Evaluation of mucin changes between daily and extended wear silicone hydrogel contact lenses



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Scan this QR code with your smart phone or mobile device to read online. **Background:** Initially, contact lenses were recommended only for daily wear because of infection and discomfort concerns. With rising demand, particularly for overnight use, extended wear lenses have gained significance. Despite concerns, intensive development of materials like Lotrafilcon B aims to meet this demand, focusing on comfort and safety.

Aim: This study aimed to evaluate the mucin quantity and quality changes between daily and extended wear (Lotrafilcon B), impacting eye health and comfort.

Setting: The study was conducted at Kirana Eye Center, Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Methods: This study was a single-blinded randomised clinical trial with two parallel groups. Forty (40) eligible subjects willingly participated. Mucin 5AC (MUC5AC) and Ferning-type tests were conducted. The 40 subjects with moderate myopia were then divided into a daily wear and an extended wear group. The MUC5AC test was performed at pre-fitting and at 4 weeks, whereas the Ferning-type tests were taken at pre-fitting and 1st and 4th weeks.

Results: For both groups, there was a significant increase in MUC5AC levels from pre-fitting to week four, but with no significant difference between them in final MUC5AC levels. Additionally, the comparison of eyes with normal and abnormal Ferning-types between the two groups showed no significant differences at pre-fitting, 1st and 4th weeks.

Conclusion: There is no significant difference in MUC5AC levels with the use of daily or extended wear (with Lotrafilcon B).

Contribution: This study compares the impact of daily and extended wear Lotrafilcon B contact lenses on eye health and comfort in moderate myopia patients.

Keywords: Lotrafilcon B; MUC5AC; Ferning-type; daily and extended wear lenses; myopia; contact lenses.

Introduction

Myopia is a global health problem that may increase to 39 million people experiencing blindness and 246 m people experiencing moderate to severe visual impairment.^{1,2} The WHO (World Health Organization) has also reported that among the 153 m people who are already visually impaired because of uncorrected refractive errors, they have expressed a desire to stop wearing spectacles. Many patients who acquire refractive correction aspire to be free from spectacles, but most are still afraid of the need to do refractive surgery.³ Hence, contact lenses may be the answer to provide the solution, as they offer many advantages over the use of spectacle lenses. Contact lenses can provide sharper vision more optimally without a limited field of view and distortion. Furthermore, contact lenses offer a more aesthetically pleasing appearance.⁴ On the other hand, soft contact lens (SCL) users usually face several risks, such as corneal hypoxia, damage to tear layer integrity, epithelial lining damage, corneal polymegathism, ptosis, blinking reflex abnormalities, meibomian gland dysfunction, and dry eye syndrome (DES), to name a few.⁵⁶ Efron stated that SCL users had a five times greater risk of DES than users of spectacles only.⁵

Originally, SCLs were designed for daily wear (DW). With increasing demand from users, extended wear (EW) is favoured by some.⁷ Thus, Silicone Hydrogel (SiH) SCL uses Lotrafilcon B that undergoes surface treatment during fabrication specifically for EW (used for six consecutive nights).⁵

Mucus on the ocular surface (in tears) has hydrophilic properties that attract and retain tear fluid to prevent drying of the tear film. In addition, mucus also functions as a lubricant for the

ocular surface when the eye blinks, supports the refraction function of the cornea to maintain visual acuity, captures and expels debris or foreign objects that enter the eye and prevents infection. Mucin 5AC (MUC5AC) is a form of mucous protein (found on the surface of the eye) with an important role in maintaining moisture and lubrication in the eye and protecting against infection and irritation.⁸⁹

Several studies have been conducted regarding changes in MUC5AC levels because of the use of SCL made of SiH, but the results obtained are still controversial.^{8,9,10} Daily wear usage is considered safer than extended wear as it is not used during sleep, thereby eliminating the risk of hypoxia and more severe corneal mechanical trauma at night.¹¹ Silicone Hydrogel contact lenses with highly modified oxygen transmissions with surface treatments are expected to minimise the occurrence of these risks and benefit from extended use. Therefore, we conducted this study to evaluate the MUC5AC level associated with extended wear of SiH contact lenses (Lotrafilcon B) and to compare differences in MUC5AC levels between daily and extended wear of Lotrafilcon B.

Materials and methods

This single-blinded randomised clinical trial study with two parallel groups was conducted from November 2016 until February 2017. Research subjects were informed about the study's benefits, possible associated risks and potential for discomfort. They voluntarily participated, signing informed consent, with the right to withdraw at any time. Subject privacy was strictly maintained for research purposes only. Fittings were conducted by experienced consultants or residents, and side effects were assessed to ensure comfort during lens wear. Subjects gained improved visual acuity with minimal side effects, and those experiencing serious side effects were promptly excluded and managed appropriately.

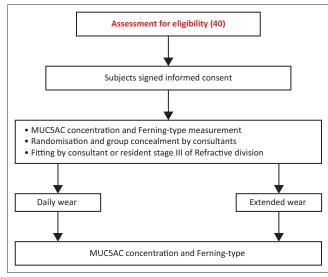
Subjects with moderate myopia and astigmatism ≤ 1 D, aged between 18 and 40 years old, were included. This study used consecutive sampling. If patients had a history of eye abnormalities, systemic disease, smoking, pregnancy or lactation history, then they were excluded. Subjects were then divided into two groups, with each group consisting of 20 subjects or 40 eyes (Figure 1). Mucin 5AC examination was performed at pre-fitting and at the 4th week using a human MUC5AC ELISA Kit from Elabscience Biotechnology Co., Ltd. Evaluation of the Ferning-type was performed on pre-fitting, 1st and 4th weeks using a 100 × magnification microscope. Subjects, who withdrew during the study, did not wear contact lenses for two days, were allergic to contact lenses and/or cleaning fluid or obtained severe complications, were excluded from analysis.

Data analysis was conducted using per-protocol analysis. Data were entered into research forms and organised into tables using SPSS version 22.0. Pre- and post-treatment data were presented in tables, with normality tested using the Shapiro-Wilks test. Mean differences before and after use were assessed using paired *T*-tests for normally distributed data and Wilcoxon tests for non-normally distributed data (p < 0.05). Mean differences between the DW and EW groups were evaluated using independent *T*-tests for normally distributed data and Mann–Whitney tests for non-normally distributed data (p < 0.05). Category differences between groups were tested using the Chi-square test or Fischer's exact test if assumptions were not met.

Results

Forty subjects met the inclusion criteria and were willing to participate in the study. One subject in the daily wear group dropped out (DO) due to an allergic reaction to the contact lenses. The basic characteristics of the subjects assessed in this study are presented in Table 1.

The results of the MUC5AC data analysis are presented in Table 2. Mucin 5AC levels at the time of pre-fitting were not



MUC5AC, mucin 5AC.

FIGURE 1: Study design.

TABLE 1: Baseline	values (N	= 39 subjects)	•

Demographic characteristic	DW EW (19 subjects) (20 subjects)		Total (N = 39)		р		
	n	%	п	%	n	%	-
Sex							0.001*
Male	0	0	9	45	9	23	-
Female	19	100	11	55	30	76.9	-
Age (mean ± range)	27.80) ± 4.40	25.30	± 3.20		-	0.006*
Spherical equivalent	-4.08	8 ± 0.88	-4.05	± 0.80		-	0.827*
Mean \pm SD ($n = 78$ eyes)		-		-		-	-
<i>Non-invasive break up time</i> (Second)	14.9	± 3.40	15.50	± 2.30		-	0.362**
Occupation							0.649ω
College student	-	-	5	25	-	-	-
Employees	10	52.60	8	40	-	-	-
Teachers	1	5.20	1	5	-	-	-
Medical personnel	8	42.10	6	30	-	-	-

Spherical Equivalent in dioptres (D) and DW and EW mean daily wear and extended wear, respectively.

DW, daily wear; EW, extended wear; SD, standard deviation.

*, Fisher test; **, Mann–Whitney test; ω, Chi square test.

homogeneous between the two treatment groups, but the statistically non-significant results were obtained at calculation during the 4th week between the two groups.

If we compare the MUC5AC levels before and after the study, there was a significant change. However, the MUC5AC level between the two groups showed no significant difference.

The Ferning-type pattern in each treatment group is described in Table 3. We compared the difference between the number of eyes with normal and abnormal Ferning types between the two treatment groups, which showed no significant change in pre-fitting, 1st and 4th weeks.

Table 4 lists complications that may occur during the use of contact lenses. Complications obtained during this study were only mild complications; thus the SCL was tolerated well.

Discussion

The successful use of contact lenses is strongly influenced by the stability of the tear layer and the oxygen transmission capability of the contact lens.¹² The mucin layer has an important role in achieving this success because it provides protection to the corneal epithelium and conjunctiva.¹⁰ Most subjects in this study were female, which is consistent with the number of contact lens users in the world, where twothirds are female.^{13,14,15,16,17} The age and sex differences between the two groups after evaluation with ANCOVA did

TABLE 2: Comparison of the average mucin 5AC levels at pre-fitting and 4th week (N = 78 eyes).

MUC5AC	Total (N	р	
	Lotrafilcon B (Daily wear) n = 38 eyes	Lotrafilcon B (<i>Extended wear</i>) <i>n</i> = 40 eyes	
MUC5AC pre-fitting (ng/mL)	2.16 (1.69–4.37)	2.55 (1.78–5.55)	0.002**
MUC5AC 4th week (ng/mL)	4.62 (1.91-5.90)	4.74 (3.88–6.38)	0.352**
p value within group	0.001#	0.001#	-
Δ MUC5AC	2.49 (-0.46-3.30)	2.08 (-0.80-3.33)	0.153**
p value ANCOVA repeated measurement	-	-	0.626***

^{*}, Wilcoxon test; **, Mann–Whitney test; ***, Mann–Whitney test, after being controlled by age and gender variables; MUC5AC, mucin 5AC; Δ , difference; ANCOVA, analysis of covariance.

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Ferning-type	ng-type Total (N = 78 eyes)				p	
		DW EW (n = 38 eyes) (n = 40 eyes)			_	
	п	%	п	%	_	
Pre-fitting						
Normal	35	92.1	34	85.0	0.482*	
Abnormal	3	7.9	6	15.0	-	
1st week						
Normal	35	92.1	35	87.5	1.000*	
Abnormal	3	7.9	5	12.5	-	
4th week						
Normal	36	94.7	36	90.0	0.676*	
Abnormal	2	15.3	4	10.0	-	

DW, daily wear; EW, extended wear.

*Fisher test.

not affect MUC5AC levels. A study conducted by Zhao et al.¹⁸ showed similar results, reporting there was no relationship between age and sex with the number of MUC5AC.

Increased mucin production by conjunctival goblet cells may be caused by several conditions, such as the initial phase of dry eye and allergic conjunctivitis.¹⁵ In the initial phase of dry eye, the process of ocular surface damage and irritation of the afferent sensory nerve triggers the parasympathetic nerve to increase the secretion of MUC5AC mucin via conjunctival goblet cells.^{15,19} Another mechanism that results in increased MUC5AC secretion in the use of SiH contact lenses is the diminished density of the corneal nerve plexus because of mechanical trauma by contact lenses.²⁰ The decreased density of the corneal nerve plexus leads to a boost in nerve growth factor (NGF), which induces goblet cell differentiation and MUC5AC.^{20,21}

This result here is different from that of Dogru et al.¹² where MUC5AC levels decreased after the daily use of contact lens Senofilcon A for 2 weeks. This difference may be attributed to Dk/t and lower modulus compared to Lotrafilcon B. The rise of MUC5AC levels may also be because of ocular surface damage caused by the chemical trauma of contact lens cleaning fluid.²² Another study by Carnt et al.²³ assessed inflammatory conditions by comparing the use of different additives between nonanoyl ethylenediamine tetra acetic acid (1%) and propylene glycol (0.2%), in a cleanser with 2-amino-2-methyl-1-propanol (AMP-95) and edetate disodium in other cleaning fluids. The results obtained indicated that the use of nonanoyl ethylenediamine tetra acetic acid (1%) and propylene glycol (0.2%) resulted in a larger inflammatory effect (10x) compared to the addition of 2-amino-2-methyl-1-propanol (AMP-95) and edetate disodium.

The DW group was more likely to use cleaning fluids than the extended wear group, and MUC5AC levels in the daily wear group were estimated to increase because of greater chemical trauma than the EW group. In contrast with the duration of contact lens wear, the EW contact lens wear group had longer exposure to the ocular surface compared to the DW group. Therefore, the ocular surface trauma risk is higher in the EW group, which resulted in increased

TABLE 4: Contact lens adverse effects between daily and exte	nded use ($N = 39$
subjects).	

Adverse effect	DW (n = 19)		<i>EW</i> (<i>n</i> = 20)		р
	n	%	n	%	-
Contact lens peripheral ulcer	-	-	-	-	-
CL induced acute red eye	1	5.3	4	20	0.364ω
Keratitis	-	-	-	-	-
Foreign body sensation	6	31.6	6	30	1.000ω
Dryness	2	10.5	2	10	1.000ω
Eye secretions	-	-	6	30	0.020ω
Mucin balls	-	-	-	-	-
Adverse effect	10	52.6	4	20	0.043ω

DW, daily wear; EW, extended wear; CL, contact lens

 $\boldsymbol{\omega}$, Chi-square test.

MUC5AC levels because of the greater NGF stimulation occurring in the extended wear group.

The presence of a substantial amount of secreted mucins is a critical factor for maintaining the health of the ocular surface.²⁴ Liu et al.²⁵ reported a wide range of MUC5AC levels in a normal subject, ranging from 32.39 ± 18.44 (4.05– 73.16) ng/mL. Therefore, despite a significant increase in MUC5AC levels after the 4th week, the values obtained were still within normal limits. The results of the MUC5AC examination on pre-fitting showed a significant difference (p = 0.002) between the two groups. However, in the 4th week, the MUC5AC level shift (Δ MUC5AC) between the two groups showed no significant difference (p = 0.153). The lack of significant changes in mucin expression in contact lens wearers may be because of the reduced sensitivity of the cornea, which makes the ocular surface irritable during extended wear.⁹

The MUC5AC concentration unit in this study is ng/mL, which shows a relative comparison of MUC5AC protein content to the amount of tears. Increased levels of MUC5AC leads to a decrease in the secretion of aqueous fluid, which helps to maintain high viscosity, consequently prolonging the tear break-up time (TBUT).²⁶

The Tear Ferning test is a simple and valuable test to evaluate the quality of tear composition. In general, there was no deterioration of mucin quality in both groups. This fact was seen from the number of eyes with normal category Ferningtype, which did not decrease between before and after the use of SCL for 4 weeks.

The increasing normal-type mucinous number may be associated with elevated MUC5AC levels by the 4th week as Ferning tests are also assessed as a means of finding out the relative ratio of mucin to total tears.²⁷ Dry eye disease also involves inflammation on the eye surface, characterised by cytokine production and infiltration of T cells and neutrophils. Cysteinyl leukotrienes, LTC4, LTD4 and LTE4, produced during eye allergy, dry eye disease or other inflammatory eye conditions, stimulate goblet cell mucus secretion, contributing to excessive mucus production observed in these diseases.¹⁵ Thus, raised levels of MUC5AC are considered one of the early signs of dry eye.

One subject in the DW group withdrew from the study because of an allergic reaction. From the data obtained, it was found that the subject has an atopic history. People with an atopic history are at least five times more likely to experience an allergic reaction during contact lens wear.²⁸

Conclusion

There was a significant increase in MUC5AC levels in both groups following one month of the study. However, the

difference (Δ) between the two groups after using Lotrafilcon

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Competing interests

The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article.

Authors' contributions

R.R. and T.R. played a role in conceptualising, which was then, together with L.E., M.S. and A.K., used to formulate the methodology, analyse data and perform validation. All authors made their respective contributions to the manuscript.

Ethical considerations

Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, University of Indonesia on 21 March 2016. The ethics approval number is 38/UN2. F1/ETIK/2017.

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Data availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

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