Temperature of the ocular surface in the projection of the ciliary body in rabbits

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Background: *Studies on local body temperatures improve the potential for analysis of biological processes in organs and tissues of the body. A study on changes in ocular surface temperature in an animal model of non-infectious uveitis for objectively assessing ocular inflammation is planned for the future.*

Purpose: *To determine normal temperatures of the ocular surface in the projection of the ciliary body in rabbits.*

Material and Methods: *Temperature of the ocular surface in the projection of the pars plana was measured in 42 Chinchilla rabbits using a thermoelectric device.*

Results: *There was no significant difference in mean temperature between the nasal ocular surface and the temporal ocular surface in the projection of the ciliary body (34.13 °C (SD=1.45) against 34.09 °C (SD=1.48), p = 0.57). In addition, there was a very weak correlation of room temperature with body temperature and ocular surface temperature. Mean ocular surface temperature for the right eye was 34.1°C (SD=1.43), and for the left eye, 34.2°C (SD=1.43), but the difference in this measure between the right and left eyes was not significant (p = 0.27).*

Conclusion: *There was no significant difference in the temperature of the ocular surface in the projection of the ciliary body between the right and left eyes in the absence of pathological changes. The mean temperature of the ocular surface in the projection of the ciliary body in intact rabbits was 34.1°C (SD=1.4). Temperature of the ocular surface in the projection of the ciliary body in rabbits is characterized by autonomic thermoregulation and is relatively stable at small environmental temperature variations. The pattern of heat exchange in rabbit's ocular surface allows for modeling of unilateral ocular pathological processes that would have a change in local body temperature in the projection of the ciliary body as an objective marker.*

Keywords:

objectivization of inflammation assessment, ocular surface temperature, ciliary body, thermoelectric device

Introduction

At least 150 conditions are known to be associated with intraocular inflammation. Uveitis is a pathogenetically complex and potentially blinding intraocular inflammatory condition whose etiology remains elusive and whose treatment continues to be a challenge despite recent advances [1-4]. The severity of ocular inflammatory injury depends on the activity and type of inflammation. The decision on the amount of immune suppression and duration of immune suppression therapy to be administered should be based on the assessment of inflammation severity. Therefore, the clinician's decision on the treatment strategy and duration of treatment should be guided by quantitative assessment of inflammation.

Currently, most studies use Standardization of Uveitis Nomenclature (SUN) and National Institutes of Health (NIH) classification schemes for assessing uveitis activity [5, 6]. However, one of the major disadvantages of these classification schemes and their methodologies used for detecting inflammation in the aqueous and vitreous is subjective grading. A study demonstrated disparity in slit lamp flare readings between clinical graders in clinical grading in 35% of eyes [7, 8].

A change in the degree of activity of the process is an important index for assessing the efficacy of therapy in patients with uveitis [9]. Laser flare-cell photometry provides an automated technique to quantify the assessment of cells and protein levels ("flare") in the aqueous humor objectively, and it has been used in a variety of research and clinical situations to assess even subclinical anterior segment inflammation [10-14]. A number of factors (the degree of mydriasis, cataract, and/or posterior synechiae) can affect the results of laser flare-cell photometry. In addition, the broad application of the technique is limited by high cost of laser flare-cell photometer and the absence of consensus on the clinical value of the methodology [15, 16].

Studies on local body temperatures improve the potential for analysis of biological processes in organs and tissues of the body. Heat energy is constantly produced in the body and the amount of heat energy produced depends on the intensity of metabolic and inflammatory processes as well as state of circulation [17].

It is at the local level associated with inflammation focus that the signs of inflammation (hyperemia, locally increased temperature, edema, pain and impaired function of the damaged organ) are revealed, the mechanisms behind these signs being the molecular and cellular inflammatory mechanisms [18].

Researchers have been searching for simple, inexpensive and reliable methods for objective assessment of intraocular inflammation for years. Since measurement reproducibility is important, especially in clinical trials, recently, researchers have been trying to gradually change subjective inflammation assessment methods in favor of objective inflammation assessment methods. Local measurements of temperature responses have been successfully used in other fields of medicine, and seem promising for objective assessment of ocular inflammation. Research on changes in ocular surface temperature in an animal model of non-infectious uveitis is planned for the future to determine whether it is possible to objectively assess inflammation using ocular surface temperature, and to match these changes with pathoanatomical changes. With this in mind, we have to determine normal temperatures using precise measurement equipment, and to determine whether rabbit eyes are suitable for this purpose.

Therefore, **the purpose** of the study was to determine normal temperatures of the ocular surface in the projection of the ciliary body in rabbits.

Material and Methods

Forty-two Chinchilla rabbits (84 eyes; weight, 2.5-3.0 kg) were included in this study. Prior to baseline, they were under quarantine for two weeks. The animals were housed under conventional vivarium conditions, and fed and watered conventionally.

All animal experiments were performed in compliance with the Law of Ukraine on Protection of Animals from Cruel Treatment No. 3447-IV dated 21.02.2006 and European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes from the European Treaty Series (Strasbourg, 1986), and approved by a local Bioethics Committee of the Filatov Institute.

Temperature of the ocular surface in the projection of the ciliary body (2-3 mm from the limbus) was measured through direct contact of the probe tip and nasal or temporal scleral conjunctiva 15 minutes after both eyes received a drop of proxymetacaine HCl (0.5%) for topical anesthesia. Real-time temperature measurements were recorded every 4 seconds. Measurements were performed at least three times in each of the compartments. Rectal temperature and room temperature were also recorded. Studies were performed under minimal indoor air velocity.

A thermoelectric device [19] developed within the framework of the partnership agreement between the Institute of Thermoelectricity of the NAS of Ukraine and MES of Ukraine, and the Filatov Institute was used for measuring ocular surface temperature. The device allows for measurements every 4 seconds within a temperature range of -10°C to + 120°C with a measurement error of ± 0.08°C.

Data is presented as mean ± standard deviation (SD). Statistical analyses were conducted using Statistica 8.0 (StatSoft, Tulsa, OK, USA) software. The level of significance $p \leq 0.05$ was assumed.

Results and Discussion

The ambient room temperature was between 18 °C and 23 °C.

Body temperature in intact rabbits followed a normal distribution (K-S d = 0.08, p>0.2) (Fig. 1).

Mean temperature of the nasal ocular surface in the projection of the ciliary body was 34.13 °C (SD=1.45), and mean temperature of the temporal ocular surface was 34.09 °C (SD=1.48). Since there was no statistically significant difference (p=0.57) between these mean values, for convenience of subsequent calculations, we were taking into account mean temperature of the ocular surface in the projection of the ciliary body.

Ocular surface temperature in intact rabbits followed a normal distribution (K-S d = 0.09, p>0.2) (Fig. 2).

Temperature of the ocular surface in the projection of the ciliary body ranged from 30.55 °C to 36.35 °C, with a mean value of 34.11 °C (SD=1.421) (Table 1).

There was a mild correlation between room temperature and body temperature (r=0.30; p=0.05). In addition, there was a very weak but not significant correlation (r=0.02; p = 0.9) between room temperature and temperature of the ocular surface in the projection of the ciliary body. Moreover, there was a very weak but not significant negative correlation (r=-0.04; p = 0.82) between body temperature and temperature of the ocular surface in the projection of the ciliary body. We found a significant positive correlation between temperatures of temporal and nasal ocular surface (r = 0,895, p = 0.0001).

It seemed strange that correlation of room temperature with body temperature and temperature of the ocular surface in the projection of the ciliary body was weak and not significant. For this reason, we additionally assessed whether there was a significant difference in mean temperature between the body and ocular surface at different room temperatures. For this purpose, we separated room temperatures into two categories: first, those below 20°C, and, second, those above 20°C. At room temperatures below 20°C, the mean body temperature was 38.97°C, and at room temperatures above 20°C, the mean body temperature was 39.17°C, but the difference was not significant (p = 0.19). In addition, at room temperatures below 20°C, the mean temperature of the ocular surface in the projection of the ciliary body was 34.3°C, and at room temperatures above 20°C, it was 33.69°C, but the difference was also not significant (p = 0.17).

A rabbit study by Schwartz [20] assessed the effect of environmental temperature on temperatures of the corneal surface, conjunctiva, intraocular media and orbit. Three ranges of environmental temperatures were used: 22.0 to 27.5 °C, 15.9 to 17.6°C, and 2.2 to 4.4 °C.

Rectal temperature was noted to decrease with a decrease in air temperature, and there was a linear relationship between a decrease in corneal surface and conjunctival temperatures and a decrease in environmental temperature. In addition, the decrease in the temperature of the cornea was five times as large as that in the temperature of the inferior conjunctival fornix, which was likely due to the avascularity of the cornea. Moreover, temperatures of all intraocular structures were noted to decrease with a decrease in environmental temperature [20].

Others reported similar findings on the effect of environmental factors on corneal surface temperature in rabbits. In addition, a linear relationship between corneal surface temperature and air temperature at zero air speed has been reported [21, 22]. Our findings of weak and not significant correlation of environmental temperature with body temperature and temperature of the ocular surface in the projection of the ciliary body could be explained by the fact that, as opposed to the above studies, the environmental temperature in the current study varied within a small range. Therefore, for this small environmental temperature range, the autonomic thermoregulation may ensure relative stability in the temperature of the ocular surface in the projection of the ciliary body.

The temperature of the ocular surface in the projection of the ciliary body was 5°C below body temperature, and this difference was significant (p=0.0001) (Fig. 3).

Mean ocular surface temperature for the right eye was 34.1°C (SD=1.43), and for the left eye, 34.2°C (SD=1.43). There was a 0.11°C difference in ocular surface temperature between the right and left eyes, but this was not significant (p = 0.27) (Fig. 4).

The absence of significant difference in the temperature of the ocular surface in the projection of the ciliary body between the right and left eyes is in line with findings of a previous study [19]. This would enable (1) modeling of various unilateral processes that result in a change in local body temperature (e.g., intraocular inflammatory processes) and (2) subsequent assessment of relationships between temperature changes and clinical and anatomical signs of the disease. In addition, the autonomic thermoregulation and stability in the temperature of the ocular surface in the projection of the ciliary body for a small environmental temperature range create good conditions for studies aimed at the development of new methods for quantifying inflammation objectively.

Conclusion

First, there was no significant difference in the temperature of the ocular surface in the projection of the ciliary body between the right and left eyes in the absence of pathological changes. The mean temperature of the ocular surface in the projection of the ciliary body in intact rabbits was 34.1°C (SD=1.4).

Second, temperature of the ocular surface in the projection of the ciliary body in rabbits is characterized by autonomic thermoregulation and is relatively stable at small environmental temperature variations.

Finally, the pattern of heat exchange in rabbit's ocular surface allows for modeling of unilateral ocular pathological processes that would have a change in local body temperature in the projection of the ciliary body as an objective marker.

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Table 1. Temperature of the ocular surface in the projection of the ciliary body in rabbits

Characteristic	Number of eyes	Mean value	Median value	Minimum	Maximum	Standard deviation (SD)
Temperature of the ocular surface in the projection of the ciliary body	84	34.1°C	34.4°C	30.6°C	36.4°C	1.4

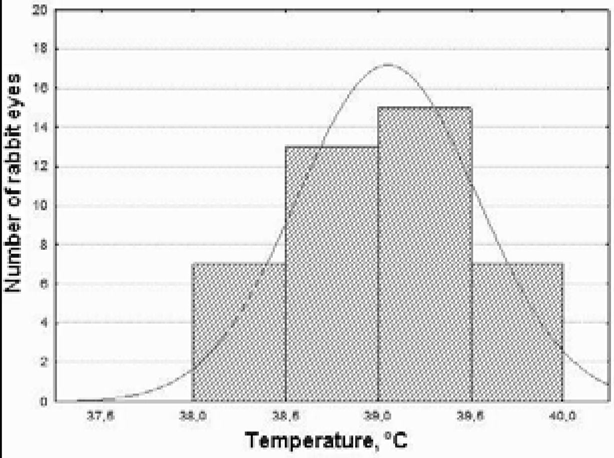

Fig. 1. Histogram of body temperatures recorded for intact rabbits

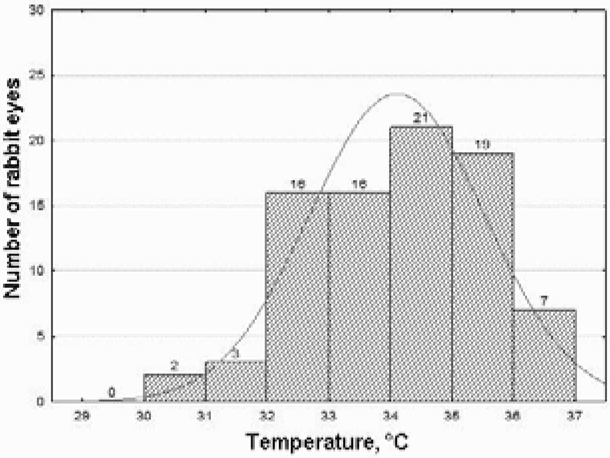

Fig. 2. Histogram of temperatures of the ocular surface in the projection of the ciliary body recorded for intact rabbits

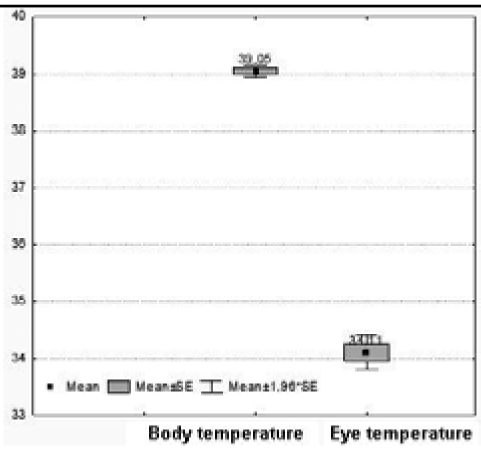

Fig. 3. Body temperature and temperature of the rabbit's ocular surface in the projection of the ciliary body

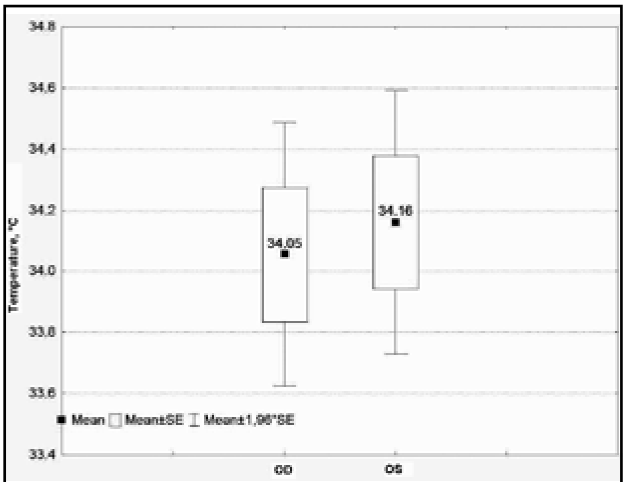

Fig. 4. Temperature of the rabbit's ocular surface in the projection of the ciliary body for the right and left eyes