CLINICAL AND EXPERIMENTAL
OPTOMETRY

ORIGINAL PAPER

The ocular response to extended wear of a high Dk silicone hydrogel contact lens

Clin Exp Optom 2002; 85: 3: 176–182

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Purpose: A four-month extended wear clinical trial was conducted to compare the ocular effects of a high Dk Balafilcon A silicone hydrogel lens and a low Dk HEMA 38.6 per cent H_2O soft lens.
Method: Twenty-four subjects who were adapted to daily wear of soft lenses wore a high Dk lens in one eye and a low Dk HEMA lens in the other eye for four months on an extended wear basis after one week of daily wear. Thirteen progress evaluations were conducted using standard clinical procedures.
Results: Eighteen subjects (75 per cent) completed the study. The high Dk lens induced significantly less bulbar and limbal injection and corneal vascularisation than the low Dk HEMA lens ($p < 0.05$). Epithelial microcysts were observed only in the eyes wearing the low Dk lens. A significant increase in myopia was found in the eyes wearing the low Dk HEMA lens (mean = 0.50 D, $p < 0.01$) compared to the insignificant myopic increase of 0.06 D in the eyes wearing the high Dk lens. Three subjects developed small infiltrates in the high Dk lens wearing eyes and significantly more post-lens debris was observed under the high Dk lens. Six subjects developed papillary conjunctivitis in the eye wearing silicone hydrogel lenses but only two of those were discontinued from the study.
Conclusion: No hypoxia-related effects were observed with extended wear of the high Dk Balafilcon A silicone hydrogel lens.

Accepted for publication: 4 April 2002

Key words: corneal swelling, epithelial microcysts, limbal injection, myopic shift, silicone/hydrogel soft lens, vascularisation

The short- and long-term effects of soft lens extended wear on the eye have been well documented.[1,12] While soft hydrogel contact lenses are generally comfortable and in most cases the lens of choice, the limitation for extended wear of all current hydrogels is their oxygen transmissibility.

As a follow-up to experiments that measured corneal swelling in response to wearing soft lenses under extended wear conditions,[13] Holden and Mertz[14] established that the critical oxygen transmissibility of a soft lens should be $87.0 \pm 3.3 \times 10^{-9}$ (cm x ml O_2)/(sec x ml x mm Hg) to avoid overnight lens induced corneal swelling.

All layers of the cornea are affected by prolonged extended wear of hydrogel lenses and while some of these effects may be minor, compromised epithelial integrity represents a potentially serious consequence, which can result in ulcerative keratitis. Some authors[15,16] believe that if oxygen transmissibility of the lens is high enough, epithelial health will not be compromised during extended wear and consequently the risk of serious adverse events is reduced. Although a cause and effect relationship between hypoxia and corneal infection has not been established, oxygen deprivation has been shown to cause epithelial microcysts,[13] loss of hemidesmosomes,[17] epithelial thinning,[6] reduced epithelial oxygen consumption[6] and increased superficial cell size of the epithelium.[18] Thus the compromised protective epithelial barrier may be an important factor in the pathogenesis of corneal infection associated with extended

	High DK eye mean ± SD	Low DK eye mean ± SD
Corneal astigmatism (D)	-0.81 ± 0.41	-0.83 ± 0.48
Refractive sphere (D)	-2.76 ± 0.89	-2.69 ± 0.76
Refractive cylinder (D)	-0.34 ± 0.23	-0.38 ± 0.30

Table 1. Ocular parameters

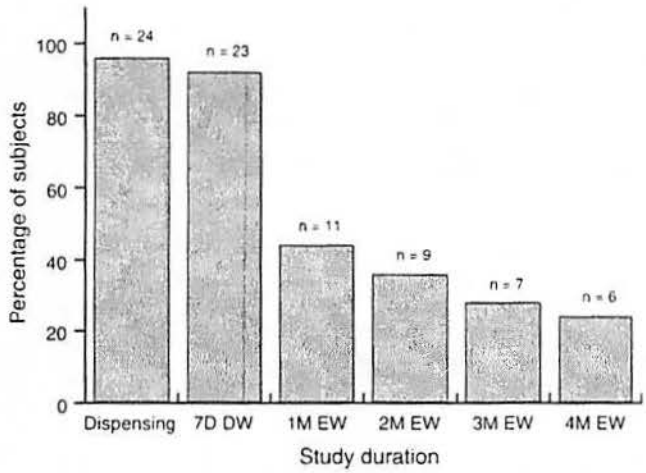

Figure 1. The percentage and number of subjects (by visit) that were able to maintain the required wearing schedule of extended wear without interruption as a function of study duration

wear of hydrogel lenses.[6,19]

Extended wear of rigid gas permeable (RGP) lenses produces unique complications[7,20-22] that appear to be unrelated to hypoxia. High Dk RGPs (Dk > 100 x 10^{-11}) have been available for years and corneal infection with this modality has been a rarity. RGP lenses are also rarely used for extended wear, probably because they are relatively more uncomfortable than soft lenses.[23]

The measurement of corneal swelling in response to wearing a contact lens can be used as an index of the oxygen transmissibility of the lens. An overnight corneal swelling study[24] was conducted on 20 adapted soft lens wearers to compare the corneal swelling response of a high Dk Balafilcon A silicone hydrogel lens (Dk/T = 110 x 10^{-9}) in one eye to Lidofilcon A 70 per cent H_2O (Dk/T = 22 x 10^{-9}) worn in the other eye. Corneal swelling induced by the Balafilcon A silicone hydrogel was 2.8 per cent compared to 8.2 per cent induced by the Lidofilcon A lens. In another similar experiment[25] conducted on unadapted subjects, the corneal swelling response to wearing high DK Lotrafilcon A silicone hydrogel lenses was 2.7 ± 1.4 per cent compared to 8.7 ± 2.3 per cent induced by Etafilcon A soft lenses. These studies clearly demonstrated that very little or no corneal swelling from overnight wear can be attributed to the high DK lenses as overnight eye closure without lens wear will produce about the same amount of swelling.[25-28]

The availability of this highly oxygen permeable Balafilcon A lens prompted a short-term study, the aim being to test the clinical/physiological response of this lens over a four-month period. The performance of Balafilcon A (which was in experimental development at the time of this study) was compared to a low water content thin HEMA lens in the contralateral eye. Since that time, a number of design changes and surface modifications to the Balafilcon A silicone hydrogel lens have been made by the manufacturer (Bausch & Lomb).

METHODS

Study design

The study was a four-month randomised, double masked clinical trial. Subjects wore the high Dk (99 x 10^{-11}) Balafilcon A silicone hydrogel 35 per cent water content lens of centre thickness 0.09 mm (Dk/T = 110 x 10^{-9}) in one eye and a low Dk HEMA Optima FW (8.5 x 10^{-11}) 38.6 per cent water content lens of centre thickness 0.035 mm (Dk/T = 24.3 x 10^{-9}) on the contralateral eye. The diameter of each lens is 14.0 mm.

Prior to subject enrolment, the study was approved by the committee on human ethics at the University of Waterloo. After obtaining informed consent from the subjects, the lenses were dispensed to be worn on a daily wear basis for one week, followed by four weeks of seven day extended wear (EW) periods. At the dispensing visit, the Optima FW and the Balafilcon A lenses were randomly assigned to each eye and it was stressed that the assignment had to remain for the duration of the study. During this first four-week extended phase, the subjects removed both lenses on the seventh night. The Balfilcon A lens was disinfected overnight and reinserted the next morning. A new Optima FW lens was inserted the next morning.

From the sixth week, the subjects were required to continue to remove and dispose of the low Dk Optima FW (control) lenses on the seventh night of extended wear and to reinsert a new lens the next morning. On the 28th night (that is, four weeks of continuous wear), the Balafilcon A lens was removed and a new lens was

Visit	Post lens debris grade	High DK soft lens n (%)	Low DK hema lens n (%)	Mann-Whitney p value
7-day 43	Grade 0	13 (62)	16 (84)	
	1	5 (24)	3 (16)	
	2	3 (14)	0 (0)	
	3	0 (0)	0 (0)	p = 0.09
8-day 50	Grade 0	14 (64)	19 (95)	
	1	5 (23)	1 (5)	
	2	2 (9)	0 (0)	
	3	1 (14)	0 (0)	p = 0.01
9-day 64	Grade 0	10 (50)	16 (89)	
	1	5 (25)	2 (11)	
	2	5 (25)	0 (0)	
	3	0(0)	0 (0)	p = 0.02
10-day 78	Grade 0	10 (50)	15 (83)	
	1	5 (25)	3 (17)	
	2	5 (25)	0 (0)	
	3	0 (0)	0 (0)	p = 0.02
11-day 92	Grade 0	9 (60)	11 (79)	
	1	5 (33)	3 (21)	
	2	1 (7)	0 (0)	
	3	0 (0)	0 (0)	p = 0.26
12-day106	Grade 0	8 (47)	13 (87)	
	1	8 (47)	2 (13)	
	2	1 (6)	0 (0)	
	3	0 (0)	0 (0)	p = 0.02
13-day120	Grade 0	10 (53)	14 (82)	
	1	3 (16)	2 (12)	
	2	5 (26)	1 (6)	
	3	1 (5)	0 (0)	p = 0.04

Table 2. Post lens debris grading

reinserted the next morning. Progress evaluations were conducted every week for the first eight weeks and every second week for the final 10 weeks. It was deemed to be unnecessary to conduct progress evaluations on a weekly basis after eight weeks of observation.

During the daily wear phase and the four weeks EW for Balafilcon A and for periods of unscheduled removal, the lenses were stored and disinfected in Bausch & Lomb Renu™ Multi-Purpose solution. Bausch & Lomb Multi-Purpose rewetting drops were used when subjects experienced dryness.

The baseline visit and 13 progress evaluations were conducted by a single observer (KM) using standard clinical procedures; this was invariably done during the morning. Prior to lens removal at each progress evaluation, high and low contrast visual acuity were measured following over-refraction and the subjects recorded their comfort and vision scores using visual analogue scales. The presence of post-lens debris was graded on a scale of zero (no debris) to three (excessive debris). Lens surface deposits and wettability were also graded (*in vivo*) on a zero to three scale. Lens centration and movement were measured using an eye piece reticle in a Rodenstock slitlamp. After lens removal, biomicroscopy was performed, which included an assessment of bulbar and limbal injection, corneal oedema, epithelial microcysts, corneal and conjunctival staining and tarsal plate characteristics, all of which were graded on a zero to three scale and the presence of adverse reactions was recorded. Automated refractive and keratometric measurements were recorded at the end of each month (five measures including baseline).

Subjects

All subjects were adapted daily soft lens wearers without ocular complications. Three males and 21 females were enrolled with a mean age of 21 ± 5 years. Although the female to male ratio was highly skewed, it is usual that more females wear contact lenses than males. The participants ocular parameters are listed in Table 1.

RESULTS

Eighteen of the 24 subjects (75 per cent) completed the four-month extended wear study. The reasons for premature discontinuation of the six subjects were: one subject found the study inconvenient, another experienced bilateral discomfort and dryness, one subject developed corneal infiltrates on repeated occasions, two subjects had tarsal conjunctival papillae in the high Dk wearing eyes and one had high levels of corneal staining in the high Dk wearing eye during the daily wear phase.

Figure 1 is a frequency histogram that shows the interruption to the scheduled extended wear protocol. Six of the 23 subjects (26 per cent) who progressed from the daily wear phase to extended wear completed the study without interruption to the specified wearing schedule of weekly EW with the Optima FW lens and monthly

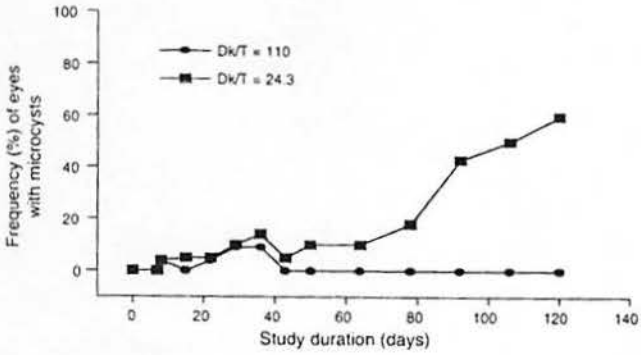

Figure 2. The percentage of eyes that developed epithelial microcysts after one month of extended wear

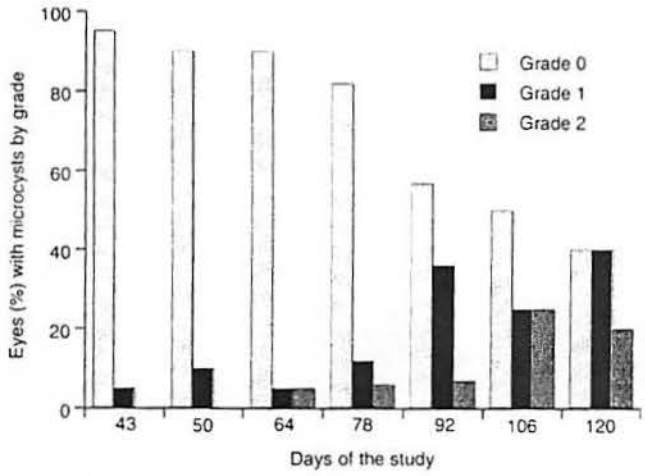

Figure 3. The percentage of eyes that developed epithelial microcysts of either grade 1 or grade 2 over the four-month study duration

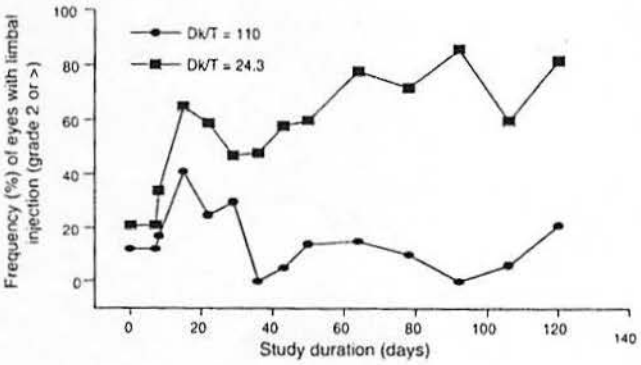

Figure 4. The percentage of eyes that developed limbal injection of grade 2 or greater

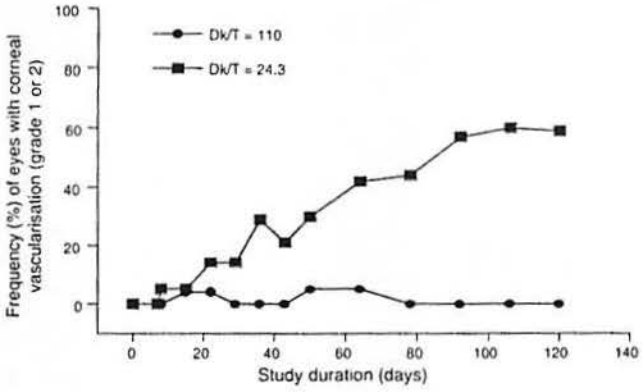

Figure 5. The percentage of eyes that developed corneal vascularisation of grade 1 or grade 2

(28 days) EW with the Balafilcon A lens. The largest number of interruptions occurred between the initiation and completion of the first month of seven day extended wear periods. Eleven subjects (46 per cent) were able to complete the first month of the extended wear section of the study without interruption (that is, without temporary removal of lenses or the development of significant biomicroscopic findings). The temporary removals were predominantly for cleaning or rewetting of either or both lenses for the relief of minor discomfort or dryness during the day. This analysis includes the six subjects who were permanently discontinued from the study.

High and low contrast visual acuity, subjective comfort and vision, lens centration and movement, *in vivo* lens surface deposits and wettability revealed no significant differences between the eyes wearing the Balafilcon A lens and those wearing the Optima FW lens.

Table 2 summarises the results of the seven visits when the subjects began extended wear of the high Dk lens for the one-month periods but continued with the low Dk lens for the seven day extended wear periods. This table shows that there was significantly more debris entrapment beneath the high Dk lens with the exception of the 11th visit.

	High Dk soft lens mean ± SD	Low Dk hema lens mean ± SD
Myopia (D) baseline	-2.76 ± 0.89	-2.69 ± 0.76
4 months	-2.82 ± 0.80	-3.19 ± 1.00
Difference	0.06 (increase)	0.50 (increase)
Keratometry (D) baseline	43.96 ±1.26	43.88 ±1.27
4 months	44.01 ±1.22	44.16 ±1.23
Difference	0.05 (steeper)	0.28 (steeper)

Table 3. Refractive and keratometric results

Figures 2, 4 and 5 illustrate those slitlamp biomicroscopy signs, where statistically significant differences were found between the high Dk and low Dk soft lenses. The formation of epithelial microcysts (which usually develop after four to six weeks of extended wear[29]) was observed only in the eyes wearing the low Dk HEMA Optima FW lens as illustrated in Figure 2. Figure 3 clearly shows the frequency of grade 1 and grade 2 microcysts increasing over time in the low Dk Optima FW lens wearing eyes. Figures 4 and 5 show a significantly greater percentage of subjects exhibiting grade 2 or greater limbal hyperaemia and grade 1 or grade 2 corneal vascularisation with the low Dk HEMA lens than the high Dk silicone hydrogel lens (Mann-Whitney $p < 0.01$). Bulbar hyperaemia results were less consistent. The low Dk lens was responsible for significantly greater bulbar hyperaemia ($p < 0.05$) at only four of the extended wear progress evaluations.

Table 3 summarises the refractive and keratometric data from the study and shows a significant increase in myopia of 0.50 D from baseline in the eyes wearing the low Dk lenses (paired t-test $p < 0.01$) compared to the insignificant myopic increase of 0.06 D in the high Dk silicone hydrogel lens wearing eyes. Keratometry of the low Dk wearing eyes showed significant steepening of the mean of the two corneal meridians by 0.28 D (paired t-test, $p < 0.0001$) but insignificant steepening (0.05 D) of the corneas wearing the high Dk lenses.

Corneal oedema in the form of vertical striae was observed only in the eyes of four subjects wearing the low Dk lenses. One of these subjects, who presented with multiple striae, was switched from wearing the low Dk lens to wearing high Dk in both eyes after the second extended wear progress evaluation.

Three subjects developed small non-staining corneal infiltrates in the eye wearing the high Dk lens. Two of these subjects (CH and MB) resumed extended wear after resolution of the infiltrates and continued to complete the study without further complication. LB presented with multiple central infiltrates that took four weeks to resolve and after a recurrence of three small non-staining peripheral corneal infiltrates in the same eye wearing the high Dk silicone hydrogel lens, was discontinued from the study. Six subjects developed grade 3 localised papillary conjunctivitis in zones 1, 2 or 3 in the high Dk wearing eyes. Two of these subjects were permanently discontinued. During the daily wear phase, diffuse peripheral punctate corneal staining at the grade 2 and grade 3 level occurred with the silicone hydrogel lenses in six eyes compared with grade 2 in only one eye that wore Optima FW.

DISCUSSION

During the clinical trial, corneal striae were observed on various occasions in four subjects but the striae manifested only in eyes wearing the low Dk Optima FW lenses. Obviously, this is a result of excessive overnight corneal oedema[30] and the inability of the cornea to deswell sufficiently during the day, while wearing the low Dk Hema lenses.

Another useful index of chronic lens-induced hypoxia is the presence of epithelial microcysts and this is clearly demonstrated in the low Dk Optima FW lens wearing eyes after approximately two months of extended wear.[31,32] Figure 3 shows the percentage of eyes with microcysts and the severity increasing with the period of wear. Epithelial microcysts were not observed in the high Dk silicone/hydrogel lens wearing eyes over the same period, which is an indication that these lenses transmitted sufficient oxygen to avoid this chronic response.

One of the most noticeable findings in this study was the degree of limbal hyperaemia induced by the low Dk Optima FW lens compared to the relatively insignificant amount from the high Dk silicone hydrogel lens. Only limbal hyperaemia of grade 2 or greater is represented in Figure 4. The plots of vascularisation in Figure 5 show similar differences. While there may be multiple causes of limbal vascular engorgement with soft lenses, such as the occlusive effect of the lens, lack of tear exchange and compression of the conjuctival vessels by the edge of the lens, we suggest that the relative difference of limbal injection and vascularisation was due to the difference in oxygen transmission. Others have made similar observations and support this hypothesis.[33-36]

Another very interesting feature of this study was the small but significant increase

in myopia of the eyes wearing low Dk HEMA lenses. The myopic 'shift' that has been associated with soft lens wear was reported many years ago by a number of investigators[37,41] and they all found corneal steepening in association with the increase of myopia. During the period of those reports (1970s), most of the soft lenses were thick with low water content and low oxygen transmissibility.

The increase in myopia in the eyes wearing low Dk lenses in this study are suggestive of a hypoxic aetiology because the eyes that were wearing high Dk silicone/hydrogel lenses did not become more myopic. Dumbleton and colleagues[41] showed an identical result comparing high and low Dk soft lenses. However, a mechanical or moulding effect by the low Dk lenses cannot be ruled out because of the associated steepening of corneal curvature. These corneas may have been more susceptible to moulding by the lens because the low Dk lenses induced more oedema.

The cause of the infiltrates in the eyes wearing the high Dk lens cannot be explained but there does not appear to be a link with hypoxia. Mertz and Holden[42] suggested that this inflammatory condition is associated with the entrapment of debris, exfoliated cells and their toxic by-products from overnight soft lens wear. Others[43,44] have demonstrated that bacteria harvested from lenses may be responsible for adverse reactions. In our study, the presence of debris including bacteria could have been a factor because of the consistently greater presence of debris observed under the high Dk lenses. The design changes that have been made to these silicone/hydrogel lenses since this study was conducted may reduce post-lens debris. The fact that these infiltrates developed only in the eyes wearing high Dk lenses may not be significant because of the small sample size of this study. In fact, the multiple central infiltrates that were observed in subject (LB) are uncharacteristic of soft lens related infiltrates. These are more likely to appear at the corneal periphery. Much larger clinical trials and retrospective analyses need to be conducted to determine whether the incidence of adverse responses is greater with high DK silicone hydrogel lenses worn under extended wear conditions.

The cases of papillary conjunctivitis in the eyes wearing high Dk silicone hydrogel lenses were attributed to the lens design causing mechanical trauma to the palpebral conjunctiva. The lenses of these subjects were sectioned and the edges were found to be thicker than would customarily be designed for a soft lens. As mentioned, the lens design of Balafilcon A has been altered from the prototype that was used in our study.

In conclusion, the results of this prospective study showed that high Dk silicone hydrogel lenses were worn successfully for up to 30 nights without removal and have essentially eliminated the hypoxic complications that have been common features of extended wear of soft lenses. However, adverse responses do occur and these effects may be related to design, modulus and surface properties of the lenses.

ACKNOWLEDGEMENTS

This study was funded by Bausch & Lomb, Rochester, New York.

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