

Evaluation of Tear Film Lipid Layer Thickness Measurements Obtained Using an Ocular Surface Interferometer in Nasolacrimal Duct Obstruction Patients

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Purpose: To compare the tear film lipid layer thickness (LLT) between patients with incomplete nasolacrimal duct obstruction (NLDO) and normal controls and to analyze the changes in tear film LLT and blinking pattern after silicone tube intubation in NLDO patients.

Methods: We reviewed the medical records of 68 eyes in 52 incomplete NLDO patients who underwent silicone tube intubation from January 2017 to July 2017. The LLT, blinking pattern, and Meibomian gland image were measured with the LipiView II ocular surface interferometer. The Meibomian gland drop-out ratio was measured using the polygon selection tool in the Image J program. Tear meniscus height, which is the other lacrimal indicator, was assessed with spectral-domain optical coherence tomography.

Results: Tear meniscus height was significantly decreased after silicone tube intubation ($p < 0.01$). Preoperative minimum, maximum, and average LLT values were 62.4 ± 24.0 , 86.7 ± 17.9 , and 71.7 ± 23.3 nm, respectively. Significant changes in the minimum, maximum, and average LLT (74.8 ± 23.6 , 98.8 ± 11.0 , and 91.6 ± 16.1 nm, respectively) were observed after silicone tube intubation ($p < 0.001$, $p = 0.001$, and $p < 0.001$). The partial blinking/total blinking ratio in 20 seconds and the Meibomian gland drop-out ratio showed no significant change after silicone tube intubation.

Conclusions: Overall, the LLT was increased after silicone tube intubation. Silicone tube intubation may be helpful in maintaining LLT with a normalized of amount of tears.

Key Words: Intubation, Lacrimal duct obstruction, Lipids, Nasolacrimal duct, Tears

A tear film consists of three layers: lipid, aqueous, and mucin. The lipid layer, which is the outer layer of tear film, is an oily secretion produced in the Meibomian glands [1].

The lipid layer is integral in the maintenance of tear film through stabilization of the tear film's surface in the spreading and redistribution of aqueous tear fluid after blinking and suppression of the evaporation of tear fluid [2-6]. In recent years, many studies have shown that lipid layer thickness (LLT) represents the condition and function of the Meibomian gland in Meibomian gland dysfunction or dry eye.

Some research has investigated the components of tears

Received: January 22, 2018 Accepted: March 16, 2018

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in patients with nasolacrimal duct obstruction (NLDO) [7,8]. According to these previous studies, these tears were more alkaline, had a higher calcium concentration, contained inflammatory cytokines, and were unstable in the proportion of tear proteins compared with normal patients [7,8]. In 2001, there was a report that tear LLT after dacryocystorhinostomy [9]. Kubo et al. [9] reported that the tear lipid layer was thicker after dacryocystorhinostomy in four patients (five eyes).

After development of an ocular surface interferometer, many studies were published regarding the tear lipid layer in dry eye or Meibomian gland dysfunction patients. However, there are few studies on the lipid layer or tear film in epiphora or NLDO patients. There have also been no studies on whether the lipid layer is increased with aqueous as the amount of tears increases in epiphora patients or whether there is no difference between these patients and normal controls.

In this study, we evaluated the LLT and blinking pattern of incomplete NLDO patients who underwent silicone tube intubation.

Materials and Methods

Clinical evaluation

We retrospectively reviewed the medical records of NLDO patients who underwent silicone tube intubation at CHA Bundang Medical Center in Seongnam, South Korea, from January 2017 to July 2017. This study was approved by the institutional review board of CHA Bundang Medical Center in Seongnam (CHAMC IRB 2018-01-027), South Korea, and was performed in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from all study participants.

All patients had been diagnosed with incomplete NLDO through examinations, including Munk's scale, syringing, and dacryocystography (DCG). The severity of epiphora was graded using Munk's scale, and patients classified as grades 2 to 4 were included [10] in the study. All participants diagnosed with incomplete NLDO had shown partial passage with regurgitation during syringing, which was confirmed by dacryocystography. Patients who passed the syringing test and were classified as having functional NLDO were excluded from our sample. Orbital computed

tomography was performed to rule out secondary NLDO resulting from causes such as orbital tumor, nasal cavity tumor, or anatomical abnormality in the bony structures. Patients with other ocular diseases, such as dry eye syndrome, corneal disease, or an eyelid disorder, were excluded. Silicone tube intubation was performed under local anesthesia with lidocaine mixed with a 1 : 100,000 dilution of epinephrine by the same surgeon in all patients. A 0.94-mm (outer diameter) silicone tube (Yuwon Meditech, Wonju, Korea) was used in all procedures. Patients with a history of previous lacrimal surgery and who were followed up for a period of less than three months were excluded.

Measurement of tear meniscus height, LLT, blinking pattern, and Meibomian gland drop-out ratio

Tear meniscus height (TMH) was assessed by one optometrist using spectral-domain optical coherence tomography (Spectralis; Heidelberg Engineering, Heidelberg, Germany). TMH was measured from the cornea-meniscus junction to the lower lid-meniscus junction with a scan line perpendicular to the mucocutaneous junction. The examination was performed twice for each patient. TMH was used for confirming the amount of tears both before and after silicone tube intubation (Fig. 1A, 1B) [11].

The LLT and blinking pattern were assessed using the LipiView II (TearScience, Morrisville, NC, USA) ocular surface interferometer by one optometrist. The LLT information included the minimum, maximum, and average for 20 seconds (Fig. 1C, 1D). The blinking pattern was obtained by determining the total blinking and partial blinking rates in 20 seconds and then calculating the partial blinking/total blinking ratio. The Meibomian gland drop-out ratio, the ratio of the Meibomian gland drop-out area to the total area, was measured using the polygon selection tool in the Image J program (National Institutes of Health, Bethesda, MD, USA) (Fig. 2) [12].

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics ver. 20.0 (IBM Corp., Armonk, NY, USA). Independent *t*-test was used to compare the overall LLT, blinking pattern, Meibomian gland drop-out ratio, and TMH of control and nasolacrimal duct patients. Paired *t*-test was used to compare the overall LLT, blinking pattern, Meibo-

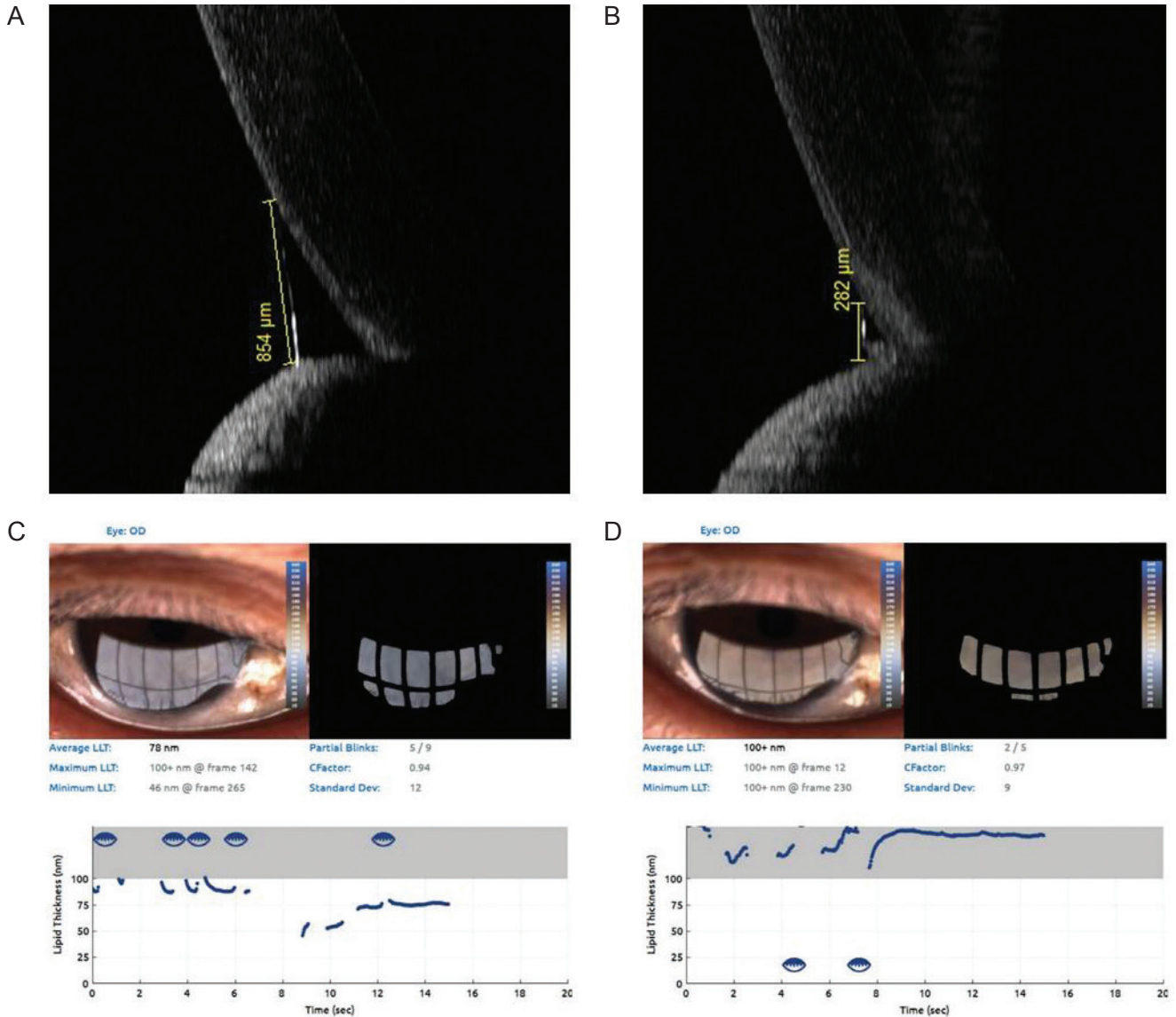


Fig. 1. Tear meniscus height, lipid layer thickness and blinking patterns before and after silicone tube intubation. (A,B) Preoperative and postoperative tear meniscus height obtained using spectral-domain optical coherence tomography (Spectralis, Heidelberg Engineering, Heidelberg, Germany). (C,D) Preoperative and postoperative lipid layer thickness and blinking patterns as measured with LipiView II (TearScience, Morrisville, NC, USA)

mian gland drop-out ratio, and TMH both before and after silicone tube intubation. A p -value <0.05 was considered to indicate significance.

Results

This study evaluated 52 incomplete NLDO patients (68 eyes), including 16 male (30.8%) and 36 female (69.2%) patients, and 21 controls (42 eyes), including 6 male (28.6%)

and 15 female (71.4%) patients. The average age and duration of incomplete NLDO patients were 60.5 ± 12.9 years and 4.82 ± 3.95 months, respectively. The mean age of the controls was 54.1 ± 10.6 years, and there were no significant differences ($p > 0.05$). The average age and disease duration were 64.5 ± 14.7 years and 5.05 ± 5.16 months, respectively, in male incomplete NLDO patients and 58.7 ± 11.8 years and 3.35 ± 4.57 months, respectively, in female incomplete NLDO patients. The mean Munk score was 4.2 ± 1.2 , 4.0 ± 1.3 in male patients and 4.3 ± 1.2 in female patients.

There were no significant differences in male and female patients ($p > 0.05$).

TMH is significantly increased in incomplete NLDO patients; it decreased to show improvement after silicone tube intubation ($p < 0.001$) (Table 1 and Fig. 3A). There was no significant difference in LLT between control and incomplete NLDO patients. Before performing silicone tube intubation, the minimum, maximum, and average LLT rates were 62.4 ± 24.0 , 86.7 ± 17.9 , and 71.7 ± 23.3 nm, respectively. Significant changes in the minimum, maximum, and average LLT (74.8 ± 23.6 , 98.8 ± 11.0 , and 91.6 ± 16.1 nm, respectively) were observed after silicone tube intubation

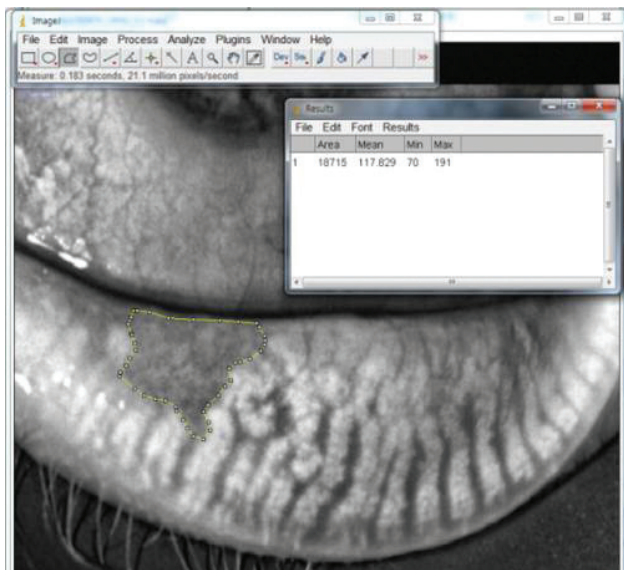


Fig. 2. Measurement of Meibomian gland drop-out ratio using the Image J program (National Institutes of Health, Bethesda, MD, USA). Meibomian gland drop-out ratio, ratio of Meibomian gland drop-out area to total area, was measured using a polygonal selection tool of the Image J program.

($p < 0.001$, $p = 0.001$, and $p < 0.001$) (Table 1 and Fig. 3B).

The numbers of total and partial blinking events in 20 seconds were 8.2 ± 3.6 and 3.9 ± 1.9 , respectively, in the control group. Preoperative total blinking and partial blinking for 20 seconds were 8.5 ± 5.3 and 4.1 ± 3.8 , respectively, while the corresponding postoperative events totaled 7.9 ± 4.9 and 4.1 ± 3.8 . There was no significant difference in partial blinking or partial blinking/total blinking ratio between the controls and the incomplete NLDO patients ($p = 0.422$, $p = 0.078$) (Table 1). In addition, there was no significant difference between the preoperative and postoperative partial blinking/total blinking ratios $p = 0.830$ (Table 1 and Fig. 3C). Finally, no significant differences in Meibomian gland drop-out ratio in control, pre, and postoperative groups ($p = 0.293$, $p = 0.628$) (Table 1 and Fig. 3D) were noted.

Discussion

According to previous studies, tear protein components in patients are more alkaline, higher in calcium concentrations and inflammatory cytokines, and unstable compared with normal persons [7,8]. Kubo et al. [9] reported that the tear lipid layer was thicker after dacryocystorhinostomy in four patients (five eyes). In their study, researchers determined the LLT by observing the specular reflected light from the tear's surface, a similar method to the ocular surface interferometer used in this study.

Tear lipids are secreted from the Meibomian glands and play an important role in maintaining the stability of the tear film. The importance of the tear lipid layer in myalgia dysfunction and dry eye has been emphasized. The LipiV-

Table 1. Comparison of LLT, blinking pattern, and TMH between control and epiphora patients

	Control	Nasolacrimal duct obstruction			p -value [†]
		Preoperative	Postoperative	p -value*	
TMH (μ m)	207.1 ± 116.9	453.9 ± 309.9	264.5 ± 169.1	<0.001	<0.001
Average LLT (nm)	70.6 ± 25.3	71.7 ± 23.3	91.6 ± 16.1	<0.001	0.897
Total blinking (times/20 sec)	8.2 ± 3.6	8.5 ± 5.3	7.9 ± 4.9	0.506	0.536
Partial blinking (times/20 sec)	3.9 ± 1.9	4.2 ± 3.8	4.1 ± 3.8	0.960	0.422
Partial blinking/total blinking ratio	41.05 ± 26.30	52.28 ± 35.33	53.34 ± 35.78	0.830	0.078
Meibomian gland drop-out ratio	8.57 ± 3.65	9.48 ± 4.76	9.56 ± 4.87	0.628	0.293

LLT = lipid layer thickness; TMH = tear meniscus height.

*Paired t -test; †Independent t -test.

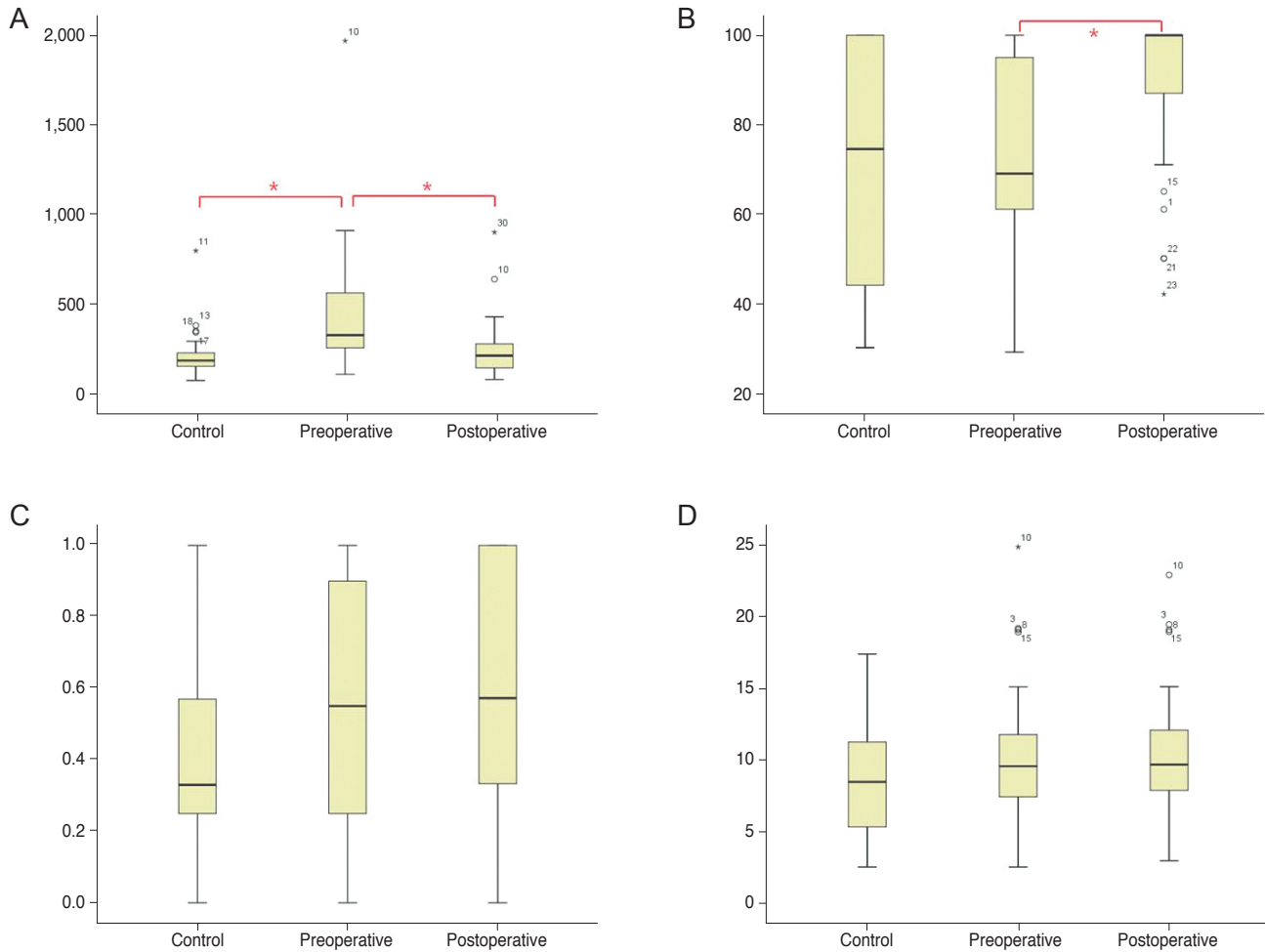


Fig. 3. Box plot of the measured values between control and epiphora patients (before and after silicone tube intubation). (A) Tear meniscus height, (B) lipid layer thickness, (C) partial blinking/total blinking ratio, and (D) Meibomian gland drop-out ratio ($p < 0.05$).

iew II ocular surface interferometer is a new measurement tool that can measure tear film thickness, eyelid blinking, and Meibomian glands structure [11,13]. More recent studies have been conducted due to its development. Most of these studies have focused on the relationship between the tear film lipid layer and Meibomian gland dysfunction or dry eye. Eom et al. [12] reported that the LLT in South Koreans is 65.0 ± 19.1 interferometry color units, which is the same value obtained with a nanometer and had a similar numeric value to our study.

In this study, we investigated the tear lipid layer and pre- and postoperative changes in patients with incomplete NLDO, a typical condition of excessive tear production. In this study, the overall tear film LLT was not different between the control and incomplete NLDO patients and in-

creased following silicone tube insertion. This finding is similar to the results of a previous study by Kubo et al. [9], who reported that the lipid layer could not be extended to the corneal surface by decreased tear volume and leads to a thicker and irregular lipid layer. However, in our study, the LLT in the postoperative group was significantly higher than that of the control group, but there was no significant difference in TMH. Therefore, we considered the following possibility. The lipid layer is increased with tearing to maintain homeostasis of the tear composition because the balance of tear film components is important for tear film stability, and a compensatory system is considered necessary in response to changes in these components [14,15]. An increased postoperative LLT might be due to the maintained high lipid layer as the amount of tears decreases and

lipid secretion does not change immediately. The other possibility is that the blinking dynamics produce a difference of LLT after silicone tube intubation. In our study, we could only obtain the blinking pattern by ratio of partial and total blinking, and there were no significant differences in the preoperative, postoperative, and control groups. We must also consider that any blinking-related Meibomian gland squeezing pressure may be affected by the silicone tube intubation. Further studies will be needed to investigate the lid blinking power along the lid margin using new instruments like cinematography to prove these ideas.

A limitation of this study is that it was carried out only by simple silicone tube insertion in incomplete NLDO. Other techniques, such as DCR, will also be needed in the future. In addition, studies on diseases causing tearing other than incomplete NLDO may be necessary. In this study, it was meaningful to measure the tear lipid layer in patients with epiphora as this has not been performed in previous tear lipid layer studies. Further study is needed to determine whether the increase of tear lipid layer after silicone tube implantation is due to normalization of aqueous tear volume or to the increase of tear lipid secretion in Meibomian glands. In addition, the correlation between the tear lipid layer and tearing symptoms must be determined.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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