https://doi.org/10.31288/oftalmolzh202531114

Objective optical densitometry-based evaluation of longitudinal changes in the inflammatory process in the treatment of bacterial keratitis

Alifanov I. S., Klopotska N. G.

Dnipro State Medical University

Dnipro (Ukraine)

Purpose: *To objectively determine longitudinal changes in corneal optical density (COD) in patients with bacterial keratitis (BK).*

Methods: *Thirty patients with unilateral BK (mean age ± standard deviation [SD], 44.7±11.5 years) underwent examination. Fellow eyes were used as controls. Optical densitometry was performed using the corneal topography system Pentacam AXL at admission and days 7 and 14 of treatment.*

Results: *At presentation and days 7 and 14 of treatment, the average median (interquartile range [IQR]) COD value for the affected eyes was 92.8 (55.6-99.6), 89.7 (51.1-97.3) and 80.6 (32.0-93.1) grayscale units (GSU), respectively ($p<0.05$), indicating a decrease in inflammatory infiltration, and the average mean (SD) COD value for the control eyes was 19.6±3.0, 19.9±2.8, and 19.7±2.6 GSU, respectively, with no statistically significant difference.*

Conclusion*: The use of optical densitometry for monitoring corneal transparency in eyes treated for BK over a two-week period enabled objective recording of a gradual reduction in median (IQR) COD values in the affected eyes from 92.8 (55.6–99.6) to 80.6 (32.0–93.1) GSU, corresponding to an improvement in the clinical status of patients.*

Keywords:

bacterial keratitis, corneal topography, optical densitometry, cornea, keratitis

Introduction

According to the 2019 WHO World Report on Vision, corneal disorders accounted for 3.46% of global vision loss [1]. Corneal opacity is most commonly caused by eye infection such as infectious keratitis; it is the fourth leading cause of blindness and was estimated to be the cause of 10% of all cases of avoidable loss of vision in the developed countries [2]. Bacteria are the most common causative agents of ocular infections. Even though the eye is hard and protected by the continuous flow of tear which contains antibacterial compounds, inflammation and scarring once occurred may not be easily resolved and requires immediate management [3].

Effective management of such infections demands knowledge of the specific etiology. Because antimicrobial antibiotic resistance is a pressing public eye health issue [4], there is a need for the development of new methods of treatment and improvements in methods of objective monitoring the state of the cornea in the course of research. However, in today's ophthalmological practice, longitudinal changes in corneal inflammation are assessed through visual acuity measurements and results of anterior segment biomicroscopy. This approach allows only for the qualitative assessment of the state of the cornea, with the results much depending on the quality of equipment and qualification of healthcare workers.

Pentacam Scheimpflug imaging system is equipped with a rotating Scheimpflug camera and allows for objective measurements of corneal optical density (COD). COD is typically measured in standardized grayscale units (GSU), ranging from 1 to 100, where 0 represents maximum transparency and 100 represents maximum opacity [5].

The purpose of the study was to objectively determine longitudinal changes in COD in patients with bacterial keratitis.

Material and Methods

This study was conducted at Department of Ophthalmology, Dnipro State Medical University, and Dnipropetrovsk Regional Clinical Eye Hospital. Informed consent was obtained from all subjects.

Medical histories of 30 patients treated for unilateral bacterial keratitis at the First Department of Ophthalmology, Dnipropetrovsk Regional Clinical Eye Hospital, were reviewed. The fellow eyes were used as controls.

Inclusion criteria were age 18 or older and a verified diagnosis of unilateral bacterial keratitis. Patients with bilateral keratitis, non-bacterial keratitis, or the presence of corneal comorbidity affecting corneal transparency were excluded.

Of the 30 patients, 17 were men and 13 women. The mean patient age was 44.7 ± 11.5 years.

Based on the bacteriological culture results, keratitis was most commonly caused by single Gram-positive organisms (53.3%), including Staphylococcus aureus (23.3

%), methycillin-resistant Staphylococcus aureus (MRSA) (6.7%), Staphylococcus epidermidis (13.3%), and Streptococcus pneumonia (10.0%). Single Gram-negative organisms were found in 16.7% of patients; these included Pseudomonas aeruginosa (6.7%), Esherichia coli (6.7%) and Klebsiellae pneumonia (3.3%). Mixed bacterial infections were found in 10.0% of patients; these included Staphylococcus epidermidis plus Staphylococcus aureus (6.7%) and Staphylococcus epidermidis plus Candida albicans (3.3%). There was no bacterial growth in cultures from 20.0% of patients.

Patients underwent a routine eye examination including visual acuity testing, intraocular pressure (IOP), and binocular ophthalmoscopy of the anterior and posterior segments (when possible; using a Katena Diamond 90D non-contact lens and SL-45 slit-lamp (Shin Nippon, Tokyo, Japan)). Additionally, they underwent spectral-domain optical coherence tomography (SD-OCT; Optovue RTVue 100-2; Optovue Inc., Fremont, CA) and B-scan ultrasonography (Compact II, Quantel Medical, Clermont-Ferrand, France).

Optical densitometry was performed using the Pentacam AXL system (OCULUS Optikgeräte GmbH, Wetzlar, Germany) at admission to the in-patient unit and days 7 and 14 of treatment. The value automatically determined at the point of maximum optical density of inflammatory infiltrate was used for statistical calculations. Examples of densitometry maps are presented in Figs. 1 (inflammatory corneal infiltration in the optical zone of the affected eye) and 2 (the healthy eye).

Empiric therapy was administered before the results of microbiological tests were available and included mira-

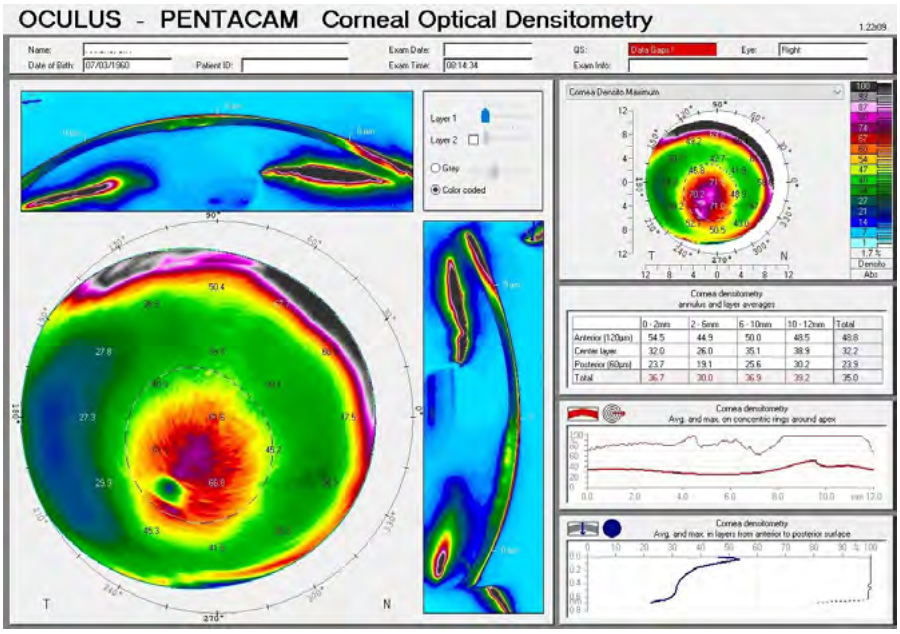

Fig. 1. Pentacam densitometry map for the affected right eye of a patient with bacterial keratitis

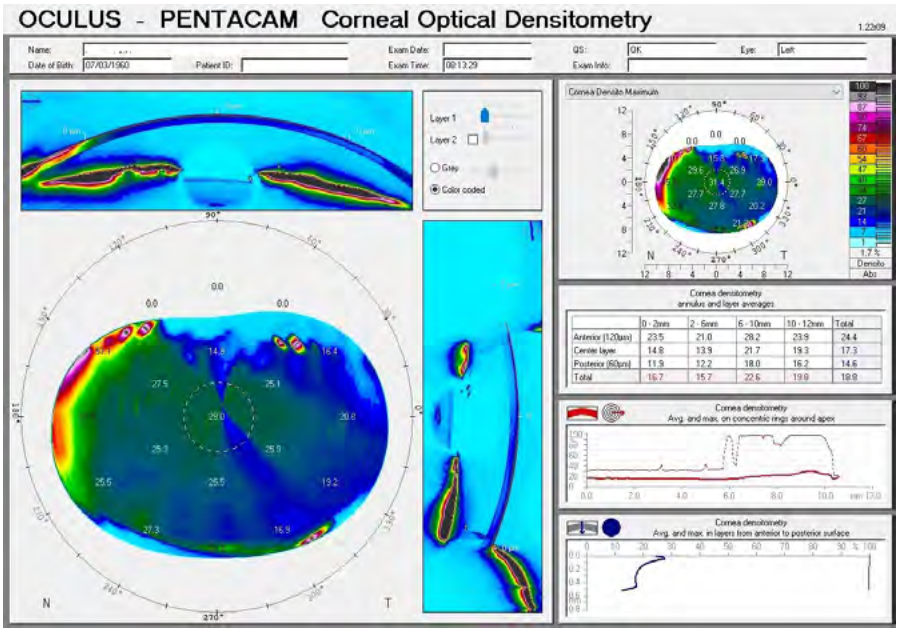

Fig. 2. Pentacam densitometry map for the healthy left eye of a patient with bacterial keratitis

mistin 0.1 mg/ml 6 times daily, ciprofloxacin 0.3% 6 times daily, and tobramycin 0.3% 6 times daily. After antibiogram results were available, the patient was administered the antibiotic agent to which the causative microorganism proved most susceptible. Additional therapy included cyclopentolate 1% twice daily and dexpantenol 2% and sodium hyalorunate 0.15 ophthalmic solution four times daily.

Statistica v6.1 software (StatSoft, Inc., Tulsa, OK; № AGAR909E415822FA) was used for statistical analysis. For normally distributed data, mean and standard deviation (SD) were calculated, and analysis of variance (ANOVA) and Tukey honestly significant difference (HSD) test were employed to determine the significance of differences between time points. For non-normally distributed data, median (Med) and interquartile range (IQR) were calculated, and the significance of differences between time points was analyzed using Friedman's rank ANOVA and Wilcoxon test for pairwise comparison. Analysis of normality was performed with the Kolmogorov-Smirnov test with Lilliefors correction, with a significant P value indicating evidence of non-normality. The level of significance $p < 0.05$ was assumed.

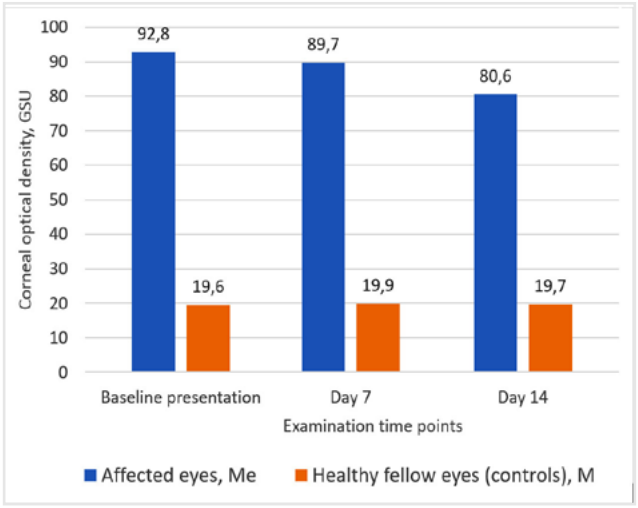

Fig. 3. Longitudinal changes in median [Me] and mean [M] corneal optical densitometry values for affected eyes and healthy fellow eyes (controls), respectively, of patients with bacterial keratitis

Results

COD values in the affected eyes were not normally distributed whereas those in the healthy fellow eyes were normally distributed.

At baseline presentation, the median COD value for the inflammatory infiltrate area in eyes with bacterial keratitis ranged from 30.2 to 100.0 GSU, and the average median (IQR) COD was 92.8 (55.6-99.6) GSU. At days 7 and 14 of treatment, the average median (IQR) value for this measure decreased to 89.7 (51.1-97.3) GSU and 80.6 (32.0-93.1) GSU, respectively, indicating a decrease in inflammatory infiltration. Overall, these data corresponded well with biomicroscopic evidence of a reduction in corneal edema, increase in corneal transparency and reduction in affected area. The difference in median COD for affected eyes between time points was statistically significant ($p<0.05$).

At baseline presentation, the mean COD value for healthy fellow eyes in with patients with bacterial keratitis ranged from 13.5 to 24.8 GSU, with a mean ± SD value of 19.6 ± 3.0 GSU. At days 7 and 14 of treatment, the mean ± SD value for this measure was 19.9±2.8 GSU and 19.7±2.6 GSU, respectively. The difference in mean COD value for healthy fellow eyes between time points was not statistically significant ($p > 0.05$) (Fig. 3).

Discussion

Several techniques for assessing corneal transparency are available for ophthalmic practice today. Slit-lamp biomicroscopy is the most popular clinical technique for assessing corneal transparency and integrity. Although this grading method is simple to use, the grading is often dependent on the experience and subjectivity of clinicians. Ultrasound biomicroscopy (UBM) with a high-frequency transducer allows identifying the location and size of corneal lesions. However, UBM is only able to assess moderate and above-moderate haze; subtle haze is not observable with UBM. In vivo confocal microscopy provides high-quality corneal visualization at the cellular level, but is sensitive to the transparency of the ocular media and cannot be used in eyes with marked corneal opacity. OCT is a high-resolution optical imaging technique that utilizes near-infrared light waves to image the microstructures of different tissue types and allows assessing corneal and retinal damage at the microscopic level. Its efficacy, however, decreases with an increase in tissue density [5].

The Pentacam AXL corneal topographer is equipped with a rotating Scheimpflug camera and is a visible light-based optical scanning tomography system. The Pentacam® analysis is a contactless examination routine that enables the assessment of corneal structure, shape and optical density in about two seconds. Any eye movement is detected by a second camera and corrected for in the process [6, 7].

Other researchers reported the results of the use of optical densitometry in health and disease of the anterior segment. Dhubhghaill and colleagues and Asrar and colleagues [8] and published the results of optical densitometry measurements with the Pentacam system in normal individuals of various age and ethnic background, demonstrating changes in COD with age, area and corneal depth. Our findings in normal eyes (the maximum COD was automatically found at the corneal apex at the level of the Bowman's membrane) are in general agreement with their findings.

There have been reports on increased COD readings after refractive [9, 10] and cataract surgery [7], corneal cross-linking in patients with keratoconus [11, 12], keratoplasty [13], etc. Our present study demonstrates that optical densitometry is an effective tool for objective monitor-

ing of corneal transparency in eyes treated for bacterial keratitis. Over two weeks of treatment, there was a gradual reduction in median (IQR) values of COD in the affected eyes from 92.8 (55.6–99.6) GSU to 80.6 (32.0–93.1) GSU, corresponding to an improvement in the clinical status of patients. There was, however, hardly any change in mean (SD) values of COD in the healthy fellow eyes over that period.

Conclusion

The use of optical densitometry for monitoring corneal transparency in eyes treated for bacterial keratitis over a two-week period enabled objective recording of a gradual reduction in median (IQR) values of COD in the affected eyes from 92.8 (55.6–99.6) to 80.6 (32.0–93.1) GSU, corresponding to an improvement in the clinical status of patients. Optical densitometry is a non-invasive technique enabling (1) easy and fast evaluation of pathological corneal changes in the region of inflammatory infiltration and (2) effective monitoring of longitudinal changes in the clinical status in patients with bacterial keratitis. The methodology presented is believed to be important and promising for further research, particularly for evaluating the efficacy of new treatments and comparing schemes for the conservative and surgical treatment of inflammatory corneal disorders.

References

1. WHO (2019). World report on vision. Geneva: World Health Organization; 2019. Available at: https://www.who.int/publications/i/item/world-report-on-vision (accessed 30 June 2020)
2. World Health Organization. Causes of blindness and visual impairment. Available at: http://www.who.int/blindness/causes/en. Accessed December 7, 2016.
3. Teweldemedhin M, Gebreyesus H, Atsbaha AH, et al. Bacterial profile of ocular infections: a systematic review. BMC Ophthalmol. 2017 Nov 25;17(1):212. https://doi.org/10.1186/s12886-017-0612-2
4. Cabrera-Aguas M, Khoo P, Watson SL. Infectious keratitis: A review. Clin Experiment Ophthalmol. 2022; 50(5): 543-562. https://doi.org/10.1111/ceo.14113
5. He Y, Ma B-S, Zeng J-H, Ma D-J. Corneal optical density: Structural basis, measurements, influencing factors, and roles in refractive surgery. Front Bioeng Biotechnol. 2023 Apr 6:11:1144455. https://doi.org/10.3389/fbioe.2023.1144455
6. Kuerten D, Plange N, Koch EC, et al. Central corneal thickness determination in corneal edema using ultrasound pachymetry, a Scheimpflug camera, and anterior segment OCT. Graefes Arch Clin Exp Ophthalmol. 2015 Jul;253(7):1105-9. https://doi.org/10.1007/s00417-015-2998-y
7. Hsieh TH, Yu HJ, Yang IH, et al. Simultaneously Monitoring Whole Corneal Injury with Corneal Optical Density and Thickness in Patients Undergoing Cataract Surgery. Diagnostics (Basel). 2021 Sep 7;11(9):1639. https://doi.org/10.3390/diagnostics11091639
8. Asrar A, Ikram B, Khan H, et al. Normal values of corneal optical densitometry using pentacam scheimpflug camera. Adv Ophthalmol Vis Syst. 2016;5(1):202–9. https://doi.org/10.15406/aovs.2016.05.00142
9. Adran D, Vaillancourt L, Harissi-Dagher M, et al. Corneal Densitometry as a Tool to Measure Epithelial Ingrowth After Laser In Situ Keratomileusis. Cornea. 2017 Apr;36(4):406-410. https://doi.org/10.1097/ICO.0000000000001114
10. Wei R, Li M, Yang W, et al. Corneal Densitometry After Small Incision Lenticule Extraction (SMILE) and Femtosecond Laser-Assisted LASIK (FS-LASIK): 5-Year Prospective Comparative Study. Front. Med (Lausanne). 2020 Nov 6:7:521078. https://doi.org/10.3389/fmed.2020.521078
11. Alnawaiseh M, Rosentreter A, Eveslage M, et al. Changes in Corneal Transparency After Cross-linking for Progressive Keratoconus: Long-term Follow-up. J Refract Surg. 2015 Sep;31(9):614-8. https://doi.org/10.3928/1081597X-20150820-07
12. Böhm M, Shajari M, Remy M, Kohnen T. Corneal densitometry after accelerated corneal collagen cross-linking in progressive keratoconus. Int Ophthalmol. 2019 Apr;39(4):765-75. https://doi.org/10.1007/s10792-018-0876-4
13. Kobashi H, Kamiya K, Shimizu K. Impact of Forward and Backward Scattering and Corneal Higher-Order Aberrations on Visual Acuity after Penetrating Keratoplasty. Semin Ophthalmol. 2018;33(6):748-756. https://doi.org/10.1080/08820538.2018.1427767.

Disclosures

Received: 04.01.2025

Accepted: 27.05.2025

Author Contributions: *Conceptualization and study design: OG, OZ, AK; Data curation and analysis: OG, WC, IN, PCh, OZ, OA, AK; Writing - original draft preparation: OG, OZ. All authors reviewed the results and approved the final version of the manuscript.*

Conflict of interest: *The authors declare no conflict of interest that could influence their views on the subject matter or materials described and discussed in this manuscript.*

Funding: *No.*

Abbreviations: *COD, corneal optical density; GSU, grayscale units*