• Clinical Research •

Endothelial parameters in central and peripheral cornea in patients wearing contact lenses

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Abstract

• AIM: To measure the parameters of endothelium in the central and peripheral parts of the cornea and evaluate the influence of wearing the hard and soft contact lenses on the mentioned parameters.

• METHODS: A specular microscope was used to measure the corneal endothelium parameters in both eyes of 139 Caucasians (a total of 278). All participants were divided into three groups: soft lens wearers, hard lens wearers and a control group. Factors, such as age, smoking, types of lens material, duration of lens wear and lens air permeability were assessed to determine their impact on the morphometric parameters of the endothelium.

• RESULTS: A lower percentage of hexagon-like cells and higher cell variation than in other groups were determined in hard contact lens wearers. The difference in density of endotheliocytes between the groups was not observed. The measurements of the morphometric parameters in soft contact lens wearers did not depend neither on the duration of lens wear, nor on air permeability. The relation between the patients' age and the variation of endothelium parameters was determined in the group of hard contact lens wearers.

• CONCLUSION: Wearing hard contact lenses provokes pleomorphism and polymegethism of the corneal endothelium, while soft contact lenses do not impact any parameters of the endothelium, most likely due to higher air permeability.

• KEYWORDS: corneal endothelium; morphometry; endothelial changes; contact lenses

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INTRODUCTION

Injuries of the corneal endothelium are related to a variety of eye diseases, such as corneal distrophies, critical reduction in the density of endotheliocytes, named as the most common cause of the corneal transplant rejection within five years after transplantation[1], and recently determined relation between density of endotheliocytes and expression of the symptoms of dry eye syndrome[2]. In order to standardize the degree of the corneal endothelial damage, the classification, based on the density of endotheliocytes and corneal changes identified during ophthalmobiomicroscopy, was suggested in 2014[3].

The studies describing the density of endotheliocytes not only in central but also in the peripheral cornea *in vivo* appeared already in 1977[4]. With the possibility of measuring endothelial parameters in the periphery using more and more automated and patient-friendly methods, this was started in order to more accurately predict endothelium changes and their effects after various interventions (*e.g.* LASIK, lamellar keratoplasty), and to specifically investigate the potential of endotheliocytes regeneration/proliferation at the corneal periphery which could be used to treat endothelial damage effectively[5-8].

The aim of this research is to measure the corneal endothelium parameters in the central and peripheral corneal areas and to determine the influence of the wear of soft and hard contact lenses on changes in these parameters in the Lithuanian population.

SUBJECTS AND METHODS

After receipt of an informed consent, 139 Caucasian patients (a total of 278 eyes) were involved to the research. Totally 31 males and 108 females at the age from 18 to 68 (33.12±19.97)y were involved. All participants had no anterior segment diseases, diabetes mellitus, no eye injuries or surgical treatment in anamnesis. All of them were divided into three groups: soft contact lens wearers (SCL), hard contact lens wearers (HCL) and a control group (CG) which included participants who have never worn contact lenses. Patients' anamnesis was collected on the following: age, sex, smoking, duration of contact lenses wear, type of contact lenses (daily-wear/ monthly-wear/ conventional-wear), type of contact lens material [silicone (Si)/ hydrogel (Hy)/ silicone-hydrogel (SiHy)/ rigid gas permeable (RGP)/ polymethyl methacrylate (PMMA)].

Central corneal thickness (CCT) and parameters of endothelium were assessed in central and six peripheral points of the cornea using a specular microscope (Topcon SP-1P). Examination

of the endothelium included endothelial cell density (ECD), polymegethism (variation of cells size-CV %) and pleomorphism (percentage of hexagon-like cells-HEX %). Only the data obtained after measuring at least 60 endotheliocytes were used in the research.

IBM SPSS® 20.0 (IBM Corporation, Armonk, NY, USA) and Microsoft Excel® 2007 (Microsoft Corporation, Redmond, WA, USA) were used for the statistical analysis. Student's *t*-test and Pearson's correlation coefficient (*r*) values were calculated. The data were considered statistically significant at $P<0.05$.

This study was approved by the Human Ethics Committee of Vilnius University Faculty of Medicine.

RESULTS

The CG included 67 participants: 20 males and 47 females aged from 21 to 68 (32.64±13.18)y. The group of the SCL consisted of 37 participants [6 males and 31 females aged from 23 to 45 (25±3.05)y] and the group of the HCL had 40 patients: 5 males and 35 females at the age from 18 to 64 (42±12.81)y.

Distribution of endothelial parameters in the examined points is shown in Table 1 (CG), Table 2 (HCL) and Table 3 (SCL). ECD varied from 1678.5 to 4421 cells/mm^2 and in superior corneal point was statistically significantly higher in all groups (P=0.002; Figure 1). ECD in the central cornea in CG and HCL groups was statistically significantly lower than in the peripheral points (P=0.002; Figure 1). Statistically significant ECD difference between all groups was not observed in any of the examined corneal points [center (C) P=0.02, superior (S) P=0.04, inferior (I) P=0.25, nasosuperior (NS) P=0.1, nasoinferior (NI) P=0.09, temporosuperior (TS) P=0.02, temporoinferior (TI) P=0.04].

The lowest CV was measured in the CG (20%), the highest in the group of HCL and the CG (52.50%). CV in HCL group was statistically significantly higher than in SCL and CG ($P<0.001$; Figure 2). The lowest HEX was measured in HCL group (28.5%), the highest in CG (81%). HEX in HCL group was statistically significantly lower than in SCL and CG ($P<0.001$; Figure 3).

Average measurement of CCT was 528.25±37.01 μm (ranged from 452 to 662 μm). CCT measured in the CG was 526.82±38.73 μm (ranged from 370 to 623 μm). In the SCL group 534.05±35.18 μm (ranged from 468 to 662 μm), HCL group 524.85±35.85 μm (ranged from 452 to 584 μm). Statistically significant CCT difference between all groups was not observed (P=0.52). Neither ECD, nor CV or HEX did not depend on CCT (P values, respectively, 0.41, 0.74 and 0.66).

There was a weak negative correlation between ECD and HEX with age in the CG (Table 4).

The CG included 9 smokers and 58 non-smokers. The group of SCL had 13 and 24, and the group of HCL had 5 and 30, respectively. In total there were 27 smokers and 112 non-smokers. In SCL group, longer time of smoking was associated

Table 1 Corneal endothelium parameters values in control group

Parameters	Localization	Mean	SD
Endothelial cell density (cell/mm^2)	Central	2899.22	295.74
	Superior	3346.52	420.70
	Inferior	2986.15	320.12
	Nasosuperior	2980.49	325.87
	Nasoinferior	2986.58	316.95
	Temporosuperior	3064.08	343.04
	Temporoinferior	3029.38	336.61
Polymegethism (%)	Central	29.91	3.34
	Superior	33.50	5.00
	Inferior	30.05	4.08
	Nasosuperior	30.56	4.46
	Nasoinferior	30.05	4.48
	Temporosuperior	31.05	4.19
	Temporoinferior	29.45	3.67
Pleomorphism (%)	Central	57.35	6.82
	Superior	55.24	7.49
	Inferior	59.80	6.69
	Nasosuperior	62.45	8.21
	Nasoinferior	60.88	7.63
	Temporosuperior	59.40	7.62
	Temporoinferior	57.35	6.82

SD: Standard deviation.

Table 2 Corneal endothelium parameters values in hard contact lens wearers

Parameters	Localization	Mean	SD
Endothelial cell density (cell/mm^2)	Central	2982.41	365.02
	Superior	3249.02	430.16
	Inferior	3078.60	401.45
	Nasosuperior	3108.00	366.33
	Nasoinferior	3089.41	428.86
	Temporosuperior	3194.80	407.21
	Temporoinferior	3078.14	423.05
Polymegetism (%)	Central	36.04	4.21
	Superior	36.32	6.08
	Inferior	34.84	5.44
	Nasosuperior	35.42	6.46
	Nasoinferior	34.10	5.53
	Temporosuperior	35.10	4.70
	Temporoinferior	33.35	3.61
Pleomorphism (%)	Central	48.52	7.27
	Superior	48.97	5.99
	Inferior	51.04	6.34
	Nasosuperior	52.54	7.78
	Nasoinferior	54.41	9.32
	Temporosuperior	51.62	6.37
	Temporoinferior	48.52	7.27

SD: Standard deviation.

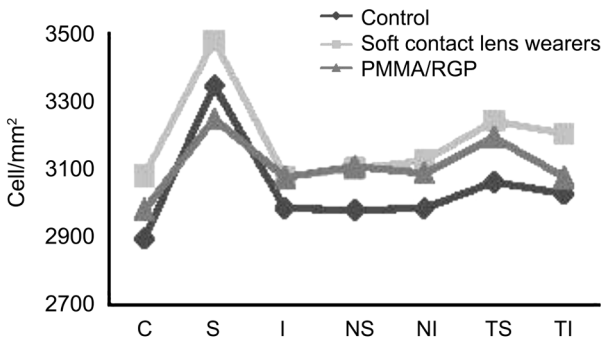

Figure 1 Distribution of the endothelial cell density in various corneal points.

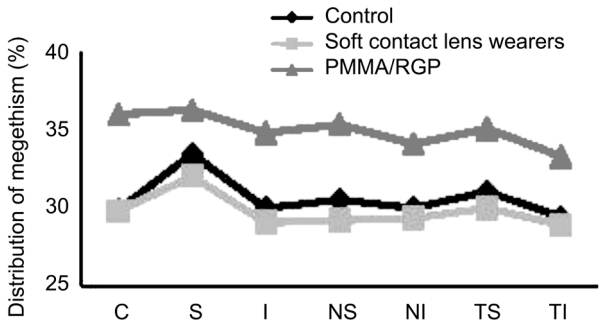

Figure 2 Distribution of megethism in various corneal points.

Table 3 Corneal endothelium parameters values in soft contact lens wearers

Parameters	Localization	Mean	SD
Endothelial cell density (cell/mm^2)	Central	3084.66	345.92
	Superior	3479.91	313.19
	Inferior	3079.31	266.93
	Nasosuperior	3103.54	352.63
	Nasoinferior	3126.75	267.89
	Temporosuperior	3241.44	270.62
	Temporoinferior	3206.72	266.24
Polymegetism (%)	Central	29.81	3.09
	Superior	32.05	4.81
	Inferior	29.08	3.25
	Nasosuperior	29.21	3.34
	Nasoinferior	29.33	3.17
	Temporosuperior	30.04	3.38
	Temporoinferior	28.94	2.93
Pleomorphism (%)	Central	56.56	6.82
	Superior	58.44	7.67
	Inferior	60.40	8.01
	Nasosuperior	63.79	7.04
	Nasoinferior	61.52	8.41
	Temporosuperior	60.75	7.40
	Temporoinferior	56.56	6.82

SD: Standard deviation.

with a reduction in the values of ECD (Table 5). According to the significance value, there was no correlation between the parameters and smoking (Table 6).

The duration of lenses wear in SCL group varied from 3 to 144mo (62.54±40.63mo). In this group, there was no correlation between duration and other parameters (Table 7). Daily-wear lenses were worn by 1 (2.7%), monthly-wear by 36 (97.3%) participants. This is why the impact of lenses wearing mode was not evaluated. Permeability of oxygen in SCL group varied from 19.7 to 175. Permeability of oxygen had no statistically significant impact on the studied parameters (Table 8). Using the linear regression method and measuring influence of permeability of oxygen, duration of lens wear and mode, on all parameters of endothelium, revealed that none of these factors had more impact than others (Table 9).

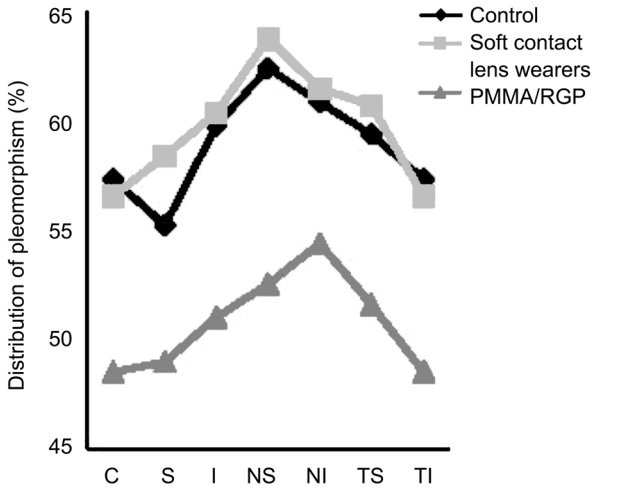

Figure 3 Distribution of pleomorphism in various corneal points.

Table 4 Correlation between endothelial parameters and age

Group	Parameters	*P* (Pearson)	Correlation
Control	Endothelial cell density	0.000	-0.490
	Polymegethism	0.273	
	Pleomorphism	0.000	-0.430
Soft contact lens	Endothelial cell density	0.131	
	Polymegethism	0.152	
	Pleomorphism	0.116	
Hard contact lens (PMMA/RGP)	Endothelial cell density	0.259	
	Polymegethism	0.033	
	Pleomorphism	0.731	

Table 5 Correlation between endothelial parameters and duration of smoking

Group[a]	Parameters (periphery)	*P* (Pearson)	Correlation
Control	Endothelial cell density	0.878	
	Polymegethism	0.098	
	Pleomorphism	0.022	
Soft contact lens	Endothelial cell density	0.004	-0.742
	Polymegethism	0.238	
	Pleomorphism	0.424	
Hard contact lens (PMMA/RGP)	Endothelial cell density	0.886	
	Polymegethism	0.396	
	Pleomorphism	0.126	

[a]All participants-smokers.

Table 6 Correlation between endothelial parameters and smoking

Group	S+/S-	Parameters	Mean	SD	*P* (Pearson)
Control	Smokers (S+)	Endothelial cell density	2896.73 cell/mm^2	312.68	0.200
		Polymegethism	32.69%	4.99	0.200
		Pleomorphism	57.95%	6.29	0.177
	Non-smokers (S-)	Endothelial cell density	3091.73 cell/mm^2	312.68	0.200
		Polymegethism	30.48%	3.72	0.078
		Pleomorphism	59.38%	5.99	0.200
Soft contact lens	S+	Endothelial cell density	3197.46 cell/mm^2	277.35	0.200
		Polymegethism	30.23%	3.40	0.200
		Pleomorphism	60.39%	6.09	0.200
	S-	Endothelial cell density	3211.05 cell/mm^2	247.77	0.200
		Polymegethism	29.53%	2.76	0.200
		Pleomorphism	60.17%	6.31	0.117
Hard contact lens (PMMA/RGP)	S+	Endothelial cell density	2880.63 cell/mm^2	411.19	0.146
		Polymegethism	32.70%	4.18	0.200
		Pleomorphism	52.31%	5.69	0.200
	S-	Endothelial cell density	3175.05 cell/mm^2	334.40	0.062
		Polymegethism	35.21%	4.58	0.200
		Pleomorphism	51.00%	5.43	0.200

SD: Standard deviation.

Table 7 Correlation between endothelial parameters and duration of soft contact lens wear

Parameters	*P*
Central-endothelial cell density	0.068
Central-polymegethism	0.109
Central-pleomorphism	0.160
Peripheral-endothelial cell density	0.508
Peripheral-polymegethism	0.384
Peripheral-pleomorphism	0.630

Table 8 Correlation between endothelial parameters and soft contact lens permeability of oxygen

Parameters	*P*
Central-endothelial cell density	0.845
Central-polymegethism	0.385
Central-pleomorphism	0.526
Peripheral-endothelial cell density	0.688
Peripheral-polymegethism	0.516
Peripheral-pleomorphism	0.381

Table 9 Various predictors impact on endothelial parameters in soft contact lens group

Parameters	Predictors	*P*
Central-endothelial cell density	Dk/t	0.948
	Duration	0.518
	Schedule	0.127
Central-polymegethism	Dk/t	0.711
	Duration	0.194
	Schedule	0.252
Central-pleomorphism	Dk/t	0.954
	Duration	0.031
	Schedule	0.200
Peripheral-endothelial cell density	Dk/t	0.319
	Duration	0.614
	Schedule	0.010
Peripheral-polymegethism	Dk/t	0.757
	Duration	0.540
	Schedule	0.303
Peripheral-pleomorphism	Dk/t	0.736
	Duration	0.119
	Schedule	0.275

In HCL group PMMA lenses were worn by 11 (31.42%) participants, RGP by 8 (22.85%) participants. Totally 16 (45.71%) patients at first wore PMMA lenses which later were changed into RGP-these participants were assessed as mixed wearers. The type of contact lens material did not make any statistically significant impact on endothelial parameters. Measuring in the central cornea (C) ECD *P*=0.206, CV *P*=0.146, HEX *P*=0.491, in the peripheral cornea (P) ECD *P*=0.029, CV *P*=0.070, HEX *P*=0.048. PMMA lenses were being worn from 12 to 492 (242.33±122.71)mo, Boston XO from 24 to 204 (112.83±53.20)mo. PMMA lenses were being worn statistically significantly longer than Boston XO (*P*=0.000). Duration of lenses wear did not have any impact on endothelium parameters (C) ECD *P*=0.903, CV *P*=0.069, HEX *P*=0.249, (P) ECD *P*=0.682, CV *P*=0.012, HEX *P*=0.011. Based on the linear regression method, participants' age had a statistically significant impact on ECD in the peripheral cornea (Table 10).

Table 10 Various predictors impact on endothelial parameters in hard contact lens (PMMA/RGP) group

Parameters	Predictors	*P*
Central-endothelial cell density	Material	0.078
	Duration of wear	0.040
	Age	0.016
Central-polymegethism	Material	0.934
	Duration of wear	0.734
	Age	0.308
Central-pleomorphism	Material	0.642
	Duration of wear	0.157
	Age	0.357
Peripheral-endothelial cell density	Material	0.016
	Duration of wear	0.010
	Age	0.001
Peripheral-polymegethism	Material	0.254
	Duration of wear	0.617
	Age	0.177
Peripheral-pleomorphism	Material	0.442
	Duration of wear	0.101
	Age	0.892

DISCUSSION

HCL group had a higher pleomorphism and polymegethism than other groups. Many of the studies published so far point out both CV and HEX changes in wearing contact lenses[9-10]. In 2001, Lee *et al*[11] wrote about the difference in the variation of cells size between those, who did not wear contact lenses, and those, who had a history of wearing lenses for at least 10y (respectively 22%-29% and 26%-33%). HEX percentage reduction was from 59.4%-71% in those not wearing lenses and up to 47.5%-70% when wearing lenses for a minimum of ten years[11]. In wearing contact lenses, a more significant variation of the parameters from the norm correlates with the corneal hypoxia[12]. Possibly, analogical changes were not discovered in SCL group because of lenses' higher oxygen permeability. It is important to note that in HCL group the average of patients' age was higher than in other groups. Different authors have contradicting opinions about the impact of age on pleomorphism and polymegethism. Some of them state that the age has no influence on rates, while others claim that they increase with age[12-14]. Some authors state that the expression of pleomorphism takes time and it is not such a change of endothelium that can be quickly revealed, yet it is a highly sensitive marker of the endothelial damage and instability[12]. Neither change of CV, nor of HEX causes corneal decompensation or clinical expression. Meanwhile, CV increase and HEX decrease are related to the subsequent reduction of ECD and are considered to be its precursors[12].

In HCL group, ECD statistically significantly did not differ from SCL and CG and its mean was not lower in this age group than the one mentioned in literature[15-21]. This does not interfere with research describing ECD when wearing contact lenses and it is explained by the fact that reduction of endotheliocytes, unlike pleomorphism and polymegethism, it is not an early reaction to stress (mainly hypoxia and hypercapnia[22-23]), but is a late outcome of wearing lens for a long time[12] or does not appear at all after wearing gas permeable lenses[24]. ECD decrease with aging, indicated by many sources[13,19,25], was observed only in HCL and CG when measuring endotheliocytes in the corneal periphery. Although it is claimed that the morphometric endothelial parameters are the most stable at the age of 15-50y[11], ECD decrease in SCL group did not show up possibly due to the group very homogenous in age (standard deviation was only 3.05) while the age of participants was more varied in HCL and CG groups.

In HCL and CG, ECD in the central cornea was lower than in the periphery. This is likely to be associated with homogenous age of participants in SCL group. It is assumed that the cause of higher density in the endothelial periphery can be the lack of space for endotheliocytes growth[26].

The corneal pachymetry performed in our investigation showed thinner corneas than the means presented in the research carried out in 2013 in which the Lithuanian population with equal age was examined[14]. Small errors are possible due to different methods of measurement.

Corneal thickness did not have any impact to the endothelial morphometric parameters. There are some studies that find no relation between CCT and ECD[26]. Others claim that thinner corneas have lower ECD[20,27]. It is found that the cornea decompensates and its oedema develops when critical reduction (400-500 cells/mm^2) of ECD is reached[26].

Smoking did not have any influence on the endothelial parameters, though it was observed that longer duration of smoking causes endothelial thinning. It is confirmed in Sayin *et al*[28] research which was performed in 2014.

In SCL group duration of lenses wear and permeability of oxygen did not influence any of the endothelial parameters. The possible impact of duration of wear was not observed due to short time (average 5y). Most sources state that more stable endothelial changes are observed when lenses are worn for at least 6y[11], although there are those who claim that 25y are required[12]. Permeability of oxygen had no impact most likely due to highly oxygen permeable contact lenses. After reaching permeability of oxygen of at least 200, open eye oxygenation is the same as without contact lenses[29]. This is why literature states that the contemporary materials of contact lenses solve hypoxia[24,30-31]. However, it is admitted that the endothelial changes depend not only on hypoxia, but also on hypercapnia[22-23]. Therefore, the future works for the manufacturers of lenses will be targeted not only at increase of Dk/t, but also at reduction of hypercapnia.

The evaluation ofthe impact of HCL materials on the corneal endothelium was impossible in this research because of a small sample of patients. Also, the majority of those who wore not oxygen permeable PMMA lenses at first, after some time changed them to oxygen permeable lenses. Although there were no significant differences inside this group, there was evident CV increase and HEX decrease in HCL group as compared to SCL and CG.

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