

The Research of the Effect of Eye Drops Containing Quercetin for Regeneration of the Cornea in the Experiment

Kliuiev GO* and Kolomiichuk SG

The Health Technology Ltd., Odessa, Ukraine

Abstract

In the research on 7 rabbits was studied the influence of the eye drops on the cornea that contain bioflavonoids-quercetin. Corneal damage was induced by application of filter paper disc, impregnated with 20% solution of ethyl alcohol with increasing time on 60 s. In the control eye were dripped saline, in the studied eye—drops containing quercetin. The severity of corneal edema was evaluated by examination of corneal thickness, by using Pachymeter Tomey SP-100. The study was performed before effect and on 1st, 3rd and 7th days after effect. There was statistically significant reduction of edema (the thickness normalization of rabbit cornea) in a shorter time under the influence of a quercetin-containing drop.

Keywords: Quercetin; Eye drops; Cornea; Edema; Cataract; Phacoemulsification; Pachymetry; Experiment

Introduction

The sufficiently common problem after ultrasound phacoemulsification of solid (brown) cataracts is damage of the corneal endothelium with the appearance of descemetitis and edema, which sometimes leads to corneal dystrophy. Also cornea suffers with various injuries and viral diseases. Therefore, the study of the application of various medications to reduce the cornea edema is very important [1-5]. Currently, special attention is giving to the development of biologically active components with anti-inflammatory and antiproliferative properties and with antioxidant action, particularly the bioflavonoids [6].

The aim of our research was to study the effects of eye drops containing the bioflavonoid quercetin on the regeneration of rabbits' cornea in the experiment.

Materials and Methods

The experimental research was performed on 7 rabbits of the breed Chinchilla weighing between 1.7-1.8 kg. The room temperature was maintained at $20 \pm 1^\circ\text{C}$ with a 12 h light/dark cycle. Food and water were given *ad libitum*. This experimental study was conducted in accordance with the provisions of the "European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes" (Strasbourg, 1986). On the animals corneal shell of the right eye (control eye) and left eye (subject eye) was putting the application disc of filter paper 10 mm in diameter, impregnated with 20.0% solution of ethyl alcohol [7] for 60 s. Then daily for 7 days on the cornea of the left eye (research eye) was dripped the eye drops that contain the bioflavonoid quercetin 3 times a day. On the cornea of control eye daily for 7 days was dripped the sodium chloride solution 0.9%.

The clinical evaluation of the eyes condition of animals was performed according to the following criteria: the degree of inflammatory response and recovery time of the epithelium of the cornea. Objective criteria for the evaluation of the effects results were the studies of the thickness of the cornea of experimental animals with the help of pachymetry "Handy Pachymeter SP-100" (Japan).

The sample size was calculated for an alpha error of 0.05 and power at 90%. Each animal measured the thickness of the cornea of right and left eyes in 8 replicates. The mean thickness of the cornea of each animal was added to the database. Data was expressed as mean and Standard Deviation (SD) in μm . P values of less than 0.05 were considered

statistically significant. The obtained data were processed with the help of the Statistica 7 program by using the nonparametric criterion for connected groups Friedman ANOVA, for pairwise comparisons—Wilcoxon test and unconnected groups Mann-Whitney test.

Results and Discussion

At observing for the experimental animals after effects of 20.0% solution of ethyl alcohol was no signs of development of purulent complications. Epithelialization of the cornea in control and research eyes occurred not later than on 7-9 days. To 7 days in the control and research eyes all signs of inflammation were stopped, the cornea remained transparent, and was covered with epithelium. In the Table 1, there are presented the parameters of descriptive statistics that present the experimental data about the effect of eye drops containing quercetin on the change of corneal thickness after modeling of corneal edema under the effect of 20.0% solution of ethyl alcohol.

At the use of the nonparametric criterion for connected groups Friedman ANOVA and Kendall Coefficient of Concordance was found that in all periods of observation in the control eyes Chi Sq. was 18.77143, $p=0.00030$; Coef. of Concordance=0.89388, Aver. rank $r=0.87619$. At processing data of the corneal thickness of the eyes treated with instillation of bioflavonoid quercetin, indicators Chi Sqr. were 15.34286, $p=0.00155$; Coef. of Concordance=0.73061, Aver. rank $r=0.68571$.

In the Table 2, there are presented data at the study of the effect of eye drops containing quercetin to change the thickness (μm) of the rabbit cornea calculated using the Wilcoxon test for pairwise comparisons. According to the obtained data in the control eyes of rabbits on the first day of observation, the corneal thickness was 426.00 ($8.2 \mu\text{m}$), that on 14.0% more compared to the original data ($p<0.02$). After 3 and 7 days of observation, thickness of the cornea in the control eyes decreased, significantly different from the original data.

*Corresponding author: Kliuiev GO, The Health Technology Ltd., Odessa, Ukraine, Tel: +38050 333 96 01; E-mail: karine@kluev.com.ua

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In the research eyes in the 1 day after instillation of eye drops containing the bioflavonoid quercetin, the thickness of the cornea was 413.7 (7.8) μm that was 109.0 % from the original data ($p < 0.02$). In the same group after 3 days, a measure of corneal thickness is still significantly differed from the original data, representing 394.1 (6.4). After 7 days of observation, thickness of the cornea in the research eyes significantly decreased, not significantly different from the original data. At comparing data of the thickness of the cornea of rabbits treated with instillation of quercetin with data in the control eyes was noted the significant differences between the groups after 1 and 3 days of the experiment (Table 3).

Conclusion

The change of the thickness of the cornea due to various causes, including the burn process or surgical intervention, can contribute the development of deeper structural and functional disturbances in the eye tissues and development of pathological processes [2,8-10].

In a number of studies were shown that the bioflavonoids (quercetin) can be widely used in the prevention and treatment of various eye diseases, including the development of metabolic and ischemic disorders in the tissues of the eye, cataract and fundus pathology [11-13].

Currently, a lot of attention is spent to the development of drugs with elevated bioavailability of physiologically active components of eye drops, especially to the degree of their penetration into the tissues of the eyes and the improvement of the effectiveness of their action [12,14,15]. The obtained data indicate that process of cornea regeneration after application method of effect of 20-% solution of ethanol under the application of eye drops containing the bioflavonoid quercetin occur in earlier periods compared with the control eyes (without treatment). Thus, the noted effectiveness of eye drops containing quercetin that we have developed at local application evidence about increasing resistance of the cornea to the damaging action of pathochemical factor that can be particularly important in pre- or post-operative period in patients with pathology of the anterior eye.

Terms	n	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	Std.Dev.
Control eyes							
Original data	7	374.00	364.00	380.00	369.00	379.00	5.62
1 day	7	428.00	409.00	435.00	424.00	429.00	8.16
3 days	7	407.00	391.00	411.00	400.00	411.00	7.33
7 days	7	388.00	379.00	394.00	381.00	393.00	5.79
Subject eyes (quercetin)							
Original data	7	381.00	368.00	386.00	375.00	385.00	6.31
1 day	7	416.00	401.00	421.00	406.00	420.00	7.76
3 days	7	393.00	385.00	402.00	388.00	400.00	6.41
7 days	7	392.00	383.00	394.00	383.00	393.00	5.20

Table 1: Parameters of descriptive statistics at the study of the effect of eye drops containing quercetin to change the thickness (μm) of the rabbit cornea.

Researched groups	Statistical indicators	The periods of observation, day			
		Before application	1 day	3 days	7 days
Control eyes	n	7	7	7	7
	Mean	373.6	426.0	405.1	387.4
	SD	5.6	8.2	7.3	5.8
	p	-	<0,02	<0,02	<0,05
	%	100.0%	114.0%	108.4	103.7
Research eyes	n	7	7	7	7
	Mean	379.7	413.7	394.1	388.9
	SD	6.3	7.8	6.4	5.2
	p	-	<0,02	<0,02	>0,05
	%	100.0%	109.0	103.8	102.4

p-level of significance of differences of data between groups for pairwise comparisons for Wilcoxon

Table 2: The effect of eye drops containing quercetin to change the thickness of the rabbit cornea (μm).

Terms	Rank Sum	Rank Sum	U	Z	p-level
Original data	37.50	67.50	9.50	1.91663	0.055286
1 day	72.00	33.00	5.00	2.49162	0.012717
3 days	70.50	34.50	6.50	2.29996	0.021451
7 days	48.50	56.50	20.50	-0.51110	0.609281

p-level of significance of differences of data between groups calculated using Mann-Whitney Test for independent samples

Table 3: The effect of eye drops containing quercetin to change the thickness of the rabbit cornea (μm) at comparing the control and the research eyes.

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