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Review

New insights into the morphology and function of meibomian glands

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ABSTRACT

Meibomian glands secrete meibum, which gives rise to the lipid layer of the tear film and thereby prevents excessive evaporation of tear fluid. Meibomian gland dysfunction (MGD) is a major causative condition of evaporative dry eye, which is more common than the aqueous-deficient type of dry eye. Noninvasive meibography relies on infrared light and an infrared-sensitive camera to reveal the morphology of meibomian glands in both the upper and lower eyelids, whereas tear interferometry allows both qualitative and quantitative evaluation of the lipid layer of the tear film. These two techniques not only provide valuable clinical information related to dry eye but also allow clinical evaluation of MGD. Tear interferometry also has the potential to distinguish the condition of the tear film between normal individuals and dry eye patients. Furthermore, combined evaluation of the noninvasive breakup time of the tear film and the interferometric fringe pattern as determined by tear interferometry allows classification of the subtype of dry eye disease.

Contents

Abbreviations: MGD, meibomian gland dysfunction; NIM, noninvasive meibography; BUT, breakup time; OSDI, ocular surface disease index; LLT, lipid layer thickness.

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1. Introduction

Meibomian glands secrete the oily components of the tear film that attenuate the evaporation of tear fluid (Mishima and Maurice, 1961). Meibomian gland dysfunction (MGD) is a major causative condition of evaporative dry eye (Lemp, 1995; Mathers, 1993; Shimazaki et al., 1995), which is more common than the aqueous-deficient type of dry eye (Lemp et al., 2012), with the result that MGD is a key cause of dry eye disease in general. The International Workshop on Meibomian Gland Dysfunction defines MGD as a chronic, diffuse abnormality of meibomian glands that is commonly characterized by terminal duct obstruction or qualitative or quantitative changes in glandular secretion (Geerling et al., 2011). Defective formation of the oily layer of the tear film associated with MGD can result in symptoms such as eye irritation, clinically apparent inflammation, and ocular surface disease. Evaluation of both the morphology and function of meibomian glands is therefore central to the diagnosis of MGD.

2. Morphology of meibomian glands as revealed by meibography

Early meibography systems visualized the structure of meibomian glands through illumination of the tarsal plate from the skin side and were thereby able to detect abnormalities in gland morphology (Mathers et al., 1994; Nichols et al., 2005; Robin et al., 1985; Tapie, 1977; Yokoi et al., 2007). However, the observation area for such systems was small, necessitating the acquisition of many images to capture all meibomian glands. The edge of the illumination light probe was also sharp and hot, resulting in discomfort to the patient during the observation (Yokoi et al., 2007). To overcome these disadvantages, we developed a noncontact meibography system consisting of an ophthalmic slitlamp microscope and an infrared-sensitive camera equipped with an infrared-transmitting filter (Arita et al., 2008). With this system, the required observation time is short and the patient experiences minimal discomfort, with meibomian glands being detected as areas of high reflectivity and lost portions of meibomian glands as areas of low reflectivity (Fig. 1). It is able to reveal various types of meibomian gland abnormality including dropout, shortening, dilation, and distortion. Several noninvasive meibography (NIM) devices are now available commercially, including BG-4M/DC-4 attached to a slitlamp microscope (Topcon, Tokyo, Japan) (Arita et al., 2008); the Meibom Pen (Japan Focus Corporation, Tokyo, Japan) (Arita et al., 2013a); the Eye Top Topographer, Sirius Scheimpflug Camera, and Cobra Fundus Camera (CSO, Florence, Italy, and bon Optic Vertriebs GmbH, Lübeck, Germany); the Keratograph 5M (Oculus, Wetzlar, Germany) (Srinivasan et al., 2012); and Meiboviewer 2.0 (Visual Optics, Chuncheon, Korea).

Examination of 17 MGD patients by NIM revealed that the loss of meibomian glands was correlated with the pattern of the oily layer of the tear film and the noninvasive breakup time (BUT) of the tear film as determined by tear interferometry as well as with the ocular surface disease index (OSDI), suggesting that NIM might be valuable for the diagnosis of MGD (Pult et al., 2012). NIM allowed us to detect shortening of meibomian glands in wearers of contact lenses with dry eye symptoms (Arita et al., 2009a), distortion of meibomian gland ducts in patients with allergic conjunctivitis (Arita et al., 2010a), and dropout of meibomian glands in individuals treated with topical antiglaucoma drugs (Arita et al., 2012a,b), indicating that these various conditions might confer risk for the development of MGD.

NIM allows both semiquantitative and quantitative analysis of meibomian gland morphology. Such quantitative analysis is applicable to evaluation of the severity of or effects of treatment on disease (Arita et al., 2009b, 2010b, 2013b, 2014, 2015; Ban et al., 2013; Koh et al., 2012; Pult and Riede-Pult, 2012). We proposed the meiboscore as a means to grade the condition of meibomian glands on the basis of partial or complete loss of the glands in each eyelid. The meiboscore ranges from 0 to 3 for each eyelid and thus from 0 to 6 for each eye (Fig. 2) (Arita et al., 2008). The cutoff value of the meiboscore as a criterion for the diagnosis of MGD was found to be $\geq$3 (Arita et al., 2009b). Different evaluation scales for meibomian gland morphology have been proposed by Nichols et al. (2005) and by Pult and Riede-Pult (Pult and Riede-Pult, 2013). Evidence for the efficacy of meibography for evaluation of meibomian glands has now been obtained by many research groups, although it remains insufficient for the diagnosis of MGD, with additional analyses such as determination of the number of expressible glands

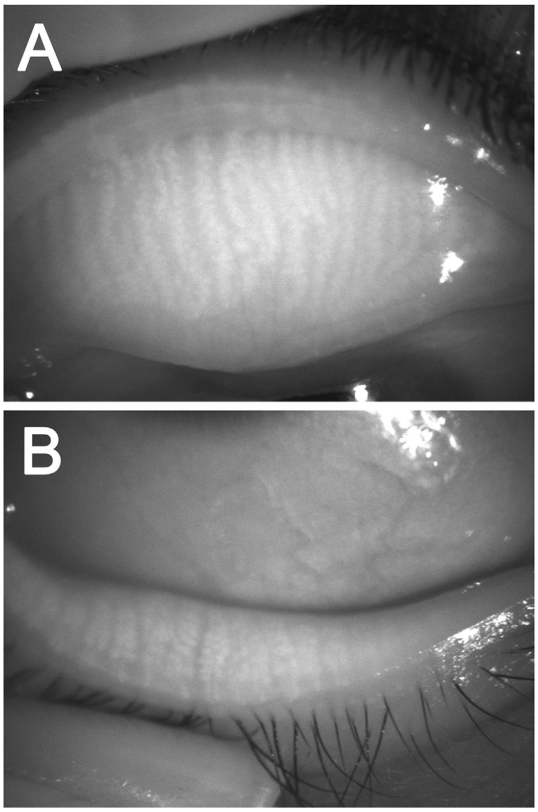

Fig. 1. Representative images of meibomian glands in the upper and lower eyelids obtained from a normal subject by noninvasive meibography. Meibomian glands are apparent as areas of high reflectivity, with those in the upper eyelid (**A**) being more slender and elongated than those in the lower eyelid (**B**).