Effects of contact lens use on the cytological status of the ocular surface and corneal healing after transepithelial photorefractive keratectomy

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Вплив носіння контактних лінз на цитологічний статус очної поверхні та загоєння рогівки після трансепітеліальної фоторефракційної кератектомії

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Abstract

Purpose*: To evaluate the effects of soft contact lens (SCL) use on the cytological status of the bulbar conjunctiva and tear film stability before and after transepithelial photorefractive keratectomy (TPRK) and to examine the association of these characteristics with postoperative healing processes.*

Material and Methods: *This prospective comparative study included two clinical groups 30 patients (60 eyes) each: group 1 (patients who had not used SCLs) and group 2 (patients who had used SCLs for the most recent five years before surgery). All patients received transepithelial PRK [1]. The status of the ocular surface was assessed by impression cytology (Nelson's classification grades 0-3) [2], Schirmer's I test and non-invasive break-up time (NIBUT) before and 2 months after surgery. Severity of corneal opacity (haze) was assessed 2 months after surgery. Mann-Whitney test, Wilcoxon test, Fisher exact test and Spearman correlation were used for statistical analysis.*

Results*: Preoperatively, the mean grade (standard deviation [SD]) of cytological changes was statistically significantly worse for group 2 than for group 1 (2.35 (0.66) versus 1.38 (0.69), $p < 0.001$). Two months after surgery, the mean grade (SD) of cytological changes in group 2 improved significantly ($p = 0.003$), but was still worse than that for group 1 (2.15 (0.61) versus 1.32 (0.54), $p < 0.001$). There was a moderate correlation of the grade of cytological changes at baseline with the severity of haze at 2 months ($\rho = 0.47$, $p < 0.001$). Additionally, the grade of cytological changes was mildly correlated with preoperative NIBUT ($\rho = -0.20$; $p = 0.033$) and two-month postoperative NIBUT ($\rho = -0.18$; $p = 0.048$).*

Conclusion: *Long-term SCL use resulted in stable pathological changes in the ocular surface epithelium, which did not disappear completely two months after the cessation of CSL use and TPRK. Abnormal cytological status is a prognostic marker associated with the risk of postoperative haze.*

Keywords: *transepithelial photorefractive keratectomy, contact lenses, cytology, haze, dry eye, ocular surface, cornea.*

Резюме

Мета. *Оцінити, як носіння м'яких контактних лінз (МКЛ) впливає на цитологічний стан бульбарної кон'юнктиви та стабільність слізної плівки до та після трансепітеліальної фоторефракційної кератектомії (ТФРК), та дослідити зв'язок цих показників із процесами післяопераційного загоєння.*

Методи. *У проспективному порівняльному дослідженні взяли участь 120 пацієнтів, розділених на дві групи: група 1 (n=60) — пацієнти, які не носили МКЛ,*

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та група 2 (n=60) — пацієнти, які протягом п'яти років перед операцією носили МКЛ. Усім пацієнтам було проведено ТФРК [1]. Стан поверхні ока оцінювали за допомогою імпресійної цитології (за класифікацією Нельсона, 0–3 ступені) [2], тесту Ширмера I та часу розриву слізної плівки (NIBUT) до операції та через два місяці після неї. Ступінь помутніння рогівки (хейз) оцінювали через два місяці. Для статистичного аналізу використовували тести Манна — Уітні, Вілкоксона, точний тест Фішера та коефіцієнт кореляції Спірмена.

Результати. *До операції пацієнти з групи 2 мали статистично значуще гірший цитологічний статус порівняно з групою 1 (середній бал 2,35 ± 0,66 проти 1,38 ± 0,69; p < 0,001). Через два місяці після операції у пацієнтів групи 2 спостерігалося статистично значуще покращення (p=0,003), однак їхні показники залишалися гіршими, ніж у групі 1 (2,15 ± 0,61 проти 1,33 ± 0,54; p < 0,001). Виявлено помірний позитивний кореляційний зв'язок між ступенем цитологічних змін після операції та вираженістю хейзу через два місяці (ρ = 0,47, p < 0,001). Також підтверджено слабкий негативний зв'язок між цитологічними змінами та показником NIBUT як до (ρ = –0,20), так і після операції (ρ = –0,18).*

Висновки. *Тривале носіння контактних лінз призводить до стійких патологічних змін епітелію очної поверхні, які не зникають повністю через два місяці після припинення їх використання та проведення ТФРК. Порушений цитологічний статус є прогностичним маркером, асоційованим із ризиком розвитку післяопераційного хейзу.*

Ключові слова: *трансепітеліальна фоторефракційна кератектомія, контактні лінзи, цитологія, хейз, сухе око, поверхня ока, рогівка.*

Introduction

Transepithelial photorefractive keratectomy (TPRK) is a major laser vision correction technique which is characterized by a contactless approach and no flap formation; this may contribute to a reduced postoperative complication rate and is better for ocular surface sparing compared to conventional photorefractive keratectomy (PRK) [3-5]. The success and outcome of surgery largely depends on the course of corneal healing which is closely associated with the status of the entire ocular surface [6]. Ocular surface is a complex functional unit comprising the corneal and conjunctival epithelium, tear film and lacrimal glands. Its homeostasis is critically important for maintaining the transparency of the media and adequate regeneration after surgical intervention [7, 8].

Wearing soft contact lenses (SCL) is a common cause of chronic ocular surface changes like epithelial microinjury, inflammatory reactions, hypoxia, tear film composition changes, and meibomian gland dysfunction [9-11]. These changes can be detected at the cellular level by conjunctival cytology, even if not experienced as symptoms of advanced dry eye syndrome (DES). Cytological changes may reflect chronic ocular surface stress and potentially affect post-surgical corneal healing and recovery.

Temporary or chronic deterioration in the status of the ocular surface and the development or exacerbation of DES symptoms is common after refractive surgery [12-14]. Risk factors of postoperative DES include female sex, advanced age, large refractive correction and a history of wearing contact lenses before surgery [15]. Damage to corneal nerve endings during laser ablation can result in the disturbance of the sensory reflex arch, leading to decreased tear production and tear film destabilization. Postoperative impaired regeneration can result in the development of subepithelial corneal opacification (haze) [16, 17].

Despite significant advances in the understanding of post-TPRK corneal recovery, there is still a need in a more detailed investigation of the effects of wearing SCLs and preoperative evidence of cytological changes on various aspects of the postoperative period. Particularly, the value of cytological changes as a predictor of corneal recovery should be investigated.

The purpose of this study was to evaluate the effects of SCL use on the cytological status of the bulbar conjunctiva and tear film stability before and after TPRK and to examine the association of these characteristics with postoperative healing processes.

Material and Methods

This prospective comparative study included two clinical groups 30 patients (60 eyes) each. Group 1 comprised 12 males and 18 females (mean age (standard deviation [SD]), 25.4 (4.1) years; mean refractive error (SD), -2.88 (1.72) D) and group 2 comprised 10 males and 20 females (mean age (SD), 26.1 (3.8) years; mean refractive error (SD), -3.80 (1.96) D).

Inclusion criteria for group 1 were age 18-45 years; informed consent for participation in the study; no history of SCL use for the most recent five years before surgery; no concomitant ocular surface disease; a myopic spherical refractive error ≤ 7 D; a planned depth of corneal laser ablation < 100 μm; a 6-7 mm laser ablation zone; no myopia progression for at least 12 months; and a preoperative corneal thickness more than 480 μm.

Inclusion criteria for group 2 were age 18-45 years; informed consent for participation in the study; history of SCL use regularly for the most recent five years before surgery; compliance with SCL wear (daily wear, no overnight wear, and timely lens replacement); no concomitant ocular surface disease; a myopic spherical refractive error ≤ 7 D; a planned depth of corneal laser ablation < 100 μm; a 6-7 mm laser ablation zone; no myopia progression for at least 12 months; and a preoperative corneal thickness more than 480 μm.

Patients exhibiting non-compliance with the study procedure were excluded from the study.

All patients received StreamLight single-step TPRK for myopia using the Alcon Wavelight EX500 excimer laser (Alcon Laboratories, Fort Worth, TX) [1].

A comprehensive eye examination was performed preoperatively and 2 months postoperatively and included the following:

Cytological study: The status of the bulbar conjunctival epithelium was assessed by impression cytology. The cytologic changes of the bulbar conjunctiva were graded according to Nelson's grading system, with grade 0 corresponding to normal findings (small and round epithelial cells with a nucleo-cytoplasmic ratio of 1:2 and abundant goblet cells), and grades 1 to 3 of increasing severity of conjunctival squamous metaplasia (epithelial cells exhibiting an increase in size and pyknotic nuclei with a reduction in the number or absence of goblet cells) [2]

Tear film analysis: Tear production was assessed by performing Schirmer's I test, and tear stability, non-invasive break-up time (NIBUT) using ocular surface analyzer

Assessment of complications: Subepithelial corneal haze was observed clinically during biomicroscopy and graded according to the Fantes scale [18, 19] 2 months postoperatively.

Statistical analysis was conducted using non-parametric tests on IBM SPSS Statistics software. Between-group comparisons used the Mann-Whitney test, and preoperative-postoperative comparisons within a group used the Wilcoxon test. Fisher exact test was used to compare the two groups for categorical data. Spearman rank correlation was utilized to assess relationships among parameters. Statistical significance was set at $P < 0.05$ for all analyses. Results are presented as mean (SD).

Results

Group comparison for cytological changes. There was a significant difference between groups with regard to cytological changes both before and after surgery (Table 1).

Preoperatively, the mean grade of cytological changes was almost one point higher for group 2 than for group 1 (2.35 versus 1.38, $p < 0.001$). At 2 months after surgery, the status of the epithelium remained stable with no significant change compared to baseline ($p = 0.317$), in group 1, but statistically significantly improved ($p = 0.003$) in group 2, indicating the onset of recovery with cessation of SCL use. Despite positive changes after surgery, the status of the conjunctiva in group 2 remained worse than that in group 1 ($p < 0.001$).

The distribution of grades of changes among patients (Table 2) was helpful to see the details of structural differences.

Preoperatively, most patients (90%) in group 2 exhibited marked (grade 2 to 3) cytological changes in the

Table 1. Grades of cytological changes before and 2 months after surgery in group 1 versus group 2

Timepoint	Group 1 (patients who had not used soft contact lenses) (mean [standard deviation])	Group 2 (patients who had used soft contact lenses) (mean [standard deviation])	P-value (between-group difference)*
Baseline	1.38 (0.69)	2.35 (0.66)	< 0.001
Two months after surgery	1.33 (0.54)	2.15 (0.61)	< 0.001
P-value (before- and-after difference) **	0.317	0.003	

Note: *P-value for comparing between groups (Mann-Whitney U test); **P-value for comparing before-and-after changes within a group (Wilcoxon test)

Table 2. Distribution of grades of cytological changes among patients of groups 1 and 2 before and after surgery

Grade	Baseline		p (before)*	After surgery		p (after)*
	Group 1	Group 2		Group 1	Group 2	
	n (%)	n (%)		n (%)	n (%)	
0	2 (3%)	0 (0%)	0.496	0 (0%)	0 (0%)	1.000
1	38 (63%)	6 (10%)	<0.001	42 (70%)	7 (12%)	< 0.001
2	15 (25%)	27 (45%)	0.035	16 (27%)	37 (62%)	< 0.001
3	5 (8%)	27 (45%)	<0.001	2 (3%)	16 (27%)	< 0.001

Note: n, number of cases; *P-value for comparing groups for the frequencies of each grade (exact Fischer test); P (before)*, comparing preoperative data; P (before)*, comparing postoperative data

epithelium (Table 2). Postoperatively, the percentage of patients with the most severe (grade 3) changes decreased from 45% to 27%, mostly due to the transition from grade 3 to grade 2. Nevertheless, the percentage of patients with mild (grade 1) changes remained rather small (12%).

Tear film analysis. Tear production was assessed by performing Schirmer's I test (Table 3), and tear stability, NIBUT (Table 4).

Preoperatively, the tear production was somewhat better in group 1 than in group 2, but the difference was not significant ($p = 0.0688$). It is important that, postoperatively, the Schirmer test score decreased significantly ($p < 0.05$) in both groups, as expected after surgery. At 2 months, the difference between groups for tear production changed from significant to non-significant ($p = 0.4034$).

Preoperatively, NIBUT was significantly shorter in group 2 (8.11 s) than in group 1 (10.55 s, $p = 0.0367$), indicating that SCL use affects tear film stability. Although the Schirmer test score decreased, the NBUT improved significantly after surgery in both groups ($p < 0.001$). This indicated that surgical intervention and postoperative medical therapy (0.2% hyaluronic acid and 0.1% dexamethasone) only had a positive effect on tear film quality and stability in group 1, whereas these two measures plus the cessation of SCL use had a positive effect on tear film quality and stability in group 2.

Despite improvements in both groups, the difference between groups was not only still significant but became more marked at 2 months ($p = 0.0036$). Tear film stability was preserved significantly better in patients who had not used SCLs (group 1).

We analyzed correlations between cytological changes in the conjunctiva and the clinical parameters examined (Table 5).

There was a correlation between the duration of SCL use and the grade of squamous epithelial metaplasia ($\rho = 0.59$; $p < 0.001$). This confirms chronic microinjury and hypoxia due to long-term effects of SCLs on the ocular surface, resulting in a stable rearrangement of the epithelial layer of the ocular surface. Additionally, the severity of cytological changes was mildly correlated with preoperative NIBUT ($\rho = -0.20$; $p = 0.033$) and 2 months postoperative NIBUT ($\rho = -0.18$; $p = 0.048$). Therefore, the progression of degenerative changes in the epithelium and the reduced density of goblet cells were associated with the deterioration of tear film stability. This created the conditions for the dry eye vicious circle, and the disease symptoms maintained postoperatively. Of note was the correlation of the cytological status at baseline and the severity of early haze at 2 months after TPRK ($\rho = 0.47$; $p < 0.001$). This finding points to the role of epithelial-stromal relationships in the healing process. Worse baseline morphological status of

Table 3. Comparisons of preoperative and postoperative Schirmer test scores for groups 1 and 2

Comparison	Preoperative Schirmer test score (mean [standard deviation])	Postoperative Schirmer test score (mean [standard deviation])	P-value (preoperative-postoperative difference)*
Group 1, n = 60	17.50 (6.40)	14.93 (4.17)	0.0001
Group 2, n = 60	15.92 (6.06)	14.45 (4.67)	0.0218
P-value (between-group difference)**	0.0688	0.4034	

Note: *, P-value for comparing preoperative-postoperative changes within a group (Wilcoxon test); **, P-value for comparing between groups (Mann-Whitney U test)

Table 4. Comparisons of preoperative and postoperative **noninvasive break-up times (NIBUT)** for groups 1 and 2

Comparison	Preoperative NIBUT (mean [standard deviation])	Postoperative NIBUT (mean [standard deviation])	P-value (preoperative-postoperative difference)*
Group 1 (patients who had not used soft contact lenses), n = 60	10.55 (5.53)	12.83 (4.58)	0.0003
Група 2 (patients who had used soft contact lenses), n = 60	8.11 (3.50)	10.56 (3.88)	< 0.0001
P-value (between-group difference)**	0.0367	0.0036	

Note: n, number of eyes; *, P-value for comparing preoperative-postoperative changes within a group (Wilcoxon test); **, P-value for comparing between groups (Mann-Whitney U test)

Table 5. Analysis of correlations of the grade of conjunctival squamous metaplasia and clinical-and-functional status of the ocular surface

Parameters that were correlated with cytological changes	Coefficient (ρ)	p
ACL use longer than 5 years	0.59	< 0.001
Preoperative NIBUT	-0.20	0.033
Two-month postoperative NIBUT	-0.18	0.048
Two-month postoperative haze	0.47	< 0.001

Note: NIBUT, noninvasive break-up time; P, coefficient of Spearman rank correlation

the epithelium was a predictor of more marked activity of keratocytes and development of corneal opacity in the early postoperative period. Therefore, preoperative cytological status can be used as a predictor of quality of reparative regeneration after laser ablation.

Discussion

The results obtained demonstrate that long-term contact lens use is a powerful factor of the development of advanced pathological changes in the ocular surface epithelium, which is in agreement with recent studies [9-12]. Although the cessation of SCL use and postoperative therapy (0.2% hyaluronic acid and 0.1% dexamethasone) contributed to partial recovery of the ocular surface, this process was slow, and ocular surface homeostasis did not become completely normal within two months after surgery. The persistence of the above changes indicates the presence of profound changes at the cellular level with a long time required for complete recovery [8]. The short follow-up period (2 months) was a limitation of this study. This follow-up duration was selected purposefully to assess the peak of early physiological haze which is most closely associated with cytological status of the ocular surface at baseline. Further long-term research is required to evaluate the effect of cytological changes on the development of late haze (≥ 3 months after surgery).

The key finding of this study was a positive association of the status of the epithelium and corneal surface healing process. A moderate correlation of cytological abnormalities with haze ($\rho = 0.47$) confirms the hypothesis that healthy epithelium plays a key role in regeneration regulation. It is likely that cellular level abnormalities result in unbalanced production of cytokines and growth factors, stimulating excessive activity of keratocytes, their transformation into myofibroblasts and excessive collagen deposition that is clinically manifested as haze. Therefore, postoperative cytological status may serve as an important prognostic marker of the development of haze.

These findings were complemented by tear film analysis. Although the surgery itself temporarily reduces tear production in all patients, a worse ocular surface in SCL wearers creates a less favorable environment for post-PRK corneal healing. The association of the cytological status of the bulbar conjunctiva and tear-film stability (NIBUT) is also natural, since squamous metaplasia is accompanied by goblet cell loss, which results in tear mucin deficiency and, consequently, tear instability.

Studies on corneal recovery and risks of complications (like haze) after refractive surgery (e.g., TPRK) confirm the need for comprehensive evaluation of anatomic and functional features of the ocular surface in patients to prevent complications and minimize discomfort in the postoperative period [12-17, 20, 21]. Studies on cytological changes in the ocular surface, however, have been not given adequate attention in the context of prediction of postoperative complications [8, 10]. Therefore, the current study not only complements the available data on the importance and features of pre-refractive surgery examination of patients, but also introduces a new view on the use of conjunctival cytological studies in refractive surgery patients. This work is the first to characterize a factor of cytological changes in the ocular surface conjunctiva as an effective prognostic marker of corneal subepithelial haze in the early postoperative period.

Therefore, a thorough assessment of ocular surface status should precede refractive surgery, especially in patients with a prolonged history of SCL use. The detection of marked cytological changes may provide grounds for performing preoperative procedures to improve the status of the epithelium and reduce the risk of postoperative complications.

To conclude: first, patients using contact lenses for more than five years had a statistically significantly worse cytological status of the bulbar conjunctival epithelium at baseline, which was characterized by marked signs of squamous metaplasia. Second, although the status of the ocular surface in these patients improved with TPRK and cessation of SCL use, it did not reach that of group 1 within two months after surgery. Third, inadequate postoperative cytological status of the ocular surface was a significant risk factor associated with a more marked development of corneal opacity (haze). Finally, cytological analysis is a valuable diagnostic and prognostic tool that enables evaluating risks of complicated corneal healing after refractive surgery, especially in patients who have worn SCLs for long periods.

Prospects of future research

The findings of this study demonstrate the need for further research into the role of cytological changes in the ocular surface as a predictor of effective and safe transepithelial PRK. It is reasonable to use longer follow-ups to evaluate long-term changes in the epithelium, effects of various SCL types and the duration of their use, and introduce molecular biological methods for conjunctival status analysis to clarify reparative mechanisms.

Author Contributions

SOS: Conceptualization, Project Management, Data Analysis and Interpretation, Writing – Original Draft, Review & Editing; KYH: Conceptualization, Project Management, Data Analysis and Interpretation, Writing - Review & Editing. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work.

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The authors declare that the views expressed in this article are their own and do not reflect the official position of the institutions.

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Conflict of Interest

The authors declare that they have no conflicts of interest that could bias their opinion regarding the subject matter or materials described and discussed in this manuscript.

Ethics Statements

This study involved human subjects, was approved by the Bioethics committee of the National Pirogov Memorial Medical University, Vinnytsia (Minutes No. 60 of 24.09.2025), and followed ethical standards as outlined in the Declaration of Helsinki. Informed consent was obtained from the all patients. This study did not include animal experiments.

Data Availability Statement

: All the data obtained or examined during this study has been incorporated into this published article.

Abbreviations

DES, dry eye syndrome; NIBUT, non-invasive break-up time; OSA, ocular surface analyzer; OSDI, ocular surface disease index; PRK, photorefractive keratectomy; SCL, soft contact lens; TPRK, transepithelial photorefractive keratectomy

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