

Conclusions. The survey results indicated that medication use and comorbid medical conditions demonstrated significant differences and may have had a substantial impact on the oral symptoms in adults who self-reported having SS.

Clinical Implications. Given the prevalence of SS, obtaining an accurate and complete medical and pharmacological history has implications for dental practitioners because medication use and comorbid medical conditions have a significant impact on oral symptoms in patients with SS.

Key Words. Autoimmune disease; Sjögren syndrome; comorbid conditions; drugs; dental care; interactions; patient safety.

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TABLE 1

Participants' characteristics, comorbid conditions and medication use (N = 151).

VARIABLE	VALUE
Sex (Female), No. (%)	145 (96.0)
Current Smoker, No. (%)	5 (3.3)
Age, in Years, Mean (SD)*	65.8 (11.5)
Number of Comorbidities, Mean (SD)	4.2 (2.9)
Number of Prescription Medications, Mean (SD)	4.9 (3.5)
Number of Over-the-Counter Medications, Mean (SD)	4.5 (2.8)
Number of Oral Products Currently Used, Mean (SD)	4.6 (1.4)

* SD: Standard deviation.

often experience problems with retention and function of prostheses due to or exacerbated by oral dryness.

According to the 2010 U.S. Census, 40.3 million people 65 years or older have retained more of their original teeth than earlier generations.⁵ Because North Americans are living longer, have more chronic conditions, take more prescription and over-the-counter (OTC) medications and retain their dentition, adverse oral events are likely to increase in association with an increase in salivary dysfunction due to autoimmune disorders and medications taken to manage chronic conditions.

We conducted an exploratory study to describe people's self-reports of current medication use, chronic illnesses and dry mouth symptoms and to determine between-group differences, stratified by medication and comorbidity, for dry mouth symptoms.

METHODS

We conducted our survey in conjunction with the Sjögren's Syndrome Foundation (SSF) (Bethesda, Md.) and MedActive Oral Pharmaceuticals (Odessa, Fla.), which sponsored the study in association with SSF and contributed to the protocol development and data collection. We analyzed the data independently. A notice about our survey was first published in SSF's quarterly newsletter, *Moisture Seekers*, and MedActive Oral Pharmaceuticals staff members sent an introductory letter announcing the survey to 3,000 randomly selected members of SSF from SSF's mailing lists for New York, Virginia, Ohio, New Jersey, Connecticut and Pennsylvania. Members of the SSF self-identified as having SS, but diagnostic confirmation was not available for our study. In the letter, we invited the recipients to contact the designated MedActive Oral Pharmaceuticals staff member to learn more about the survey and to volunteer to participate. Three hundred one SSF members responded, and we sent them a survey as part of a clinical product trial conducted by MedActive Oral Pharmaceuticals to assess the effect of its oral relief products on oral symptoms such as dry mouth.

Of the 301 respondents, 151 provided written informed consent and completed a survey of symptoms and provided a medical history including prescription and OTC medications they used.

Survey. In the survey, we asked participants to report their basic demographic information (age, sex, tobacco use), comorbid medical conditions, medications used (prescription and OTC) and oral products used to manage their SS symptoms. Participants also completed a survey based on the Vanderbilt Head and Neck Symptom Survey Version 2.0 (VHNSS 2.0),⁶ which originally was developed to assess dry mouth symptoms and oral function in a population of patients with head and neck cancer. In VHNSS 2.0, participants rate symptoms and functions on an 11-point scale in which 0 indicated the lowest level of the symptom experienced and 10 indicated the highest level of the symptom experienced. Although this survey was validated in a head and neck cancer population, its primary aim is to assess the symptoms of dry mouth and oral function, which are the same as those for SS; therefore, on the basis of the clinical and research expertise of the authors of this tool and because the population we studied was patients with symptoms of dry mouth and oral function, we did not conduct any further validation testing. The survey results are comparable to those obtained in a clinical setting in which a health history that includes medical diagnoses and medication use is acquired by means of patient self-report.

Data analysis. We reported participant characteristics, comorbid medical conditions and medication use from the survey responses as means (standard deviation [SD]) for continuous variables and as percentages for dichotomous variables. For our exploratory analysis of symptom severity for participants who required more medical management than did the other participants, we grouped participants by reported number of comorbidities and number of prescription and OTC medications. We analyzed between-group symptom comparisons for dry mouth, pain, dietary problems, taste or diet changes and oral complaints by using independent samples *t* tests. We performed analyses by using statistical software (SPSS 18, SPSS, Chicago), and we set statistical significance at $P < .05$.

RESULTS

Participant characteristics and oral care product use for SS symptoms. A total of 96 percent of the sample was female, and 1.3 percent of the participants did not identify their sex (Table 1). The mean (SD) age was 65.8 (11.5) years. Five (3.3 percent) of the participants reported being smokers with a mean (SD) pack per day use of 0.75 (0.4). The mean (SD) number of oral care products—

ABBREVIATION KEY. OTC: Over the counter. SS: Sjögren syndrome. SSF: Sjögren's Syndrome Foundation. VHNSS 2.0: Vanderbilt Head and Neck Symptom Survey Version 2.0.

TABLE 2

Participants' self-reported medical status.*	
MEDICAL CONDITION	PARTICIPANTS, NO. (%)
Allergies	58 (38.4)
Arthritis	64 (42.4)
Asthma	20 (13.2)
Bronchitis	9 (6.0)
Cancer	10 (6.6)
Chronic Obstructive Pulmonary Disease	9 (6.0)
Chronic Pain	58 (38.4)
Depression/Anxiety	42 (27.8)
Diabetes	9 (6.0)
Fibromyalgia	39 (25.8)
Gastroesophageal Acid Reflux	68 (45.0)
Heart Disease	17 (11.3)
Hypertension	37 (25.4)
Insomnia	41 (27.2)
Lupus	14 (9.3)
Overactive Bladder	15 (9.9)
Osteoporosis	44 (29.1)
Rheumatoid Arthritis	35 (23.2)
Scleroderma	9 (6.0)
Sleep Apnea	13 (8.6)

* Comorbid conditions experienced by at least five percent of 149 participants (two participants were excluded from the analysis owing to missing data). Less than five percent of participants reported kidney conditions, stroke, multiple sclerosis, emphysema and mental illness. No participants reported having attention-deficit/hyperactivity disorder, dementia, bulimia, Parkinson disease, Alzheimer disease or human immunodeficiency virus/AIDS.

which included toothpaste, mouthrinse, floss, mouth spray, gum, lozenges, gel, prescription saliva stimulants (sialagogues) and other miscellaneous oral products—used was 4.6 (1.4).

Current medical status, comorbid conditions and daily medication use. Two participants (1.3 percent) were missing comorbidity data, and we excluded them from our analysis and from the between-group analysis.

Gastroesophageal acid reflux was the most frequently reported chronic condition (45.0 percent) followed by arthritis (42.4 percent), allergies (38.4 percent), chronic pain (38.4 percent), osteoporosis (29.1 percent), depression/anxiety (27.8 percent), insomnia (27.4 percent), fibromyalgia (25.8 percent), hypertension (24.5 percent) and rheumatoid arthritis (23.2 percent) (Table 2). Table 2 shows the comorbid conditions present in at least 5 percent of participants. Less than 5 percent of participants reported kidney conditions (2.6 percent), stroke (2.0 percent), multiple sclerosis (1.3 percent), emphysema (0.7 percent) or mental illness (0.7 percent). No participants reported attention-deficit/hyperactivity disorder, dementia, bulimia, Parkinson disease, Alzheimer disease or human immunodeficiency virus/AIDS.

TABLE 3

Self-reported daily prescription medication use.*	
MEDICATION CLASS	NO. (%) OF PARTICIPANTS TAKING PRESCRIPTION MEDICATION
Antianxiety	21 (13.9)
Antidepressant	46 (30.5)
Antihistamine	20 (13.2)
Antihypertensive	54 (35.8)
Anti-inflammatory	44 (29.1)
Asthma	13 (8.6)
Cholesterol Lowering	35 (23.2)
Corticosteroid	22 (14.6)
Diuretic	12 (7.9)
Gastroesophageal Acid Reflux	37 (24.5)
Heart	19 (12.6)
Pain Reliever	50 (33.1)
Sedative	10 (6.6)
Other Medications	49 (32.5)

* Prescription medications that at least five percent of participants reported taking (n = 116; 36 participants were excluded owing to missing data). Less than five percent of participants reported taking oral hypoglycemic agents for diabetes, antibiotics, anticoagulants, decongestants, amphetamines or insulin.

Daily prescription medication use was reported by 74.9 percent of participants, and the mean (SD) number of prescription medications participants reported taking was 4.9 (3.5) (Table 1). The mean (SD) number of OTC medications participants reported taking was 4.5 (2.8). Table 3 shows the classes of prescription medications that were taken by at least five percent of the participants (n = 116; we excluded 36 participants owing to missing data). Antihypertensive agents were reported most frequently (35.8 percent) followed by pain relievers (33.1 percent), antidepressants (30.5 percent), anti-inflammatory agents (29.1 percent), gastroesophageal acid reflux agents (24.5 percent) and cholesterol-lowering medications (23.2 percent). Less than 5 percent of participants reported taking oral hypoglycemic agents for diabetes (4.6 percent), antibiotics (4.0 percent), anticoagulants (4.0 percent), decongestants (3.3 percent), amphetamines (3.3 percent) or insulin (2.6 percent).

Comorbidity and medication use between-group comparisons for differences in oral symptoms. Because having multiple comorbid conditions was common among participants, we divided them into two groups to determine if oral symptoms differed between those reporting having few (< four) comorbid conditions versus those reporting having several (≥ four) comorbid conditions. We based stratification on whether participants had fewer than four comorbid conditions (n = 75, 49.7 percent) and four or more chronic conditions (n = 74, 49.0 percent). As we mentioned above, two par-

TABLE 4

Oral symptom severity ratings for the total sample and comorbid condition stratification.				
ORAL SYMPTOMS	TOTAL SAMPLE, MEAN RATING (SD*) (N = 151†)	FEWER THAN FOUR COMORBID CONDITIONS, MEAN RATING (SD) (n = 75)	FOUR OR MORE COMORBID CONDITIONS, MEAN RATING (SD) (n = 74)	P VALUE
Problems With Dry Mouth	7.6 (2.1)	7.1 (2.2)	8.2 (1.7)	.001
Problems With Dry Mouth Make Chewing and Swallowing Hard	5.7 (2.9)	5.2 (2.9)	6.3 (2.8)	.020
Problems With Dry Mouth Affect Ability to Sleep	4.8 (3.3)	4.0 (3.1)	5.6 (3.3)	.003
Problems With Dry Mouth Affect Ability to Talk	5.3 (3.1)	4.5 (3.0)	6.1 (3.0)	.002
Thick Saliva (Mucus or Phlegm)	4.3 (3.5)	3.7 (3.4)	4.8 (3.6)	.047
Lost Weight Due to Dry Mouth Affecting Eating Habits	1.6 (2.8)	1.3 (2.6)	1.8 (2.9)	.228
Trouble Maintaining Weight Due to Swallowing Problems	0.9 (2.3)	0.6 (1.8)	1.2 (2.7)	.079
Trouble Eating Certain Solid Foods	6.0 (3.4)	5.2 (3.4)	6.8 (3.2)	.003
Food Gets Stuck in Mouth Due to Dryness	5.9 (3.4)	5.2 (3.3)	6.5 (3.5)	.028
Food Gets Stuck in Throat Due to Dryness	4.7 (3.2)	4.2 (3.1)	5.2 (3.3)	.082
Great Effort to Swallow Due to Dry Mouth	3.8 (3.0)	3.2 (2.9)	4.5 (3.0)	.009
Painful Sores in Mouth or Throat	3.0 (3.4)	2.0 (2.8)	4.0 (3.6)	<.001
Hard to Take Medications Due to Dry Mouth	2.7 (3.1)	2.0 (2.7)	3.4 (3.4)	.007
Mouth or Throat Pain Causes Difficulty Speaking	2.6 (3.1)	1.8 (2.7)	3.4 (3.3)	.002
Average Mouth Pain Level Over the Last Week	2.9 (2.8)	2.0 (2.5)	3.7 (2.9)	<.001
Worst Mouth Pain Level Over the Last Week	3.3 (3.3)	2.4 (3.0)	4.2 (3.3)	.001
Pain Causes Difficulty Sleeping	2.1 (3.1)	1.2 (2.3)	3.1 (3.5)	<.001
Trouble Speaking	3.7 (3.0)	2.9 (2.6)	4.4 (3.1)	.002
Voice Is Hoarse	4.3 (3.0)	3.1 (2.7)	5.4 (2.8)	<.001
Trouble Being Understood Due to Speaking or Hoarse Voice	2.8 (3.0)	2.0 (2.4)	3.7 (3.2)	<.001
Trouble Wetting/Softening Food Due to Dry Mouth	3.9 (3.4)	3.2 (3.1)	4.6 (3.5)	.011
Taste Is Altered or Reduced	4.2 (3.4)	3.4 (3.1)	5.0 (3.6)	.006
Less Desire to Eat Due to Taste Change	2.3 (3.1)	1.7 (2.7)	3.0 (3.4)	.017
Chosen Foods to Eat Altered Due to Taste Changes	3.1 (3.5)	2.1 (3.2)	4.1 (3.6)	.001
Decrease in Food Eaten Due to Taste Changes	2.2 (3.1)	1.6 (2.7)	2.8 (3.3)	.019
Difficulty Chewing Due to Teeth/Dentures	2.8 (3.3)	1.8 (2.8)	3.8 (3.5)	.001
Teeth Are Sensitive to Hot/Cold/Sweet Foods	4.3 (3.7)	3.5 (3.6)	5.2 (3.6)	.006
Trouble With Dentures	3.8 (3.8)	1.7 (2.5)	6.3 (3.7)	.001
Burning Sensation in Lining of Mouth and Throat	4.1 (3.4)	3.2 (3.0)	4.9 (3.6)	.003
Lining of Mouth/Throat Is Sensitive to Spicy/Hot/Acidic Foods	5.9 (3.5)	4.9 (3.5)	6.8 (3.3)	.001
Lining of Mouth/Throat Is Sensitive to Dryness	6.6 (3.0)	5.5 (3.0)	7.6 (2.7)	<.001
Burning Pain in the Lining of Mouth/Throat Changes Food Choice	4.1 (3.9)	2.9 (3.6)	5.2 (3.8)	<.001
Burning Pain in Lining of Mouth/Throat Prevents Brushing of Teeth	0.8 (1.9)	0.5 (1.5)	1.1 (2.2)	.087

* SD: Standard deviation.
† Total sample has 151 participants. Two participants were excluded from the comorbidity between-group analysis owing to missing data. Rating scale ranges from 0, indicating the lowest level of the symptom experienced, to 10, indicating the highest level of the symptom experienced.

ticipants (1.3 percent) were missing data, and we excluded them from this analysis. Six participants (4.0 percent) had no comorbid conditions; five of these participants were taking at least one medication, and we excluded the sixth participant from the analysis owing to missing data.

Almost all of the oral symptoms had statistically significant differences between the groups (Table 4), and the four-or-more-comorbid-conditions group had higher rat-

ings for all oral symptoms than did the fewer-than-four-comorbid-conditions group. "Trouble with dentures" had the largest between-group difference (mean difference = -4.6; 95 percent confidence interval [CI], -7.0 to -2.2; $P = .001$) followed by "voice is hoarse" (mean difference = -2.3; 95 percent CI = -3.2 to -1.4; $P < .001$), "burning pain in the lining of mouth/throat changes food choice" (mean difference = -2.3; 95 percent CI = -3.5 to -1.0;

$P < .001$), “lining of mouth/throat is sensitive to dryness” (mean difference = -2.1 ; 95 percent CI = -3.0 to -1.2 ; $P < .001$) and “difficulty chewing due to teeth/dentures” (mean difference = -2.0 ; 95 percent CI = -3.2 to -0.9 ; $P = .001$).

Similar to what we did when we analyzed differences in comorbidity, we divided participants into two medication use groups to determine if oral symptoms differed between those who reported taking fewer than four prescription and OTC medications ($n = 61$, 40.4 percent) and those who reported taking four or more prescription and OTC medications ($n = 54$, 35.8 percent). As we mentioned previously, we excluded 36 participants from the analysis owing to missing data. We compared all variables listed in Table 4 for comorbidity between medication use groups, and we found that the differences were not statistically significant for any variables (data not shown) except for “voice is hoarse” (mean difference = -1.6 , 95 percent CI = -2.6 to -0.6 , $P = .003$) and “trouble being understood due to speaking or hoarse voice” (mean difference = -1.1 , 95 percent CI = -2.2 to -0.9 , $P = .034$), indicating higher symptom ratings in the four-or-more-medications group.

severity of dry mouth or may be the cause of the symptoms.

Using an 11-point scale in which 0 indicated the lowest level of the symptom experienced and 10 indicated the highest level of the symptom experienced, participants reported that dry mouth had a considerable impact on their daily living activities (for example, eating and speaking) (Table 4); overall reports of problems indicated that they were severe (mean [SD], 7.6 [2.1]; $n = 151$), especially in participants who had four or more comorbidities (mean [SD], 8.2 [1.7]; $n = 74$) compared with those who had fewer than four comorbidities (mean [SD], 7.1 [2.2]; $n = 75$). All participants rated similar reports of problems with oral function as moderate to severe. These problems had a statistically greater impact in participants with four or more comorbidities (for example, problems with eating certain foods, chewing and swallowing, food sticking in mouth or throat, impact on speech and affecting sleep). The impact of taste changes, decreased oral comfort, and burning mouth and throat were rated as moderately severe with respect to diet and intake of food and beverages (Table 4). These findings indicated the significant impact of dry mouth reported by the

**Patients should report Sjögren syndrome symptoms
to their dental providers, as they may have a significant impact
on oral function if they are not addressed.**

DISCUSSION

Given the evidence that people in North America live longer, have more chronic conditions, take more prescription and OTC medications and retain their dentition longer in life,⁵ adverse oral events are likely to increase and aggravate autoimmune disorder symptoms. As SS is the second most common autoimmune disorder, affecting 0.06 to 4.8 percent of the world's population, oral health care professionals are particularly aware of it given its propensity to cause a decrease in saliva production, as well as dry mouth.⁴ Oral dryness leads to difficulty swallowing and is associated with an increased rate of dental caries and other oral complications.⁷ These oral complications can be exacerbated further by a decreased sense of taste and a change in oral flora, including an increase in oral candidiasis.⁵

Participants reported that dry mouth had a substantial impact on their oral function, which may reflect that advanced dry mouth was their reason for being members of SSF and for their interest in responding to the survey. Since diagnostic confirmation of SS was not available for our study, our sample may have represented people with SS and people with dry mouth symptoms, although it is unlikely that people who do not have SS are members of the SSF. Participants also had high numbers of comorbid conditions and of prescription and OTC medications taken, which may increase the risk of developing and

participants. Patients should report symptoms to dental providers, as they may have a significant impact on oral function if they are not addressed.

We compared differences in oral symptoms between participants taking fewer than four prescription and OTC medications ($n = 61$; 40.4 percent) and those taking four or more prescription and OTC medications ($n = 54$; 35.8 percent). We selected a cutoff of fewer than four prescription and OTC medications because there was a natural demarcation in our study groups at this number (almost one-half were above this number and one-half were below). In our analysis, we found that differences were not statistically significant for any variables except for “voice is hoarse” (mean difference = -1.6 , 95 percent CI = -2.6 to -0.6 , $P = .003$) and “trouble being understood due to speaking or hoarse voice” (mean difference = -1.1 , 95 percent CI = -2.2 to -0.9 , $P = .034$). The higher oral symptom ratings for “voice is hoarse” and “trouble being understood due to speaking or hoarse voice” occurred in the four-or-more-medications group. These results are not surprising as many of the most frequently reported medications used by our cohort were antihypertensive agents (35.8 percent), pain relievers (33.1 percent), antidepressants (30.5 percent), anti-inflammatory agents (29.1 percent), gastroesophageal acid reflux agents (24.5 percent) and cholesterol-lowering medications (23.2 percent), for which dry mouth is a

potential adverse effect either alone or in combination with other medications. Missing data were problematic in this analysis, so we propose our conclusions from this analysis tentatively.

Drug-induced dry mouth is likely to exacerbate oral complaints and increase the risk of oral complications, regardless of the number of prescription or OTC medications taken. The xerostomia-inducing drugs taken by our study population were antianxiety agents, antidepressants, antihistamines, anti-inflammatory agents, antihypertensive agents, asthma medications, diuretics, pain relievers and sedatives. The incidence of dry mouth with these drugs is 10 percent or greater.⁸⁻¹⁰ The mean (SD) number of prescription medications reported in our study population was 4.9 (3.5) and the mean (SD) number of OTC medications used was 4.5 (2.8). These results are similar to those of other reports demonstrating that people older than 65 years take up to five medications concurrently.^{11,12}

Although many commonly reported chronic conditions alone or in combination may be responsible for clinically significant dry mouth symptoms, the potential impact these conditions could have on oral care and dental hygiene, as well as dental damage, can lead to increased oral disease.

Medications that are commonly used in dentistry typically fall into five drug classes: analgesics and anti-inflammatory agents, antibiotics, local anesthetics, sedatives and emergency medications (albuterol, aspirin, diphenhydramine, epinephrine, glucose, nitroglycerine, oxygen, naloxone and flumazenil).¹³ Our study results show that taking more than one xerostomia-inducing drug (medication duplication) could exacerbate the oral symptoms of SS, since almost two-thirds of our participants already took pain relievers (33.1 percent) and anti-inflammatory agents (29.1 percent). Although only 6.6 percent of our participants routinely took sedative agents and only 4.0 percent took antibiotics, these drug classes still represent a potential for medication duplication secondary to a dental visit. These findings emphasize the importance of obtaining an accurate and up-to-date medication history that includes OTC medications and herbals supplements to avoid medication duplication, which could lead to additional unintended negative sequelae, ranging from exacerbation of oral symptoms to inadvertent medication overdosing.

Other potential drug interactions between the prescription and OTC medications our participants reported taking and medications commonly administered by dentists extend beyond the avoidance of therapy duplications. Antihypertensive agent use was reported most frequently by our cohort (35.8 percent), and much has been written about a conservative approach to local anesthetic administration in patients with underlying cardiovascu-

lar disease.¹⁴ Use of antidepressants was reported by 30.5 percent of participants. These agents are known to have a number of anticholinergic side effects that can exacerbate the oral symptoms of both SS and increase the drug-induced xerostomia that occurs when analgesics, anti-inflammatories and sedatives are administered by dentists. Our participants reported taking decongestants (3.3 percent) and amphetamines (3.3 percent), which can lead to the same interactions. A total of 24.5 percent of participants reported taking prescription medications to manage gastroesophageal acid reflux, which 45.0 percent of all participants reported having. These findings indicate that more than 20 percent of these participants may manage their condition with OTC products such as antacids. Antacids can have a significant interaction when combined with tetracycline antibiotics (tetracycline, minocycline and doxycycline), as these agents will chelate with positively charged elements in antacids, as well as those in dairy products and other medications, to

form an insoluble complex so that these antibiotics are simply excreted rather than absorbed.¹⁵⁻¹⁹ This interaction also can lead to reduced calcium and other elemental absorption owing to this physical binding, which can further undermine dental health.

Data from the Centers for Medicare and Medicaid Services, National Institutes of Health, indicate that more than 50 percent of patients older than 65 years have an average of three chronic medical conditions that matched those of our cohort.²⁰ The most common comorbidity reported, gastroesophageal acid reflux (45.0 percent), is of concern as it aggravates mucosal irritation and introduces a risk of developing dental demineralization in patients with dry mouth, which reinforces the need for patients to achieve the best possible control of gastroesophageal acid reflux. There initially appeared to be a mismatch between the prevalence of this comorbidity and the percentage of patients reporting gastroesophageal acid reflux agent use (25.0 percent). However, many patients manage this and other comorbidities by using OTC products. This finding emphasizes the need for dental professionals to obtain an accurate and complete pharmacological history for all patients.

Although many of these commonly reported chronic conditions alone or in combination may be responsible for clinically significant dry mouth symptoms, the potential impact these conditions could have on oral care and dental hygiene, as well as dental damage, can lead to increased oral disease. These conditions can be additive

in regard to risk and oral symptoms in patients with a comorbidity of dry mouth due to SS. Of greatest concern, however, is in consideration of the prescription and OTC medications used to treat these commonly reported chronic conditions, since their use also could lead to clinically significant dry mouth symptoms, either alone or in combination.

The additional effect of comorbidity on the exacerbation of oral symptom severity secondary to SS was illustrated by the statistically significant differences between the four-or-more-comorbid-conditions group and the fewer-than-four-comorbid-conditions group, with the former having higher ratings for all oral symptoms. We selected a cutoff of fewer than four comorbid conditions because there was a natural demarcation in our study population; almost one-half were above this number and one-half were below. This is important information for oral health care providers who treat patients with SS, as they could much more easily stratify patients' risk based simply on the number of comorbid conditions present. This quick risk-stratification strategy would be an easy and quick differential diagnosis that could be made before performing dental procedures, which could help mitigate any additional risk and improve patient safety. In our study, 37.7 percent of participants ($n = 57$) reported using oral lubricants; the question asked only if they used, not the frequency of use.

Although 96 percent of our sample was female, this fact likely does not represent methodological bias because the epidemiology of SS has a 9:1 ratio in preference of females.^{1,4} The usual onset of SS is in middle age (40-50 years of age), which also closely resembles our cohort. As only five of our participants were smokers who smoked less than a single pack per day, we did not feel that this variable was a confounder in our study, because smoking could be an additional risk factor for oral dryness and produce additional negative oral symptoms. It was encouraging to find tobacco use uncommon in our study population.

Study limitations. Our research results showed associations between medication use, chronic diseases and SS symptoms that merit further investigation and provided new data to help guide patient care. However, we recognized that our study had certain limitations. Although the nature of self-reported survey data is subjective, which can result in bias, in a clinical setting, dentists obtain patients' health histories and current medication use by means of self-reported data. We conducted a post hoc power analysis to detect a small effect size, which indicated that power was sufficient (0.99) in the 151-person cohort with an α of 0.05 or less.

Participants rated the common oral symptoms they had experienced by means of the VHNSS 2.0, a tool that has been validated in patients with head and neck cancer in whom dry mouth had an impact on oral function but that has not been validated specifically in patients

with SS.⁶ It also is possible that an inherent bias could have been introduced by our partnering with SSF, which announced the trial to 3,000 randomly selected SSF members from their mailing list. These members lived in New York, Virginia, Ohio, New Jersey, Connecticut and Pennsylvania, which may have introduced a regional bias and, thus, prevented the reporting of important differences that could exist in patients from other regions.

We viewed the respondents as likely to be motivated to participate in our study owing to personal concerns about symptoms associated with dry mouth. Therefore, they may represent patients with advanced SS or advanced dry mouth symptoms that may be aggravated by other causes. This potential selection bias could have an effect on the overall generalizability of our findings. In addition, as diagnostic confirmation of SS was not available for our study, the SS in this population could have represented a mixture of people with SS and people with dry mouth symptoms.

Despite these limitations, given the prevalence of SS in combination with other concurrent chronic diseases and the increase in prescription and OTC medications taken to manage it and comorbid diseases, it is clear that recording all chronic diseases and medications and herbal supplements used accurately and completely when compiling the patient's medication profile can help guide contemporary dental practice. Medication use and information regarding a patient's medical history can inform practitioners about medical diagnoses that may have implications regarding the patient's oral condition and for delivery of dental care. There may be additional concerns regarding potential interactions between frequently used medications and medications that are commonly used in dentistry. Close consideration of these issues will help mitigate risk and will further ensure patient safety.

CONCLUSIONS

The results of our study showed that the number of concomitant medications patients who report having SS may take and the number of chronic medical conditions they may have substantially affects the level of oral symptoms they experience. Having accurate and complete documentation of medication use that is used to compile the patient's medication profile and a thorough medical history that includes concomitant chronic diseases can help guide practitioners when treating patients and warrant close consideration so as to mitigate risk and help ensure patient safety, especially in patients with SS. ■

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1. Qin B, Wang J, Yang Z, et al. Epidemiology of primary Sjögren's syndrome: a systematic review and meta-analysis (published online

ahead of print June 17, 2014). *Ann Rheum Dis*. doi:10.1136/annrheum-dis-2014-205375.

2. Tincani A, Andreoli L, Cavazzana I, et al. Novel aspects of Sjögren's syndrome in 2012. *BMC Med* 2013;11:93. doi:10.1186/1741-7015-11-93.
3. Gaubitz M. Epidemiology of connective tissue disorders (published correction appears in *Rheumatology [Oxford]*. 2008;47[2]:234-235). *Rheumatology (Oxford)* 2006;45(suppl 3):iii3-iii4.
4. Ramos-Casals M, Brito-Zerón P, Sisó-Almirall A, Bosch X. Primary Sjögren syndrome. *BMJ* 2012;344:e3821. doi:10.1136/bmj.e3821.
5. U.S. Census Bureau. 2010 Census. Population by sex and age. www.census.gov/2010census/. Accessed Sept. 15, 2014.
6. Cooperstein E, Gilbert J, Epstein JB, et al. Vanderbilt Head and Neck Symptom Survey Version 2.0: report of the development and initial testing of a subscale for assessment of oral health. *Head Neck* 2012;34(6):797-804.
7. Mavragani CP, Moutsopoulos HM. Sjögren syndrome. *Annu Rev Pathol* 2014;9:273-285.
8. Sreebny LM, Schwartz SS. A reference guide to drugs and dry mouth. *Gerodontology* 1986;5(2):75-99.
9. Guggenheimer J, Moore PA. Xerostomia: etiology, recognition and treatment. *JADA* 2003;134(1):61-69.
10. Donaldson M. Impacts and interrelationships between medications, nutrition, diet and oral health. In: Touger-Decker R, Mobley C, Epstein JB, eds. *Nutrition and Oral Medicine*. 2nd ed. New York City: Humana Press; 2014:83-110.
11. Qato DM, Alexander GC, Conti RM, Johnson M, Schumm P, Lindau ST. Use of prescription and over-the-counter medications and

dietary supplements among older adults in the United States. *JAMA* 2008;300(24):2867-2878.

12. Donaldson M, Touger-Decker R. Dietary supplement interactions with medications used commonly in dentistry. *JADA* 2013;144(7):787-794.
13. Donaldson M, Goodchild JH. Pregnancy, breast-feeding and drugs used in dentistry. *JADA* 2012;143(8):858-871.
14. Godziba A, Smektała T, Jędrzejewski M, Sporniak-Tutak K. Clinical assessment of the safe use local anaesthesia with vasoconstrictor agents in cardiovascular compromised patients: a systematic review. *Med Sci Monit* 2014;20:393-398.
15. Prescribing information. Tetracycline. Sellersville, Pa.: Teva Pharmaceuticals USA; 2009.
16. Prescribing information. Minocin (minocycline). Cranford, N.J.: Triax Pharmaceuticals; 2010.
17. Prescribing information. Vibramycin (doxycycline). New York City: Pfizer; 2007.
18. Prescribing information. PhosLo (calcium acetate). Waltham, Mass.: Fresenius Medical Care North America; 2011.
19. Jung H, Peregrina AA, Rodriguez JM, Moreno-Esparza R. The influence of coffee with milk and tea with milk on the bioavailability of tetracycline. *Biopharm Drug Dispos* 1997;18(5):459-463.
20. Centers for Medicare and Medicaid Services. *Chronic Conditions Among Medicare Beneficiaries: Chartbook—2012 Edition*. Baltimore: CMS; 2012. www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Chronic-Conditions/Downloads/2012Chartbook.pdf. Accessed Sept. 15, 2014.