Clinical Guidelines for Management of Dry Eye Associated with Sjögren Disease

Gary N. Foulks, MD, FACS,[1] S. Lance Forstot, MD, FACS,[2] Peter C. Donshik, MD,[3] Joseph Z. Forstot, MD, FACP, FACR,[4] Michael H. Goldstein, MD, MM,[5] Michael A. Lemp, MD,[6] J. Daniel Nelson, MD, FACS,[7] Kelly K. Nichols, OD, MPH, PhD,[8] Stephen C. Pflugfelder, MD,[9] Jason M. Tanzer, DMD, PhD,[10] Penny Asbell, MD, MBA, FACS,[11] Katherine Hammitt, MA,[12] and Deborah S. Jacobs, MD[13]

ABSTRACT **Purpose: To provide a consensus clinical guideline for management of dry eye disease associated with Sjögren disease by evaluating published treatments and recommending management options. Design: Consensus panel evaluation of reported treatments for dry eye disease. Methods: Using the 2007 Report of the International Workshop on Dry Eye (DEWS) as a starting point, a panel of eye care providers and consultants evaluated peer-reviewed publications and developed recommendations for evaluation and management of dry eye disease associated with Sjögren disease. Publications were graded according to the American Academy of Ophthalmology Preferred Practice Pattern guidelines for level of evidence. Strength of recommendation was according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines. Results: The recommendations of the panel are briefly summarized herein. Evaluation should include symptoms of both discomfort and visual disturbance as well as determination of the relative contribution of aqueous production deficiency and evaporative loss of tear volume. Objective parameters of tear film stability, tear osmolarity, degree of lid margin disease, and ocular surface damage should be used to stage severity of dry eye disease to assist in selecting appropriate treatment options. Patient education with regard to the nature of the problem, aggravating factors, and goals of treatment is critical to successful management. Tear supplementation and stabilization, control of inflammation of the lacrimal glands and ocular surface, and possible stimulation of tear production are treatment options that are used according to the character and severity of dry eye disease. Summary: Management guidelines for dry eye associated with Sjögren's disease are presented.**

KEY WORDS **Anti-inflammatory agents, autologous serum, corticosteroids, cyclosporine, dry eye disease, mucolytics, omega 3 essential fatty acids, punctal occlusion, therapeutic contact lenses, secretogogues, Sjögren disease**

Accepted for publication December 2014.

From [1]University of Louisville Department of Ophthalmology and Vision Science, Louisville, KY, [2]Corneal Consultants of Colorado, Denver, CO, [3]University of Connecticut Health Center Division of Ophthalmology, Farmington, CT, [4]Rheumatology Associates of South Florida, Boca Raton, FL, [5]Tufts University School of Medicine, Boston, MA, [6]Georgetown University, Washington, DC, [7]HealthPartners Medical Group, St. Paul, MN, [8]University of Alabama Birmingham School of Optometry (formerly University of Houston School of Optometry, Houston, TX), [9]Baylor College of Medicine, Houston, TX, [10]University of Connecticut School of Dental Medicine, Farmington, CT, [11]Icahn School of Medicine at Mount Sinai, NewYork, NY, [12]Sjogren's Syndrome Foundation, Bethesda, MD, [13]Boston Foundation for Sight, Needham, MA.

Funding support: The Sjogren's Syndrome Foundation organized site meetings of the Committee for Ocular Clinical Guidelines in the Management of Dry Eye Associated with Sjogren Syndrome. No compensation was paid to any author.

Financial disclosures: All participating authors completed Conflict of Interest forms of the American College of Rheumatology, a co-sponsor of the Sjogren Syndrome Clinical Guidelines project, and the ICMJE-AJO forms. Consultant or advisory positions (SLF, GNF, MG, MAL, KKN, JDN, SCP, PA); speaker bureaus or lecture fees (SLF, PCD, MAL, KKN, SCP, JF, JMT, PA); grant support (MG, KKN, SCP, PA); equity payments (GNF, MG, MAL, KKM, SCP); and expert witness testimony (JDN).

Contributions of authors: Design and conduct of the panel (SLF, GNF, KH); collection, management, analysis, and interpretation of the data (SLF, GNF, PCD, MG, MAL, KKN, JDN, SCP, PA, DJ); and preparation, review, or approval of the manuscript (SLF, GNF, JF, PCD, MG, MAL, KKN, JDN, SCP, JMT, PA, DJ).

Single-copy reprint requests to Gary N. Foulks, MD, FACS (address below).

Corresponding author: Gary N. Foulks, MD, FACS, 3103 Joy Place, Wilmington, NC 28409. Fax: 910-769-4369. E-mail address: foulksgary@gmail.com

 The Ocular Surface ISSN: 1542-0124. Foulks GN, Forstot SL, Donshik PC, Forstot JZ, Goldstein MH, Lemp MA, Nelson JD, Nichols KK, Pflugfelder SC, Tanzer JM, Asbell P, Hammitt K, Jacobs DS. Clinical guidelines for management of dry eye associated with sjögren disease. 2015;13(2):118-132.

I. INTRODUCTION

The Sjögren's Syndrome Foundation initiated development of clinical guideline recommendations for medical practitioners in 2010. Representatives from rheumatology, oral medicine/dentistry, and eye care

OUTLINE

I. Introduction
II. Evaluation of Dry Eye Disease
  A. Symptoms
  B. Signs/Tests of Tear Function
III. Management of Dry Eye
  A. Topical Tear Substitutes and Lubrication
  B. Anti-inflammatory Therapy
    1. Topical Corticosteroids
    2. Topical Cyclosporine
    3. Omega 3 Essential Fatty Acids
  C. Secretogogue Therapy
  D. Punctal Occlusion
  E. Autologous Serum
  F. Mucolytic Therapy
  G. Therapeutic Contact Lenses
  H. Management of Eyelids
VI. Summary and Recommendations

providers were enlisted to evaluate recent literature and develop recommendations for those guidelines. This preliminary perspective from the eye care subcommittee is provided prior to the ultimate publication of the entire committee and is based upon agreement of the subcommittee members, all of whom contributed to the guidelines and agreed upon the recommendations.

The definition of dry eye provided by the 2007 International Dry Eye Workshop (DEWS) report is: "Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface."[1]

An alternative description of the disease is "dysfunctional tear syndrome" to emphasize that the tear film dysfunction can occur in the presence of normal tear secretion.[2] The discomfort is often described in various ways, such as burning, stinging, grittiness or sensation of something in the eye (foreign body sensation), itching, and, occasionally, pain. A recent survey of the members of the Sjögren's Syndrome Foundation revealed that the symptoms of dry eye were the most annoying and activity-limiting aspect of Sjögren disease. Sjögren disease is an autoimmune disease affecting primarily the exocrine glands of mucous membranes, resulting in dry eye and dry mouth, but often with additional musculoskeletal disturbance and damage to other body systems.[3] Visual disturbance is often noted as fluctuation of vision, particularly during reading or working at a computer, and blinking often clears the vision.

Dry eye is usually classified into two major categories: aqueous-deficient dry eye, in which tear production is reduced, and evaporative dry eye, in which the evaporation of the tear film is abnormally high.[1] Both categories have increased concentration of tear film constituents, as manifested by elevated osmolarity and rapid tear film breakup time (**TFBUT**).[4-7] Although the mechanisms of production of dry eye are easily separated, both conditions often occur simultaneously.

Inflammation of the lacrimal gland and ocular surface occur both as an inciting event in many cases and as a secondary effect as the dry eye disease worsens, prompting the name as keratoconjunctivitis sicca (**KCS**). Further classification of aqueous-deficient dry eye specifies dry eye that is associated with Sjögren disease versus dry eye not associated with Sjögren disease; this is done in recognition of the greater severity of aqueous-deficient dry eye as well as the greater inflammation associated with Sjögren disease.[1,8] It should be noted, however, that aqueous-deficient dry eye and evaporative dry eye have both been associated with Sjögren disease.[9,10]

An additional approach to categorizing dry eye, which has become more frequently used in determining the management strategy, involves the gradation of severity of the dry eye based upon level of discomfort, interference with activities of daily living, degree of clinically observable inflammation, and response to previous therapy.[11]

The literature evaluating the management of dry eye specifically in Sjögren disease is limited, and the options for therapy most often are evaluated in non-Sjögren patients. In this review, the studies that specifically included Sjögren disease patients are identified, although the management options evaluated in non-Sjögren patients are presented when considered essential or helpful in management of Sjögren dry eye disease. Publications were graded according to the American Academy of Ophthalmology Preferred Practice Pattern guidelines for level of evidence (Table 1).

Eye care practitioners frequently encounter patients with dry eye symptoms, as there are more than an estimated 20 million people with dry eye in the United States.[1] Although most patients complaining of dry eye disease do not have Sjögren disease, it is incumbent upon the practitioner to consider Sjögren disease when features of the dry eye suggest it as a possible etiology. More severe disease and more severe inflammation or difficulty in controlling the dry eye should prompt questions about concurrent dry mouth, arthritis, or other systemic evidence of inflammation or autoimmune disease. Patients with these associations should be referred to a dentist and rheumatologist for oral and systemic disease diagnosis and management.

II. EVALUATION OF DRY EYE DISEASE

A. Symptoms

Dry eye is usually symptomatic, although recent studies demonstrate that more than 40% of subjects with clear objective evidence of dry eye disease are asymptomatic.[12] The first diagnostic clue is often the patient's report of either eye discomfort and/or fluctuating vision. Many questionnaires have been developed to assess symptoms of dry eye,