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Tear levels of Transforming Growth Factor-β1 and Interleukin 1-β, and clinical correlations in new contact lens users

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ABSTRACT

Purpose: To assess alterations in the tear Transforming Growth Factor (TGF)-β1 and Interleukin (IL1)-β concentration in new contact lens wearers; and explore correlations with tear film stability, and ocular physiological response.

Methods: In this clinical setting, 12 neophytes (5 males), with an average age of 24.0 ± 5.0 years were fitted with delefilcon A contact lenses. Physiological responses (bulbar and limbal hyperemia), Pre-corneal (NIBUT), Pre-lens (PL-NIBUT) non-Invasive Break-Up Times, and tear samples were collected in the morning (before lens insertion; 9 – 10 a.m.) and afternoon (before lens removal; 7 – 8p.m.) of the same day. NIBUT and PL-NIBUT were measured using a tearscope. Tear samples were assayed for TGF-β1 and IL1-β concentrations using Enzyme-Linked Immunosorbent Assay kits. An 11-members control group (6 males) aged 25.0 ± 5.0, served to assess biomarker levels in non-contact lens wearers' tears.

Results: Subjects wore lenses for an average of 7 h and 20 min (range: 6 to 9 h). Bulbar and limbal hyperemia increased significantly throughout the day ($p < 0.001$). PL-NIBUT were lower than NIBUT (4.7 ± 2.0 Vs. 12.2 ± 8.8 s; $p < 0.001$). The IL1-β levels were higher in neophytes than controls (3.2 ± 4.7 Vs. 0.1 ± 0.1 pg/ml; $p = 0.05$), correlating significantly with bulbar ($r = 0.405$, $p = 0.008$) and limbal hyperemia ($r = 0.499$, $p = 0.027$). No substantial changes were reported for TGF-β1.

Conclusion: The presence of TGF-β1 in tears does not appear significantly affected by lens wear. The association between physiological parameters and IL1-β levels suggests that lenses may disrupt ocular surface homeostasis by altering cytokine regulatory mechanisms. However, due to its low concentration, IL1-β's role in the subclinical inflammatory response to lens wear is limited.

1. Introduction

The tear film plays an essential role in ocular physiology by maintaining the integrity and functionality of the anterior eye surface. In addition to enhanced lubrication, which allows a smooth interaction between the tarsal conjunctiva and cornea, the tear film preserves an transparent surface between the air and the eye [1]. This dynamic structure, consists of a hydrated mucus layer between the lipid outer cover and the glycocalyx that lines the corneal epithelium [2]. The stability of the film depends not only on the production and distribution of tears by the lacrimal functional unit but also on the appropriate secretion of its components [3]. The frequency and completeness of the blinks allow for proper dispersion and turnover of the film [4]. Apart from environmental factors, the pre-corneal tear film stability varies throughout the day, decreasing in the early morning [5]and at the end of the day [5–6] This variability may also depend on the individual's tear components and anatomical features [5].

Tear components, including enzymes, glycoproteins, and immunoglobulins, are dissolved in the aqueous layer, thereby protecting the ocular surface against foreign bodies and invading microorganisms [7]. The ocular inflammatory response is tightly controlled by endogenous mechanisms that preserve the immune privilege of the cornea. Among these, microanatomic characteristics, immunosuppressive soluble factors and molecules expressed at the surface of the cells are responsible for retaining the effects of acute inflammatory events on the integrity and transparency of the tissue [8–9]. Transforming Growth Factor-β1 (TGF-β1) is a multifactorial cytokine produced by the lacrimal gland, [10] conjunctival, and corneal epithelium [11]. It is involved in wound

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healing by controlling cellular proliferation and differentiation [12–13] and acting as an immune system regulator, inhibiting cell growth and the expression of inflammatory cytokines [14]. TGF-β1 is known to be increased in pathological conditions, such as Dry Eye Disease (DED) [14–15]. The presence of a contact lens (CL) can disturb ocular surface homeostasis and induce the secretion of several cytokines by the corneal epithelium through activation of the Interleukin-1R-associated kinase (IRAK) pathway [9]. Interleukin 1-β (IL1-β) is a potent mediator of inflammation and, among other functions, contributes to signaling the downstream release of other cytokines (IL-6 and IL-8) to prolong the tissue's inflammatory condition [16]. The cytokine is known to trigger matrix metalloproteinase (MMP) enzymes in corneal stromal cells, [17] boost the centripetal movement of Langerhans cells, [8] regulate keratinocyte apoptosis, and recover by increasing keratinocyte growth factor (KGF) production [18].

CL wear has been described as eliciting a subclinical inflammatory response [19–20] and the effect of using these devices on tear biomarkers has been discussed previously [21]. Meanwhile, the existing scientific evidence in this context is not very strong, [19–20,22–28] and more studies are needed to understand the interaction of these materials with the ocular surface. Therefore, this study aims to (i) determine changes in tear concentrations of TGF-β1 and IL1-β in new CL wearers over the course of a day and (ii) assess potential correlations between these findings, tear film stability, and ocular vascular response.

2. Materials and methods

2.1. Study characterization

This research is comprised of both clinical and laboratory component. The study protocol received approval from the Ethics Committee of the University of Minho for Life and Health Sciences and followed the principles of the Declaration of Helsinki [29]. Participants provided signed informed consent after a clear explanation of all the procedures. Twenty-three subjects took part in the study, divided into two groups. Of these, 12 were fitted with delefilcon A CL for the first time, forming the neophyte group. The remaining eleven were included in the control group. Table 1 provides descriptions of the CL used in the study.

Candidates were selected following a refractive and slit-lamp examination. The inclusion criteria were no prior previous CL wear, absence of dry eye symptoms, no active ocular infection or inflammation, no allergies, clear ocular media, absence of systemic diseases, no use of ocular or systemic medication within 12 weeks before and during the trial, and no history of eye surgeries. Additionally, participants age was between 18 and 40 years old and had a correctable vision of at least 08/10 or better in each eye.

At the second appointment, CL were fitted for all neophyte participants, ensuring adequate lens centration and movement in all the eyes: The CL sat symmetrically to the cornea center, moving between 0.2 and 0.4 mm after blinking. Clinical assessments and tear collection were conducted in the morning (prior to lens insertion; 9–10 a.m.) and afternoon (prior to lens removal; 7–8p.m.) on the same day, with an average wearing time of 7:20 h. Tear collection for the control group followed the same schedule.

Table 1
Characteristics of the contact lens used in the study.

USAN	**Delefilcon A**
Company	Alcon Vision Care
FDA Group	V
EWC, %	33–80
DK/t (−3 D), Barrer	156
Main monomers	Si-Hy; DPMC

USAN: United States adopted name; **FDA**: Food and Drugs Administration; **EWC**: Equilibrium Water Content; **DK/t**: Oxygen transmissibility (units: X 10-9 (cm/s) (ml O2/ml.mm Hg)); **DMPC**: phosphatidylcholine; **Si-Hy**: silicone hydrogel; Data collected from manufacturers and FDA reports.

2.2. Clinical outcomes

The parameters assessed comprised measurements of tear stability and the quantification of physiological responses. The procedures are described in detail below.

2.3. Tear stability measurements

The tear stability was assessed using a tearscope (Keeler Instruments Ltd, Windsor, UK), which measures the noninvasive break-up time (NIBUT), indicating when tear film rupture occurs [30]. The tearscope, equipped with a chronometer and several filters, was connected to a slit lamp for observations at 16-x magnification.

A mesh filter was projected onto the corneal surface, and participants were instructed to blink and keep their eyes fixed until any change in the reflected pattern was observed. This process was repeated three times for each eye and recorded using a video camera for subsequent analysis. After data collection, an independent investigator analyzed the recordings randomly to determine tear break-up time in seconds (s), calculated as the interval between the last blink and the first appearance of a break or disruption in the film.

The average of the three measurements was calculated to increase reliability. Assessments were performed in the morning on the precorneal surface (NIBUT) and in the afternoon with the lens *in situ* – Pre-Lens (PL-NIBUT). The room temperature varied between 18 and 20 °C, and the average humidity was 57 % during the procedures.

2.4. Physiological responses

Physiological responses were rated using the Cornea and Contact Lens Research Unit (CCLRU) grading scale (CCLRU, Sydney, Australia), [31] which comprises a series of photographic images that allow the classification of various ocular conditions. Bulbar and limbal hyperemia were quantified based on the observations recorded on a numerical scale: 1 (very slight), 2 (slight), 3 (moderate), and 4 (severe), as recommended by the CCLRU.

A digital camera was attached to the slit lamp observation system to capture eye images under consistent illumination and magnification conditions. Images of both eyes were taken considering the four quadrants (nasal, temporal, superior, and inferior) for subsequent classification with assessments conducted randomly. The scale was decimalized to increase its sensitivity for detecting clinically significant changes.

2.5. Tear samples collection and storage

Tear samples were collected from the inferior temporal tear meniscus of the eyes by using capillary tubes (Drummond Scientific Co., Philadelphia, USA). Corneal anesthetics were not administered, and precautions were taken to prevent contact with the corneal surface. Reflex tearing was controlled to avoid dilution effects by determining the tear fluid flow in the capillary, which corresponds to the ratio between the tear sample volume and the collection time (in minutes). Only samples below 3 μL /min were admitted for analysis [22]. After collection, all tear samples were stored in a refrigerator at −80 °C.

2.6. Laboratory analysis

Tear samples were assayed for TGF-β1 and IL1-β using commercially available enzyme-linked immunosorbent assay (ELISA) kits (*Invitrogen*, Waltham, USA). This technique represents an easy-to-perform and cost-effective method for measuring the concentration of a molecule in a sample [32]. The tear samples were processed by transferring them to Eppendorf tubes and centrifuging to remove debris. For ELISA, samples

were prepared and analyzed according to the manufacturer's protocols. The accurate biomarker concentration was calculated based on the corresponding standard curves after spectrophotometry analysis at 450 and 570 nm. The limits of detection were 0.1 ng/mL and 0.1 pg/mL for TGF-β1 and IL1-β, respectively. The detection rates were calculated for each biomarker corresponding to the percentage of samples that contained the molecule relative to the total number of analyzed samples.

2.7. Statistical analysis

The sample size was calculated using the Massachusetts General Hospital Biostatistics online freeware (available at https://hedwig.mgh.harvard.edu/sample_size/size.html). A sample size of twenty-four subjects, twelve in each group, was sufficient to detect a difference of 10.0 ± 8.0 pg/mL in IL1-β concentration between groups using a two-tailed *t*-test of difference between means with 80 % power and a 0.05 level of significance. The discrepancy was relevant after previous studies analysis in which the concentration of the molecule was determined in groups of CL wearers and non-wearers [23,25].

Statistical analysis was performed using Statistical Package for Social Sciences version 23 (*SPSS Inc*., Chicago, USA). The normality of the data distribution was evaluated using the *Shapiro–Wilk* test. Bulbar ($p = 0.062$, Shapiro–Wilk) and limbal ($p = 0.498$, Shapiro–Wilk) hyperemia were normally distributed, and morning and afternoon scores were compared using parametric paired t-tests. The NIBUT ($p < 0.001$, *Shapiro–Wilk*) and PL-NIBUT ($p < 0.001$, *Shapiro–Wilk*) IL1-β and TGF-β concentrations ($p < 0.001$, *Shapiro–Wilk*) were analyzed using nonparametric tests because the data were not normally distributed. *Wilcoxon* signed-rank test was used to compare the variables between morning and afternoon. Group comparisons were performed using the *Mann–Whitney U* test. Correlations between quantities were established using the *Pearson* coefficient for normally distributed data or *Spearman* if normality principles were not verified.

3. Results

3.1. Sample characterization

The neophyte group comprised 12 individuals (5 males), with an average age of 24.0 ± 5.0 years and a mean refraction of −0.8 ± 1.4 Diopters (D). In comparison, the control group included 11 subjects (6 males), with an average age of 25.0 ± 5.0 and refraction of −0.9 ± 2.1 D.

3.2. Tear stability assessment

The results for the NIBUT and PL-NIBUT are presented in Table 2.

Overall, NIBUT was greater than PL-NIBUT ($p < 0.001$, Wilcoxon) and had a higher standard deviation. No significant correlation was found between the two variables ($p = 0.372$; *Spearman*).

3.3. Physiological responses quantification

Table 3 provides a description of the physiological responses.

Both bulbar and limbal hyperemia increased after the CL wearing period ($p < 0.001$, *independent t-test*). When detailing the analysis for each quadrant, bulbar hyperemia registered a significant increase in the nasal (1.9 ± 0.5 Vs 2.1 ± 0.5, $p = 0.019$, *paired t-test*), temporal (1.9 ± 0.5 Vs 2.1 ± 0.4, $p = 0.007$, *paired t-test*) and inferior quadrants (1.6 ± 0.5 Vs 2.0 ± 0.4, $p < 0.001$, *paired t-test*). The results for limbal hyperemia revealed a substantial variation in the nasal (1.6 ± 0.5 Vs 2.0 ± 0.6, $p = 0.008$, *paired t-test*), superior (1.5 ± 0.5 Vs 1.8 ± 0.6, $p = 0.016$, *paired t-test*), and inferior quadrants (1.2 ± 0.2 Vs 1.9 ± 0.6, $p < 0.001$, *paired t-test*). Therefore, the most meaningful changes were observed in the inferior ocular region (Fig. 1).

Table 2
Descriptive statistics of the neophytes pre-corneal (NIBUT) and pre-lens (PL-NIBUT) Non-Invasive Break-Up Times (n = 12).

	Minimum	Maximum	Median	Mean	Standard deviation
NIBUT (s)	5.6	38.1	9.1	12.2	8.8
PL-NIBUT (s)	2.4	9.5	4.2	4.7	2.0

Table 3
Mean scores and standard deviation (SD) for the bulbar and limbal hyperemia registered in the morning and afternoon for the neophyte's group (n = 12).

	Morning (Mean ± SD)	Afternoon (Mean ± SD)	P
Bulbar hyperemia	1.8 ± 0.4	2.1 ± 0.3	**<0.001**
Limbal hyperemia	1.4 ± 0.3	1.8 ± 0.4	**<0.001**

3.4. Laboratory analysis

The average tear fluid flow was 0.7 ± 0.5 μL/min and 0.8 ± 0.4 μL/min for the control and neophyte groups, respectively. No differences were found between the morning and afternoon assessments ($p > 0.05$). Fig. 2 shows both groups' TGF-β1 concentration at the two time points of the day, respectively.

TGF-β1 was detected in 10 of the 42 analyzed samples. Six were in the tested group, and the others (4) were controls. The median TGF-β1 levels were zero for both neophytes and controls, regardless of the time of day – Fig. 2. Table 4 details each participants' IL1-β concentration in the morning and afternoon.

No statistically significant differences were found for IL1-β between the time points. Molecule detection in the neophyte samples was higher in the morning (80 %) than in the afternoon (58 %). Seven samples reported a concentration of 0 pg/ml: two in the morning and 5 in the afternoon. The control group registered similar detection rates (30 %) in both periods, with six samples (three in each group) out of 20 reporting the biomarker's presence– Table 4. Fig. 3 presents the changes in IL1-β levels between the two time points in both groups.

No significant differences were observed in the morning between neophytes and controls in IL-1β levels ($p > 0.05$). However, in the afternoon, a significant increase was noted in neophytes compared to controls ($p = 0.05$, *Mann-Whitney U*) – Fig. 3.

3.5. Correlations between measured parameters

The IL1-β levels were correlated with clinical outcomes, taking into account the time of the day (Tables 5 and 6).

Bulbar and limbal hyperemia exhibited strong correlations in both

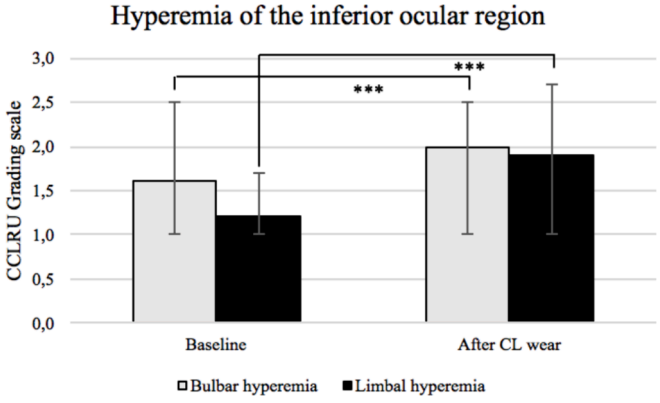


Fig. 1. Graphical representation of the inferior bulbar and limbal hyperemia for the neophyte group.

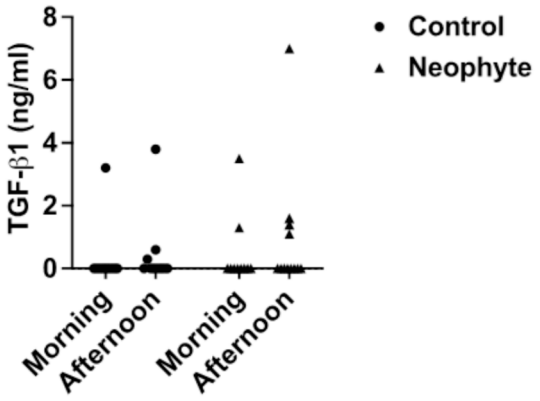


Fig. 2. Scatter-plot representing the TGF-β1 concentration for neophytes and controls in the morning and afternoon assessments.

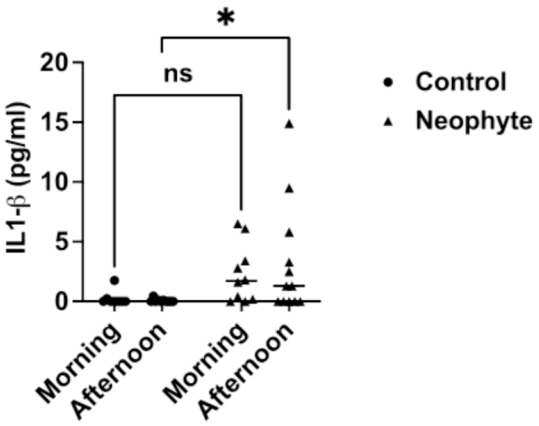


Fig. 3. Scatter-plot representing the IL1-β concentration for neophytes and controls in the morning and afternoon assessments *p = 0.05. ns: non-statically difference.

the morning ($p < 0.001$, *Pearson*) and afternoon ($p < 0.001$, *Pearson*). Additionally, moderate correlations were observed between IL1-β levels and bulbar ($p = 0.008$, *Pearson*), as well as limbal ($p = 0.027$, *Pearson*) hyperemia, but only in the morning (Fig. 4).

4. Discussion

In this pilot clinical study, 12 subjects were fitted with delefilcon A CL for the first time, and their progress was monitored throughout the day of wear. Primary clinical metrics, including tear stability measures (NIBUT and PL-NIBUT), ocular physiology response (bulbar and limbal hyperemia), and detection of tear biomarkers (TGF-β1 and IL1-β), were evaluated.

Tear stability was assessed using a tearscope for NIBUT interpretation, providing a non-invasive method that does not interfere with the film properties and is considered more repeatable than TBUT (with fluorescein) and corneal topography systems [33]. Several authors used the same equipment to measure tear stability and obtained values between 2.7 and 53.8 s in 160 healthy volunteers aged 20 to 29 years [1,4–5,33–35]. In the present study, NIBUT was within the defined range, with a registered median of 9.1 s (5.6 to 38.1) seconds – Table 2. This form of variability may be attributed to intersubject changes in tear components and their secretion rates [5]. When a CL is inserted in the eye, the POTF is divided into pre- and post-lens portions [36]. The pre-lens tear film is thinner and more unstable than the POTF due to the reduction of the aqueous phase and lipid contamination [36–37]. Consequently, it is expected that the tear film will break up sooner over the lens than on the cornea surface resulting in a lower PL-NIBUT than NIBUT (PL-NIBUT 4.7 ± 2.0 vs. NIBUT 12.2 ± 8.8 s, $p < 0.001$, Table 2). These results were confirmed by other studies that applied different methodologies, such as videokeratoscopy, [38–41] corneal topography, [42–46] interferometry, [42–43] and Integrated Clinical Platform Ocular Surface Analyzers (ICPOSA) [47–48] and CL materials, to analyze the pre-lens tear film.

Also, it has been suggested that mechanical trauma, [19–20] and hypoxia, [49] are responsible for the conjunctival vascularization during CL wear [50]. *Papas et al.* [49] demonstrated that hydrogel CL with high oxygen transmissibility [DK/t 5 x 10^{-11} (cm^2/s) (ml O_2/ml x mm Hg])] produced less conjunctival injection compared to low DK/t CL (30 x 10^{-11}). In this experiment, a slight but statistically significant increase in

Table 5
Correlation coefficients and levels of significance for the NIBUT; bulbar and limbal hyperemia; and IL-β concentration collected in the morning.

	Morning assessment			
	NIBUT	*Bulbar hyperemia*	*Limbal hyperemia*	*IL1-β concentration*
NIBUT	1	−0.321	−0.314	−0.164
Bulbar hyperemia	–	1	**0.700****	**0.405***
Limbal hyperemia	–	–	1	**0.499***
IL1-β	–	–	–	1

Values in **bold** represent statistically significant correlations.
*p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001.

Table 4
Individual IL1-β concentration, mean values and detection rates for the control and neophyte groups during the morning and afternoon assessments.

Control	IL1-β pg/ml			**Neophyte**	IL1-β pg/ml		
Participant#	*Morning*	*Afternoon*		*Participant#*	*Morning*	*Afternoon*	
1	0.0	0.0		**11**	1.6	0.0	
2	0.0	0.1		**12**	0.4	0.0	
3	0.0	0.0		**13**	–	14.9	
4	0.2	0.0		**14**	0.2	0.0	
5	0.0	0.0		**15**	0.0	1.3	
6	–	0.5		**16**	0.0	0.0	
7	0.0	0.1		**17**	–	0.0	
8	0.0	0.0		**18**	2.8	5.8	
9	1.8	0.0		**19**	1.8	3.3	
10	0.0	0.0		**20**	3.4	2.5	
11	–	–		**21**	6.5	9.5	
			P-Value	**22**	6.1	1.3	*P-Value*
Mean ± SD	0.2 ± 0.6	0.1 ± 0.2	0.461	**Mean ± SD**	2.3 ± 2.4	3.2 ± 4.7	0.859
Detection rate (%)	30	30		**Detection rate (%)**	80	58	

Detection rate represent the percentage of samples that contain IL1-β. SD Standard Deviation

Table 6
Correlation coefficients and levels of significance for the PL-NIBUT; bulbar and limbal hyperemia; and IL1-β concentration collected in the afternoon.

	Afternoon assessment			
	PL-NIBUT	*Bulbar hyperemia*	*Limbal hyperemia*	*IL1-β concentration*
PL-NIBUT	1	0.136	0.077	−0.045
Bulbar hyperemia	–	1	**0.792****	0.090
Limbal hyperemia	–	–	1	−0.301
IL1-β	–	–	–	1

Values in **bold** represent statistically significant correlations.
*p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001.

vascular response was recorded ($p < 0.001$, Table 3), indicating that factors beyond DK/t might be associated with increased hyperemia, considering the high oxygen transmissibility of the CL (156×10^{-11}) and the short testing period. The delefilcon A polymer has an aqueous gradient in its structure, which allows the transition from a silicone hydrogel core (EWC 33 %) to a hydrophilic outer surface (EWC>80 %, Table 1) [51–52]. The lens also contains and releases phosphatidylcholine (DMPC) into the tear film. These combined characteristics may also explain the mild impact of the material on ocular physiology [46,53–54].

TGF-β1 and IL1-β were studied due to their involvement in modulating the corneal subclinical inflammatory response [16,18]. TGF-β1 levels in human tears typically vary between 0.0 to 38.5 ng/ml, [13,15,55–57] with ELISA being the most common analysis method [13,55,57]. However, more evidence is needed in the literature regarding the limits of detection, with only one clinical trial reporting a 37 % detection rate [13]. In the present study, median concentrations were 0.0 ng/ml for neophytes and controls, and detection rates were below 33 %, confirming the low detection rate of this cytokine. Although this biomarker is known to be elevated after corneal refractive surgery [12–13] and in patients with DED,[15]CL application and use throughout the day did not appear to significantly impact the TGF-β1 level (Fig. 2).

The presence of IL 1-β in the tears of healthy individuals is still questionable because some studies detected the molecule, [23–25,58–61] while others did not confirm its existence, [26,62–64] possibly due to differences in the analysis methods. Reported values obtained with ELISA were between 0 and 70 pg/ml, [58,63–64] multiplex bead array assays, such as Luminex, were between 0 and 1040 pg/ml [23–25,59–62]. The IL1-β levels reported in this study were within the expected values, with detection rates comparable to those documented by *Willcox et al.* [65] who reported rates ranging from 30 to 60 % for this biomarker – Table 4. No significant changes were found in IL1-β levels throughout the day in either group. This result is consistent with previous studies that examined molecule circadian fluctuations in CL wearers [28,65] and non-wearers [66–67]. To our knowledge, only one study [67] reported a slight increase in biomarker concentration in the morning and late evening in the tears of 28 volunteers. It is also worth noting the mild increase in the IL1-β concentration during the afternoon compared to the controls (3.2 ± 4.7 Vs. 0.1 ± 0.1 ρg/ml, $p = 0.05$, Fig. 2), consistent with previous findings by *Gallardo and colleagues* [24] that observed an increased IL1-β concentration after one day of continuous CL use compared with controls (380 ± 90 vs. 70 ± 40 ρg/ml, $p < 0.001$). IL1-β appeared to decay after one week and returned to baseline values after one month. In contrast, a separate clinical trial, [65] reported a decrease in IL1-β levels in 90 subjects fitted with galyfilcon A lenses worn on a daily disposable basis for ten days compared to the molecular concentration recorded without CL ($p = 0.05$). However, participants were instructed to remove their tears, and the laboratory analysis method (multiplex bead assay) differed from that used in this study, which may justify the differing results obtained. *Fukada et al.* [63] elucidated the primary role of IL1-β in the acute phase of corneal inflammation. The authors reported concentrations ranging from 29 to 218 ρg/ml in tear fluid samples from eyes with corneal disease. After disease resolution, the biomarker was no longer detected in the affected eye. The relationship between IL1-β levels and clinical parameters revealed a moderate correlation with bulbar ($r = 0.405$, $p = 0.008$) and limbal hyperemia ($r = 0.499$, $p = 0.027$) in the morning – Fig. 4, suggesting cytokine involvement in the angiogenic response. However, this relationship was not observed in the afternoon assessment, indicating potential alterations in cytokine regulatory mechanisms due to CL presence. Lower IL1-β detection rates in the afternoon compared to the morning further suggest a possible interaction between IL1-β and CL material, warranting further laboratory studies to confirm this hypothesis.

Indeed, in a recent study, *Ramamoorthy et al.*[68] stated that the molecule could adhere to the CL material, being depleted from the tear film.

Key limitations of this study include its small sample size and the detection rates of biomarkers, restricting the generalizability of the findings to the broader population. Additionally, testing only one lens type prevents extrapolation to the wider spectrum of CL available.

5. Conclusion

The daily wear of delefilcon A CL alters tear film stability, increases vascular response, and elevates the concentration of tear IL1-β compared to controls. Meanwhile, the presence of TGF-β1 in tears appears to be reduced and unaffected by lens wear. The association between physiological parameters and IL1-β levels suggests that the presence of the CL might alter the cytokine regulatory mechanisms, thereby disturbing ocular surface homeostasis. However, due to its low concentration, the molecule's role is residual concerning the subclinical inflammatory response to CL wear. More longitudinal studies are needed to understand

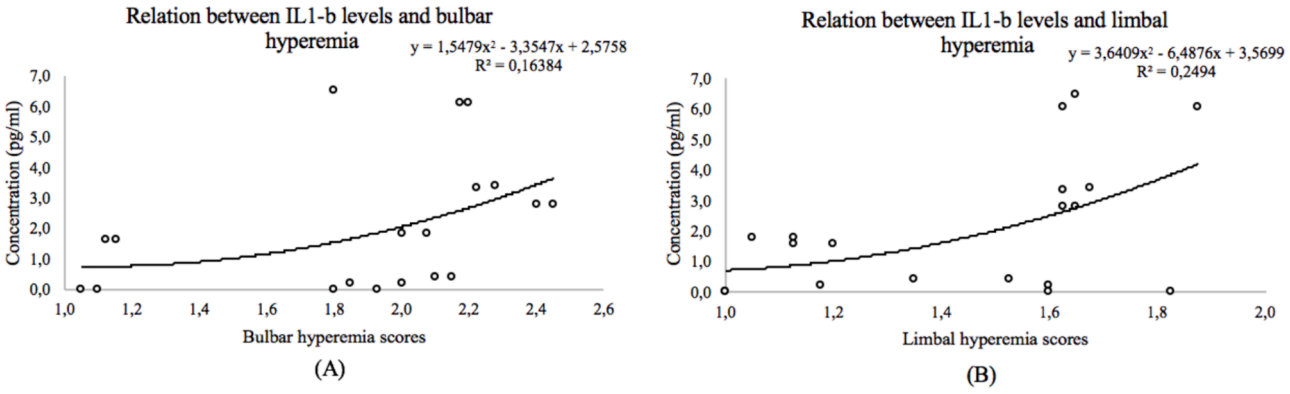


Fig. 4. Graphical representation of the correlation between IL1-β concentration, bulbar (A) and limbal hyperemia (B).

the cellular and molecular mechanisms underlying this inflammatory condition and the impact of different materials on ocular physiology.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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