

ORIGINAL ARTICLE

# Comparison of Corneal Thickness and Endothelial Cell Morphology in Myopic Patients with Daily Wear Hydrogel (Nelfilcon A) and Silicon Hydrogel (Lotrafilcon B) Contact Lenses: A Pilot Study

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## ABSTRACT

**Background:** To compare corneal thickness and endothelial cell morphology in myopic patients wearing 1 month hydrogel conventional and silicon hydrogel contact lenses in daily wear.

**Methods:** This is a prospective, single blind, randomized study. Seventeen (34 eyes) myopic patients were randomly assigned to receive either nelfilcon A or lotrafilcon B. Central corneal thickness (CCT), coefficient of variation (CV), and percentage of six-sided cell (6A) were examined using specular non-con robo Konan microscope. Changes in CCT, CV, and 6A were evaluated before contact lenses fitting as well as 1 week and 1 month after the treatment. Patients were also evaluated for any subjective side effects and complications during the treatment period.

**Results:** There were 64.7% subjects with history of contact lens wearers and 52.9% of them was hydrogel wearers. After 1 month daily wear of nelfilcon A and lotrafilcon B, no statistically differences changes in CCT ( $p=0.285$ ; Mann Whitney test), CV ( $p=0.587$ ; unpaired t-test), and 6A ( $p=0.353$ ; unpaired t-test). General linear model analysis in follow up evaluation with test of within subject effect revealed decreased in CCT ( $p=0.001$ ) and CV ( $p=0.001$ ), also increased in 6A ( $p=0.022$ ) in all subjects.

**Conclusion:** There were no statistically difference in CCT, CV, and 6A between daily wear of nelfilcon A and lotrafilcon B. Subjects with history of contact lens wearers gained advantages in oxygen availability, which decrease corneal thickness and improve endothelial cell morphology.

**Keywords:** nelfilcon A, lotrafilcon B, simple myopic, corneal thickness, endothelial cell morphology

**M**yopia is the refractive anomaly of the eye where parallel light rays from an object are focused

by the eye in front of the retina.<sup>1</sup> An eye with simple myopia has spherical equivalent (SE) less than 6 dioptri (D) and axial length

less than 25 mm.<sup>2</sup> Prevalence of simple myopia reached 22.4% and the incidence is increasing significantly every decade.<sup>3</sup>

Since introduced, contact lenses have become therapy of choice to correct refractive errors, especially simple and high myopia. It offers many advantages, including better visual acuity and cosmesis, no visual field restriction and distortion, as well as less aniseikonia.<sup>1,2</sup>

Fitting a contact lens on the eye leads to significant reduction in the oxygen supply to the cornea, thus the consequences is hypoxia with corresponding hypercapnia. If the oxygen concentration decreases below a critical level, the cornea tissue switches metabolism from aerobic to anaerobic glycolysis by Embden-Meyerhof pathway. This condition causes accumulation of lactate, end product of anaerob glycolysis. Lactate together with the accompanying hypercapnia results in stromal acidosis. Low ATP production and acidic pH dampens the pumping action of corneal endothelium, inducing corneal edema.<sup>4,5</sup> Central corneal thickness is a sensitive indicator to demonstrate corneal edema caused by contact lens wearing in short term period.<sup>6</sup>

Stromal acidosis also disturbs endothelial cell stability and morphology, produces endothelial polymegethism and pleomorphism. Polymegethism refers to a greater-than-normal variation of corneal endothelial cell size while pleomorphism can be defined as increase in the variations in cell shape distinct from the classical, uniform six-sided endothelial cell appearance. The possible method for estimating degree of polymegethism in the endothelial mosaic is to examine the coefficient of variation (CV) of the cell area, while endothelial pleomorphism could be evaluated by percentage of six-sided cell (6A).<sup>5,6</sup>

Holden and Mertz<sup>7</sup> reported that oxygen transmissibility (Dk/t) of a contact lens must be at least 24 for daily wear lenses and 87 for extended wear in order to prevent corneal edema above the normal limit of 4%. Nelfilcon A is a conventional hydrogel contact lens contain polyvinyl alcohol

(PVA) with Dk/t 26, suitable for daily wear, and has been used worldwide.<sup>8</sup> Silicone hydrogel contact lenses were initially developed to supply high oxygen levels to the cornea for extended wear. Lotrafilcon B is one of silicon hydrogel contact lens with Dk/t 138. Because the main pathologic condition in all contact lens related problems is corneal hypoxia, silicone hydrogel lenses with superior oxygen transmissibility have been reported in various studies as causing fewer adverse effect in daily wear by reducing corneal hypoxia.<sup>9-12</sup>

Performance and safety of contact lenses in maintaining physiologic metabolism of cornea depends on oxygen transmissibility to minimize hypoxia and hypercapnia because a contact lens completely without negative effects on corneal physiology has so far not been manufactured. To our knowledge, there has been no study about comparison of daily wear nelfilcon A and lotrafilcon B investigating corneal edema as well as endothelial polymegethism and pleomorphism related to hypoxia.

The purpose of this study was to compare corneal thickness and endothelial cell morphology in myopic patients wearing 1 month nelfilcon A and lotrafilcon B contact lenses in daily wear.

## MATERIAL AND METHODS

This is a randomized, single blind study conducted in RSCM Kirana between December 2014 and May 2015. Patients with SE between -3.00 to -6.00 D aged 18 to 40 years old, and astigmatism less than 1.5 D were included. Patients who are willing to participate in this study signed the informed consent.

Patients were excluded if: had dry eyes (Schirmer I test under 10 mm); endothelial cell density under 2000 cell/mm<sup>2</sup>; had history of intraocular surgery; ocular trauma; intraocular disease; allergic to contact lenses and disinfection solution. Pregnant and lactating women, uncooperative patient, and subjects with unacceptable contact lenses fitting were also excluded.

**Table 1.** Baseline characteristic

Baseline Characteristics	Group N (n=16 eyes)	Group L (n=18 eyes)	Total
<b>Sex</b>			
Male	4 (25%)	4 (22.2%)	8 (23.5%)
Female	12 (75%)	14 (77.8%)	26 (76.47%)
<b>Age (median±range)</b>	22±(20-30)	24±(19-31)	
<b>History of contact lens wear</b>			
Negative	6 (37.5%)	6 (33.3%)	12 (35.3%)
Positive	10 (62.5%)	12 (66.7%)	22 (64.7%)
<b>Keratometry (mean±SD)</b>			
Horizontal keratometry	7.69±0.340	7.66±0.305	
Vertical keratometry	7.50±0.343	7.47±0.320	
<b>Spherical equivalent/SE (mean±SD)</b>	-4.64±1.06	-4.20±0.970	

Patients were randomized to receive either nelfilcon A or lotrafilcon B. History taking, best corrected visual acuity (BCVA), slit lamp biomicroscopy examination, intra-ocular pressure (IOP) measurement, CCT, CV, and 6A measurement (obtained with specular non-con robo Konan microscope) were performed before the study. Patients were instructed to wear contact lenses 12±2 hours every day for 30 days (1 month). Patients were then requested to return after 1 week and 1 month to evaluate their CCT, CV, and 6A measurment as well as asked for any subjective side effects and complication throughout the study. When measurement was taken, patients were also asked not to wear contact lenses, so the examiners were blinded throughout the study. Subjective side effect was evaluated from questionnaire by Cornea and Contact Lens Research Unit (CCLRU).<sup>13</sup>

Data analysis was performed with IBM SPSS version 20 for MacIntosh. CCT, CV, and 6A between group were analyzed using unpaired t-test or Mann Whitney test. Analysis of general linier model was also performed to compare CCT, CV, and 6A between follow up measurement for test within subject effect then continue with post hoc analysis.

**RESULTS**

Twenty eight patients were enrolled earlier in this study. Unfortunately, three patients were unable to complete the study, thus a total participant of 25 patients were enrolled.

During February 2015 through May 2015, a technical error occurred forcing us to use another specular microscope on eight patients. Therefore, those eight patients were also excluded to control measurement bias. A total of 17 patients (34 eyes) were analyzed and randomized into nelfilcon A group (group N; 8 patients; 16 eyes) and lotrafilcon B group (group L; 9 patients; 18 eyes). All patients completed the study, thus all patients were analyzed. The baseline characteristics are shown in Table 1. In this study, 76.47% subjects were female with mean age of subject was 22-24 years old. There were 64.7% subjects with positive history of contact lenses wear before and 52.9% was hydrogel contact lens wearers. Keratometry and SE data were comparable between two groups.

The CCT between both groups was not significantly different as shown in Table 2. There were pattern of a small increase CCT in 1 week follow up, then CCT decrease in 1 month to its initial baseline and even more. The CV and 6A between both groups was not significantly different (Table 3 and 4).

Figure 1A and 1B shows comparison CCT and CV values between baseline, 1 week, and 1 month of daily wear both contact lenses. Both CCT and CV values

**Table 2.** Comparison of CCT between groups

CCT (µm)	Mean/median±SD (µm)		
	Pre-fitting	1 week	1 month
Group N	538±41.88	559.87±43.20	521±43.22
Group L	517±30.87	535.33±35.37	520.16±29.37
p value	0.032 <sup>#</sup>	0.082 <sup>*</sup>	0.285 <sup>#</sup>

<sup>#</sup>Mann Whitney test; <sup>\*</sup>unpaired t-test

**Table 3.** Comparison of CV between groups

CV	Median±SD		
	Pre-fitting	1 week	1 month
Group N	39.62±6.07	39.75±5.05	36.87±5.85
Group L	43.83±7.89	43.44±7.24	37.88±4.77
p value*	0.089	0.092	0.587

\*unpaired t-test

**Table 4.** Comparison of 6A between groups

6A	Mean/median±SD		
	Pre-fitting	1 week	1 month
Group N	50.5±7.11	50.75±5.57	55.00±10.18
Group L	46.5±8.31	50.00±9.31	51.88±8.89
p value	0.396 <sup>#</sup>	0.775*	0.353*

<sup>#</sup>Mann Whitney test; \*unpaired t-test

displayed significant decrease after 1 month follow up ( $p=0.001$ ;  $p=0.001$  respectively). Figure 1C shows 6A values with the same comparison.

The 6A values displayed significant increase after 1 month follow up ( $p=0.022$ ).

## DISCUSSION

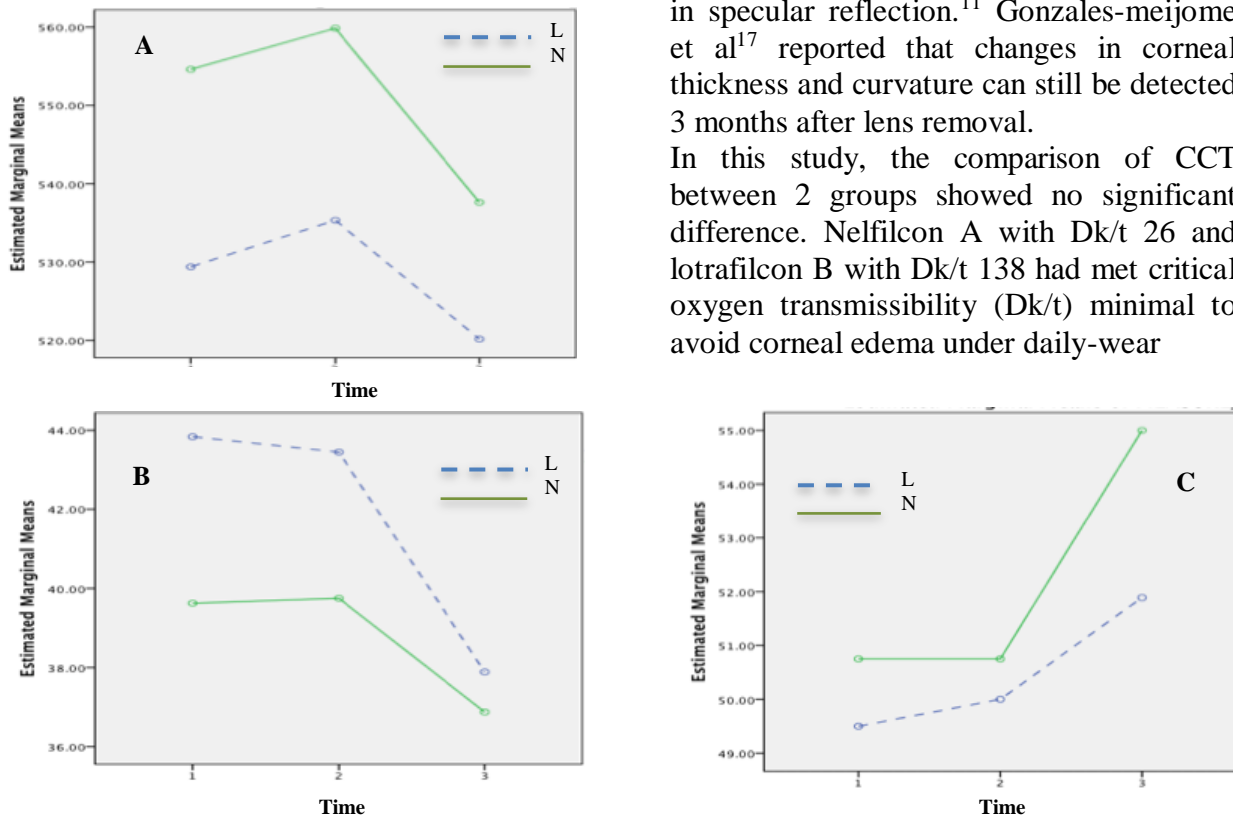
Since the introduction of soft contact lenses more than 3 decades ago, contact lenses technology has significantly improved. One of the key factors for health contact lens

wear is availability of adequate levels of oxygen. Contact lens influences corneal physiology in different ways, one of which is a change in corneal thickness and endothelial cell morphology.<sup>4,5,6</sup> Specular microscope is the current technique for evaluating endothelial morphology and is also reliable in measuring corneal thickness. Focusing on the endothelium, this machine provides specular images and gives the focal distance, which can be calculated as the corneal thickness.<sup>14</sup>

Baseline characteristics of this study showed 76.47% subjects were female and the median age of both groups are 22-24 years old. This is in line with multicenter study conducted in United Kingdom<sup>15</sup> and Malaysia<sup>16</sup> which showed that 64-70% contact lens wearers were female with median age of 20-29 years old. Unbalanced male to female ratio of contact lens wearers were found worldwide.

Among 64.7% subjects with history of contact lenses wear before, 52.9% of them was hydrogel contact lens wearers. History of wearing contact lenses could change the corneal thickness and morphologic appearance of the corneal endothelial cell layer as viewed in specular reflection.<sup>11</sup> Gonzales-meijome et al<sup>17</sup> reported that changes in corneal thickness and curvature can still be detected 3 months after lens removal.

In this study, the comparison of CCT between 2 groups showed no significant difference. Nelfilcon A with Dk/t 26 and lotrafilcon B with Dk/t 138 had met critical oxygen transmissibility (Dk/t) minimal to avoid corneal edema under daily-wear

**Fig 1.** Linear graphic of A) CCT; B) CV; and C) 6A

conditions which is 24.1.<sup>7</sup> Both transmissibility of nelfilcon A and lotrafilcon B were inadequate to induce significant changes of corneal thickness in daily wear. However, the change in CCT for both groups in 1 month daily wear showed significant decrease compared to baseline. This result is comparable to study by Doughty et al<sup>11</sup> that reported decreased CCT after re-fitting patient with silicon hydrogel lenses in patient with history of hydrogel lens wearers. This changes can be associated with improved oxygen availability and reduced hypoxia. Highly silicone hydrogel lenses have several advantages over low oxygen transmissible lenses. Many complications that develop from wearing lower Dk/t hydrogel lenses respond quickly when patient switch to higher Dk/t lenses.<sup>10,11</sup>

Majority of subjects showed pattern of a small increase CCT in 1 week follow up, then CCT decreases in 1 month. A study by Kaluzny et al<sup>18</sup> also showed the same result. Increased corneal thickness after 2 weeks of contact lens wear can be caused by a disturbance of endothelial pump activity by direct effect of hypoxia. The deterioration of CCT after 1 month shows that there is metabolic adaptation for the lower oxygen supply. Aerobic breakdown of glucose in the corneal cells shifts to the penthose phospate pathway under lens induced hypoxic conditions, which could produce an alternative source of cellular metabolic energy.<sup>18</sup>

Corneal thickness itself is reported by different studies to have increased or decreased during lens wear. Yeniad et al<sup>9</sup> reported decrease of central and inferior corneal thickness after continuous wear of silicon hydrogel lens in subjects with no history of contact lens wear before. Biochemical changes in the cornea and increased tear osmolarity have been reported to cause corneal thinning during contact lens wear. These increases indicate that silicon hydrogel may have an effect on corneal metabolism.<sup>9</sup>

CV and 6A between both groups were not significantly different also in this study. Changes in endothelial cell after hypoxia

related contact lens with continuous wear occurred after 6 months. One month of daily wear, possibly insufficient enough to induce endothelial polymethism and pleomorphism.<sup>5</sup> Esgin and Erda<sup>19</sup> reported significant changes in and percentage of 5-sided and 7-sided cell after 1 week of rigid gas permeable lenses with daily wear. Ratio of maximum/minimum endothel cell is a more sensitive indicator of endothelial damage or instability than the CV of cell size. The percentage of hexagonal cells making up the endothelial mosaic decreases in hard, soft, and extended wear contact lens wearers, and there is a compensatory increase in cells of other than six sides. Percentage of 5-sided and 7-sided cell are also more sensitive indicator to evaluate endothelial pleomorphism.<sup>19</sup>

On the other hand, there was significant decreased CV and increased 6A after 1 month daily wear compared to baseline for both groups. Doughty et al<sup>11</sup> found comparable result with this study. After 6 months of re-fitting with silicone hydrogel lenses in continuous wear, there were decreased CV and increased 6A. As described before, this condition possibly associated with reduced hypoxia and hypercapnia that alter the endothelial cells. Changes in corneal thickness (resolved of corneal edema) result in a reorganization of the corneal endothelium where value of CV and 6A return to its physiologic baseline thus improve endothelial cell morphology.<sup>10-12</sup>

Subjective side effect and complication were evaluated from score by Cornea and Contact Lens Research Unit (CCLRU). No patients complained of any complication, which is in line with other studies stated that nelfilcon A and lotrafilcon B are safe.

Limitation of this study were the unequal history of contact lens wear and short duration of follow up. A longer follow up for proper assessment of endothelial cell morphology was required because endothelial cell changes occur in 6 months. Also, there was technical error in specular microscope that forced us to further reduce our sample size. These issues needs to be further investigated in larger studies. Considering

all of the issues above, this study can be further used as a pilot study.

## CONCLUSION

There were no statistically differences in CCT, CV, and 6A between daily wear of nelfilcon A and lotrafilcon B. Subjects with history of contact lens wearers gained advantages in oxygen availability, which is decreased corneal thickness and improved endothelial cell morphology.

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