Dry Eye and Dry Mouth in the Elderly

A Population-Based Assessment

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Background: Symptoms of dry eye and dry mouth are common in the elderly and are often debilitating. Previous research on small populations has been inconsistent regarding the contribution to sicca symptoms of autoimmune markers, medication use, and other factors. The objective of this study was to determine the population prevalence of symptoms of dry eye and dry mouth and to evaluate possible risk factors.

Methods: This is a population-based study of 2481 individuals, aged 65 to 84 years, residing in Salisbury, Md, and identified by the Health Care Financing Medicare database. The main outcome measures included information on sicca symptoms, medical history, medication use, and joint examination results collected in a standardized manner. Autoimmune status was assessed in 1200 individuals by measuring antinuclear antibody, rheumatoid factor, and autoantibodies to the soluble nuclear antigens Ro/SS-A and La/SS-B by double immunodiffusion.

Results: Approximately 27% of the population reported dry eye or dry mouth symptoms to be present often or all the time and 4.4% reported both. The prevalence of dry mouth (but not dry eye) symptoms increased with age, female sex, and white race. No association of sicca symptoms was found with rheumatoid arthritis, smoking, alcohol consumption, reproductive hormonal status, or the presence of autoantibodies. A strong, dose-response relationship was observed between sicca symptoms and the use of certain medication classes. The proportion of the population prevalence of sicca symptoms attributable to the use of drying medications was estimated at 62% for dry eye and dry mouth and 38% for dry eye or dry mouth symptoms.

Conclusions: Sicca symptoms are common in the elderly, and medication side effects appear to be a major underlying factor. Our results do not indicate an association between autoimmune status and sicca symptoms and do not support immunologic testing in persons with sicca symptoms in the absence of other important systemic features.

Arch Intern Med. 1999;159:1359-1363

SYMPTOMS OF dry eye and dry mouth are common in the elderly and are frequently debilitating. When an individual presents with sicca symptoms, particularly if accompanied by musculoskeletal or other systemic complaints, considerations relating to the diagnosis of Sjogren syndrome arise, and an evaluation for evidence of an autoimmune process may ensue. In the United States, research on the epidemiology of sicca symptoms has largely been limited to selected populations such as outpatient clinics or nursing homes1-5 where a variety of selection biases are likely to play a significant role in both estimates of the prevalence of symptoms as well as their relationship to systemic disease or other factors. We have previously reported the relationship between tests (Schirmer and Rose Bengal) and symptoms of dry eye and the prevalence of dry eye by varying definitions.6,8 In summary, no significant association was seen between report of dry eye symptoms and either Rose Bengal or Schirmer testing nor was there any meaningful association between the results of Rose Bengal and Schirmer tests. Overall, 14.6% of the population reported symptoms of dry eye to be present often or all the time, and 3.5% were symptomatic and had either Rose Bengal scores or Schirmer test results in the lowest decile. Symptoms of dry mouth were found in 17% of the population and were closely associated with a measure of salivary production, the Saxon test.9,10

From a practical, clinical perspective, physicians are frequently presented with patient symptoms of dry eye, dry mouth, or vaginal dryness, particularly
PARTICIPANTS AND METHODS

POPULATION AND SETTING

The overall methodology for the Salisbury Eye Evaluation (SEE) Project has been previously described. Salisbury is located 106 miles from Baltimore on Maryland’s eastern shore. The metropolitan area has a total population of 41,430, of whom 7004 are aged 65 years and older. Fifteen percent of the elderly population are African American.

The SEE Project contains 4 research projects whose overall purpose is to study visual function in the elderly from a common population-based perspective. The goal of the population recruitment was to enroll a random sample of 2300 men and women aged 65 to 84 years from Salisbury to have a home interview and a clinical examination at the SEE Project headquarters. The study size was chosen based on estimates of the prevalence of visual disability, and the actual sample was selected from the Health Care Financing Administration Medicare database. Eligibility criteria stipulated the following: (1) age between 65 and 84 years as of July 1, 1993; (2) residence in the Salisbury metropolitan area and alive at the time of contact; (3) noninstitutionalized status, ability to communicate in English and travel to the clinic for the assessments (housebound or extremely ill subjects were considered ineligible); and (4) a score of 18 or higher on the Mini-Mental State Examination. Recruitment was based on initial contact by letter and a subsequent visit from a study interviewer. After the home interview, an appointment at the SEE facility was made where the participant completed a series of vision and functional status tests, questionnaires, and clinical assessments that included the dry eye and dry mouth evaluation described below. The representativeness of the cohort examined has been reported in detail elsewhere.

ASSESSMENT OF SICCA SYMPTOMS

A dry eye symptom questionnaire consisting of questions relating to 6 symptoms was administered in a standardized fashion by a trained technician. Symptoms of dry mouth were assessed by asking each participant the questions “Does your mouth feel dry?” and “Do you wake up at night feeling your mouth is so dry that you need to drink fluids?” Each time a respondent indicated the presence of a dry eye or dry mouth symptom, he or she was asked to indicate whether the symptom was experienced rarely, sometimes, often, or all the time.

TESTS OF AUTOIMMUNITY

A total of 2199 (87.3%) of participants consented to blood drawing and the serum specimens from a sample of 1200 subjects were selected for immunologic testing. The sample was chosen to provide a population that included adequate representation from various subgroups selected on the basis of symptoms and test results. Specifically, the basis of symptoms and test results. Specifically, the

38% of the subjects with no symptoms or signs of dry eye or dry mouth (n = 600). Antinuclear antibodies were detected by incubating dilutions of sera with commercially prepared Hep-2 cells (Zeus Wampole, Raritan, NJ) followed by incubation with a polyclonal fluorescein isothiocyanate antihuman immunoglobulin. A quenching buffer containing 1 part 0.3-mol/L triethylenediamine, 0.1-mol/L Tris-hydrochloride (pH 9.0), and 9 parts glycerol (all from Sigma-Aldrich Corporation, St Louis, Mo) was applied, and slides were read under a Zeiss fluorescent microscope. A positive antinuclear antibody at a titer of 1:320 or greater is considered abnormal. Autoantibodies to soluble nuclear antigens Ro/SS-A and La/SS-B were detected by Ouchterlony double immunodiffusion against extracts of bovine spleen and rabbit thymus, prepared as described by Clark et al and compared with control sera with known specificities. Titers of IgM rheumatoid factor were determined using latex agglutination.

OTHER RISK FACTORS

A standardized medical history and exposure (smoking, alcohol, etc) questionnaire was completed on each individual, and a trained physician examiner evaluated each subject for clinical evidence of rheumatoid arthritis. A medical comorbidity score from 0 to 15 was constructed for each participant based on the number of self-reported histories of the following 13 conditions: arthritis, hip fracture, back problems, myocardial infarction, angina, congestive heart failure, intermittent claudication, high blood pressure, diabetes, emphysema, asthma since age 50 years, stroke, Parkinson disease, cancer in the past 5 years, and vertigo. A complete list of currently used medications determined by self-report was recorded for each participant and entered into the database using either the Drug Products Information Coding system or the Iowa Nonprescription Drug Products Information Coding System. For analysis, all drugs were recorded according to the Iowa Drug Information System.

STATISTICAL METHODS

Associations with potential risk factors for sicca symptoms are presented as crude and adjusted odds ratios. Adjustment for age, race, and sex was performed using logistic regression models with age as a continuous variable. Each medication class in the Iowa Drug Information System (eg, antihistamine) was examined to assess its association with sicca symptoms. To assess the correlation among medication classes, pairwise odds ratios were estimated. In the analysis, medication classes with all pairwise odds ratios less than 3 were considered to have low correlations (less likely to be taken simultaneously). Those medication classes that had only low correlation with other classes were tested in a univariate fashion for their associations with the presence of dry eye and/or dry mouth (symptoms reported often or all the time). Medications with pairwise odds ratios of 3 or higher were considered highly correlated (more likely to be taken simultaneously), and the associations with dry eye and/or dry mouth were tested jointly in a single model. Those medication classes that had an independent association with dry eye or dry mouth of P<.10 and were in current use by at least 2% of the population were retained for further analysis.
among the elderly. These symptoms are usually interpreted in the absence of physiologic tests of tear or salivary production. We report herein the population distribution of symptoms of dry eye and dry mouth and their association with putative risk factors.

Table 1 illustrates the distribution of sicca symptoms. Approximately 27% of the population reported (present often or all the time) dry eye or dry mouth symptoms, and 4.4% reported both. Report of dry eye or dry mouth symptoms was associated with increasing age, female sex, and white race. However, these associations were driven largely by symptoms of dry mouth, since no such associations were seen for dry eye symptoms, and 4.4% reported both. Report of dry eye symptoms is presented often or all the time) dry eye or dry mouth symptoms.

Table 2 summarizes the relationship between classes of medications and symptoms of dry eye and/or dry mouth. Only medications used by more than 2% of the population and associated with sicca symptoms at a level of P < .10 are listed. The accompanying odds ratios indicates the association of each class of medication with symptoms of dry eye and/or dry mouth, adjusted for other classes of medication that were commonly used in conjunction by subjects.

Table 3 presents the association of potential risk factors with symptoms of dry eye and/or dry mouth. Each of the associations is presented in crude form and adjusted for age, sex, and race. No association of sicca symptoms was found for rheumatoid arthritis, smoking, alcohol, or the presence of autoantibodies (either individually or in combination). A strong association in a dose-response fashion was observed with both the number of reported comorbid medical conditions and use of certain medication classes. We explored the possibility that sicca symptoms are mediated through medication use rather than underlying medical comorbidities by computing the association (adjusted for age, sex, and race) of each medical comorbidity with dry eye and/or dry mouth. We reasoned that if the underlying comorbidities themselves were important risk factors on a population basis, that they should fall in order in a way that might reflect some biologic plausibility; however, they did not. For example, the medical conditions most closely associated with sicca symptoms were congestive heart failure and Parkinson disease. Arthritis ranked ninth of the 15 comorbidities assessed, and, as previously mentioned, a history of rheumatoid arthritis was also not associated with sicca symptoms. The proportion of the population prevalence of sicca symptoms attributable17 to the use of drying medications was estimated at 58% for dry eye and dry mouth symptoms and 37% for dry eye or dry mouth symptoms. Vaginal dryness was reported by 8.8% of the population and was associated with symptoms of dry eye and dry mouth (odds ratio, 3.7; 95% confidence interval, 2.1-6.4). No association was seen between vaginal dryness and medication use except for those using 6 or more of the “drying” medication classes.

Potential risk factors for sicca symptoms relevant only to the female population were examined separately. No association (or protective effect) was found for oophorectomy, current estrogen use, age of menarche or menopause, or total reproductive years with reported symptoms of dry eye or dry mouth.
In the Salisbury elderly population, 27.4% reported experiencing dry eye or dry mouth symptoms often or all the time, and 4.4% experienced both. An extrapolation to the US population for those aged 65 to 84 years \(^1\) yields an estimate of more than 8 million with symptoms of dry eye or dry mouth and 1.3 million with both.

Our population-based sample does not support a significant association of autoimmunity (as assessed by rheumatoid factor, antinuclear antibody, and precipitins) with sicca symptoms. Of course, this does not mean that such an association does not exist for individuals with definite Sjögren syndrome or other connective tissue disease. However, in the general elderly population, sicca symptoms are unlikely to have an autoimmune basis, and our data do not provide a rationale for routine immunologic evaluation of elderly subjects who complain of sicca symptoms. Furthermore, the lack of association persisted after restricting the sicca group to those with both symptoms and test results in the lowest deciles (data not shown).

In the Salisbury population, a significant association between the current use of certain medications and sicca symptoms was observed. The strong dose-response relationship and biologic plausibility of this relationship suggest a causal association. The mechanisms by which medications may cause symptoms of dry eye and dry mouth are multifactorial (e.g., direct effect on gland function or dehydration). It is possible that some of the medication classes listed in Table 2 may have only an indirect or confounded association with symptoms. However, we have attempted to minimize this possibility by using statistical techniques to separate out those medication classes with independent effects.

The proportion of the population prevalence of sicca symptoms potentially attributable to drying medications was estimated at 62%, supporting the notion that medication side effect is a significant factor underlying sicca symptoms among the elderly. We also found a significant association of sicca symptoms and the number of comorbid medical conditions. It is likely that this association is mediated through the use of drugs rather than the comorbid conditions themselves since medical conditions known to cause dry eye and dry mouth were rare in this population and, when present (e.g., rheumatoid arthritis), were not found to be independently associated with sicca symptoms.

From a practical or public health perspective, however, one cannot choose one’s comorbidities, but there may be an opportunity to reduce or alter medication therapy. The results of this epidemiological investigation suggest that elderly patients should be queried about sicca symptoms and their medications be reviewed. If the sicca symptoms are present and bothersome, consideration may be given to altering the medical regimen.

Accepted for publication October 14, 1998.

This work was supported by grant P01-A10184 from the National Institutes of Health, Bethesda, Md, and performed at the Johns Hopkins University School of Medicine, Baltimore, Md.

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REFERENCES


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**Table 3. Association of Dry Eye and/or Dry Mouth Symptoms With Potential Risk Factors**

<table>
<thead>
<tr>
<th>No. of comorbid conditions</th>
<th>Dry Eye or Dry Mouth</th>
<th>Dry Eye and Dry Mouth</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Crude OR</td>
<td>Adjusted OR† (95% CI)</td>
</tr>
<tr>
<td>0</td>
<td>9.6</td>
<td>1.0 ( . . . )</td>
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<tr>
<td>1-3</td>
<td>68.9</td>
<td>2.2 (1.4-3.2)</td>
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<tr>
<td>&gt;3</td>
<td>21.5</td>
<td>4.2 (2.8-6.4)</td>
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</table>

<table>
<thead>
<tr>
<th>No. of medication classes associated with drying symptoms</th>
<th>Dry Eye or Dry Mouth</th>
<th>Dry Eye and Dry Mouth</th>
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<tbody>
<tr>
<td>0</td>
<td>17.8</td>
<td>1.0 ( . . . )</td>
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<tr>
<td>1</td>
<td>26.3</td>
<td>1.4 (1.0-1.8)</td>
</tr>
<tr>
<td>2</td>
<td>22.9</td>
<td>1.5 (1.1-2.1)</td>
</tr>
<tr>
<td>3</td>
<td>16.0</td>
<td>2.6 (1.8-3.5)</td>
</tr>
<tr>
<td>4</td>
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</tr>
<tr>
<td>5</td>
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<tr>
<td>≥6</td>
<td>3.4</td>
<td>4.6 (2.5-6.9)</td>
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<table>
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<tr>
<td>No</td>
<td>94.1</td>
<td>1.0 ( . . . )</td>
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<tr>
<td>Yes</td>
<td>5.9</td>
<td>1.3 (0.9-1.9)</td>
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</tbody>
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*OR indicates odds ratio; CI, confidence interval; ANA, antinuclear antibody; RF, rheumatoid factor; and ellipses, not applicable.†Adjusted for age, race, and sex.
The following letter, which appeared in the February 8, 1999, issue of the ARCHIVES (1999;159:316), was inadvertently published with an incomplete author listing. The letter is reproduced in full below with all authors given proper credit.

Haemophilus influenzae Pyelonephritis in Adults

Haemophilus influenzae has rarely been implicated as the causative agent of urinary tract infections in adults. The isolation of H influenzae from a urine sample was first reported in 1898 when Kretz recovered influenzae bacillus from the urine sample of a 36-year-old man with hematuria and polyuria. Since then, only 20 cases have been reported that implicate Haemophilus influenzae as the cause of adult urinary tract infections. We report an additional case of H influenzae pyelonephritis in a 90-year-old man and discuss the possible underestimation of the true incidence of H influenzae in urinary tract infections.

A 90-year-old man was seen in the emergency department with complaints of fever, dysuria, and left-sided flank pain of 2 days' duration. His medical history was notable only for symptomatic prostatic enlargement, for which he was being treated with phenoxymazine. Positive findings on physical examination included a temperature of 38.3°C and suprapubic and left-sided costovertebral angle tenderness. A clean voided urine specimen revealed 25 to 30 white blood cells and several gram-negative coccobacilli per oil immersion field. Subsequent growth yielded more than 10^5 colony-forming units per milliliter of a beta-lactamase-negative H influenzae sensitive to ampicillin. Moreover, 2 blood culture bottles yielded beta-lactamase-negative H influenzae, also sensitive to ampicillin. The patient defervesced with resolution of his dysuria and costovertebral angle pain and tenderness following treatment with ampicillin.

Haemophilus species colonize the upper respiratory tract where they may spread to cause infections of the surrounding tissues such as the lower respiratory, meninges, epiglottis, and middle ear. Haemophilus influenzae has rarely been implicated as the causative agent in urinary tract infections in adults, most cases affecting men with anatomical or functional genitourinary abnormalities. The true incidence of H influenzae genitourinary infection is unknown. The apparent rarity of H influenzae urinary tract infection may be ascribed to 3 factors: the bacteriologic media commonly used for the recovery of uropathogens do not support the growth of this organism; the organism is not generally part of the genitoperineal flora; and growth of H influenzae is inhibited by urine even when it is supplemented with the necessary growth factors. Furthermore, the incidence of culture-negative pyelonephritis in patients who have not received prior antibiotics is unknown. Haemophilus influenzae is likely a more common pathogen in urinary tract infections than is currently appreciated. Perhaps more sensitive culture techniques and greater physician awareness to the genitourinary pathogenicity of H influenzae, particularly in male patients with anatomical or functional genitourinary abnormalities, would enhance the detection of H influenzae urinary tract infection.

Correction