Central corneal thickness increases with age in cattle

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SUMMARY

The aim of this study was to identify the physiological reference values for central corneal thickness (CCT) and the age-related changes in CCT in healthy dairy cattle. The age of 50 dairy cows was recorded in days and the CCT values of both eyes were measured using an ultrasonographic pachymeter device. The mean age of the cows was 781.38 days and the mean CCT value was 799.44 µm. There was a positive correlation between age and CCT ($p<0.001$, $y = 751.34 + 0.0616x$, $R2=0.2104$). Knowing the corneal thickness and age-related changes is important physiologically and pathologically. Medical treatment costs in eye diseases, injury due to extra procedure, decreased weight gain, decreased milk production and the transfer of animals that do not respond to treatment cause economic loss. In literature searches, no studies were found on this subject, except for a few studies (one of them postmortem) conducted about 25 years ago. The present study is the first study conducted on dairy cattle in the same environmental conditions in an organic farm. According to the presented study corneal thickness increases with age. In conclusion, corneal thickness in cattle changes over their lifetime and is similar to that reported in other mammals. Knowing the age-related physiological change of corneal thickness has diagnostic, epidemiological and pathological importance.

KEY WORDS

Bovine, cattle, central corneal thickness, cornea, ultrasound pachymeter, pachymetry.

INTRODUCTION

The integrity of the optic surface against threats coming from outside the cornea is important to be able to perform the act of seeing. The structure of the corneal epithelium, and the cellular and chemical components of the conjunctiva and tear film layer protect the corneal surface against pathogen agents and micro-organisms[1].

Light passes into the eye because of the clear and avascular structure of the cornea. Refracting light rays passing through the lens are transformed to electrical and chemical energy by reaching the retina. The signals obtained are analysed through transmission to the brain by the optic nerve and are perceived as an image. As the external surface of the cornea is convex, it protects intra-ocular organs, maintains intra-ocular pressure, and provides light refraction[2] The cornea consists of 5 layers, which from inner to outer are the epithelial layer, the lamina limitans anterior, stroma layer, Descemet membrane, and endothelial layer. The corneal surface has a specific structure. Although cells in the corneal epithelium are non-keratinised, they are named keratocytes, and are accepted as the continuation of the bulbar conjunctiva. Keratocytes are multi-layered. The corneal epithelium is formed of 3 different types of cells. These are 2-3 rows of surface cells, 2-3 rows of wing cells and 1 row of a columnar basal cell layer. Only basal cells show proliferation activity [3,4]. The lamina limitans anterior is a thin and uniform structure of the epithelium expressed by basal cells. The Descemet membrane is the basal membrane of the epithelium. The endothelial layer is formed of a single layer of cells, and the anterior chamber is bordered [5].

Corneal thickness was first measured by Blix [6] on human eye but until the mid 20th century, no studies were conducted related to corneal thickness. In 1951, David Maurice [7] designed the pachymeter and for human cornea thereafter, many studies of corneal thickness were conducted. In two studies on bovine corneal thickness, it was reported that measurements were made by ultrasound after slaughter [8,9]. The biological variations of corneal thickness depend on changes in the amount of collagen fibrils and interfibrillar substance which form the corneal stromal tissue in both human and veterinary ophthalmology. In healthy individuals, corneal thickness is therefore, a measure of tissue mass and corresponding biomechanical parameters such as bending rigidity[10].

There are many methods of measuring corneal thickness. The ultrasonographic pachymeter device makes contact with the cornea and measures corneal thickness with the principle of ultrasonography. In literature, there are many comparative studies in veterinary and human subjects [11-14]. The ultrasonographic pachymeter device is extremely sensitive with up to 0.004 mm difference in repeated measurements [15] .

Corneal thickness shows a difference according to species and even according to breed. Age-related changes are seen in both animal and human corneal thickness [1,4]. It has been reported that there is an increase in corneal thickness due to stromal hydration. This means that based on the data, corneal thickness can be used as an index of endothelial damage[16]. Decreased corneal thickness is seen in many corneal dystrophies and secondary to ulcerative inflammatory diseases of various origins.

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It is thought that in these situations, the decrease in corneal thickness is caused by loss or re-distribution of corneal tissue. The thickness of the cornea is not only related to physiology and pharmacology, but variations in normal thickness are also of diagnostic, epidemiological and pathological importance. Therefore, great interest has been shown in sensitive and accurate measurement methods. Diseased eyes can cause a great deal of pain to patients, as those who have personally experienced corneal erosions or other painful ocular conditions will attest. In caring for cattle, treatments should be directed at preventing ocular disease whenever possible.
The purpose of this study was to identify the physiological reference values for central corneal thickness (CCT) and the age-related changes in CCT in healthy dairy cattle.

MATERIAL AND METHODS

The study was conducted on the Arif Gürdal Dairy Farm with the approval of ADÜ - HADYEK (64583101/2020/095). Evaluation was made of 100 eyes of 50 healthy cattle aged 389-2970 days. The measurements for each eye were obtained using ultrasonographic pachymetry to determine CCT. All the measurements were taken by the same surgeon on the same day between 11:00 am and 3:00 pm (Figure 1).
Ophthalmological examination was performed before the cattle were included in the study. The ophthalmological examination and CCT measurements were made in head-lock barriers. All cattle eyes were free of inflammation or other ocular disease. Ultrasonographic pachymeter (Pocket II One Touch Ultrasound Pachymeter) utilizes ultrasound energy to measure CCT. The probe was gently touched to the central cornea without pressure or indentation. The device automatically calculates the average value of 5 consecutive measurements.

Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS vn.22 software (Statistical Package for Social Sciences), Jamovi (1.1.9) and Microsoft Excel programs. Conformity of the data to normal distribution was examined with the Shapiro Wilk test and the Levene test. Measurements of the right and left eyes were evaluated with the Dependent Samples t-test and correlations between age and CCT with the Pearson Correlation test. A value of $p<0.05$ was accepted as statistically significant.

Figure 1 - Central corneal thickness measurements.

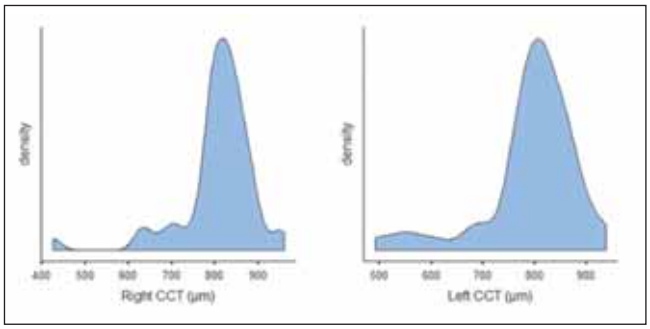

Figure 2 - Distribution of the central corneal thickness values for the left and right eyes.

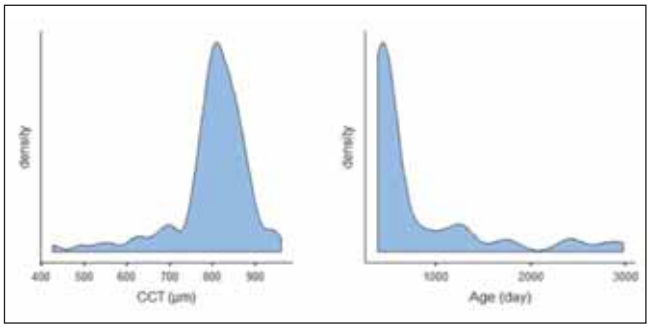

Figure 3 - Central corneal thickness and age distribution.

RESULTS

All cattle eyes were free of inflammation or other ocular disease. Measurements were taken of 100 eyes of 50 cattle. The study population consisted of healthy dairy cattle. The ages of the cattle varied between 389-2970 days and CCT between 425-960 µm. The results are shown in detail in Tables 1 and 2. The mean age of the cattle was 781.38 days. The mean CCT value was 799.44 µm. The mean CCT value was 806.58 µm (range 425-960 µm) for the right eyes and 792.30 µm (range 491-938 µm) for the left eyes (Figure 2). According to the Dependent Samples t-test, no statistically significant difference was determined between the right and left eyes in respect of CCT ($p=0.363$) (Tables 1, 2). The age distribution of the CCT of these

Table 1 - Central corneal thickness (CCT, µm) values in the left and right eyes.

	Right CCT (µm)	Left CCT (µm)
N	50	50
Mean	806,58	792,3
Std. error mean	11,99	12,81
Minimum	425	491
Maximum	960	938

Table 2 - The average central corneal thickness (CCT, µm) and age of the animals.

	Age (day)	CCT (µm)
N	50	100
Mean	781,38	799,44
Std. error mean	92,74	8,76
Minimum	389	425
Maximum	2970	960

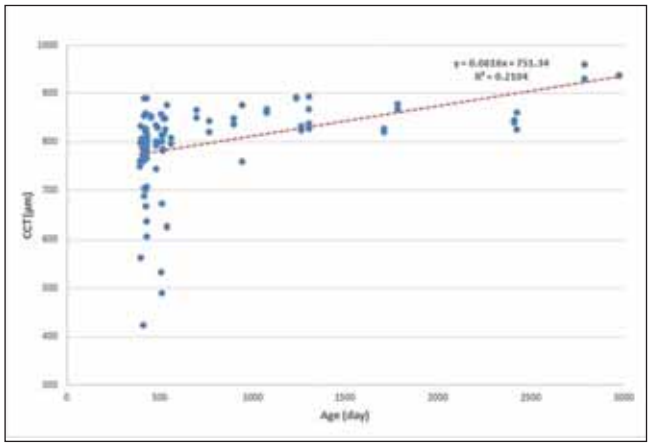

Figure 4 - Scatterplot demonstrating the age and corneal thickness values of the cattle.

subjects is summarized in Figure 3. A significant positive correlation was observed between age and CCT in these measurements of 50 dairy cows ($p<0.001$, $y = 751.34 + 0.0616x$, $R2=0.2104$) (Figure 4). According to these results, it is seen that the cornea gets thicker as the age increases. Based on the analyses, right and left CCT are similar.

DISCUSSION

The aim of this study was to establish the normal CCT values of dairy cattle and to investigate the relationship between CCT and age. The ultrasound pachymeter device is widely preferred for the measurement of CCT as it is inexpensive, easy-to-apply and repeatable. Of the techniques available, the ultrasound pachymeter shows the least variance and may therefore be the most accurate method [17]. Contact with the cornea is the greatest disadvantage of this method, and placement of the probe at the correct angle without pressing the cornea is important for accurate measurement [18].

In comparisons of pachymetry and other CCT measurement methods, there has been reported to be no difference in the results, but unlike other methods, pachymetry does not require sedation [17,19,20]. For these reasons, ultrasound pachymetry was selected for use in this study.

In previous studies in literature, CCT in cattle has been reported as 805 µm [21], 1015 µm [22], 725-936 µm [23]. In the current study of 50 dairy cows aged 389-2970 days, the mean CCT was determined as 799.44 µm, ranging from 425 µm to 960 µm.

This study was planned on the hypothesis that there could be a correlation between age and corneal thickness in cattle. Just as in all living creatures, tissues in cattle show age-related changes [24]. The repair capacity of corneal endothelial cells is known to be extremely limited. Knowledge of the normal values and age-related changes is necessary not only to determine the physiological limits, but also to reveal abnormal conditions. Previous studies have shown that corneal thickness changes depending on age [25-27].

It has been reported in previous human studies that a decrease is seen in corneal thickness as age increases. Although corneal thickness varies according to species and race, the mean corneal thickness is in the range of 0.5-0.8 mm. The periphery is generally thicker than the centre. The cornea in elderly animals can thicken up to 0.9 mm because of endothelial cell dysfunction. In studies performed on cattle eyes collected after slaughter, values of 1.29 ± 0.03 mm[8] and 1.4±0.011 mm[9] were reported. In cats, the cornea continues to develop until the age of 1-2 years. CCT increases together with age, and has been reported to be 0.55 mm at 16 weeks and 0.57 mm at 67 weeks. In dogs, there is thinning in the cornea up to 6 weeks of age, after which thickening develops together with age and the mean thickness is 0.56 mm[1,4 25,28-33]. While corneal thickness has been reported to be thinner in young llamas than in older llamas, no significant age-related difference has been observed in alpacas [34]. Studies of horses [35,36], sheep [37], dogs [38,39], and cats [40] have shown an age-related increase in corneal thickness measurements. Another study reported a negative correlation between age and corneal thickness in horses [41].

In this study, the mean CCT value was 799.44 µm and the average age was 781.38 days. The results of the current study showed a positive correlation between age and corneal thickness in dairy cattle, which was similar to the findings of other animal studies. The accumulation of new material in Descemet's membrane over their lifetime may partially explain this finding [16].

The ophthalmologic disease in the dairy farms can result in significant economic losses to producers. Along with economic impacts, the ophthalmologic disease can lead to individual pain and suffering and therefore negatively affects animal welfare [42]. In corneal diseases, the increase in corneal thickness is due to hydration. A decrease in corneal thickness is seen in corneal dystrophy and ulcerative inflammatory diseases. The thickness of the cornea is not only related to physiology and pharmacology, but a change in normal thickness is also of diagnostic, epidemiological and pathological importance[43]. Therefore, it is important that the corneal thickness is measured definitively and accurately.

There were some limitations in conducting out study due to the farm conditions. Only 50 cattle over 1 year old were included and under 1 year old could not be evaluated. However, the data obtained from the study clearly showed that cornea thickness is related to age. In this context, this study revealed the need of both to evaluate the corneal thickness measured starting from the weekly age and whether gender has an effect on the corneal thickness has to be evaluated.

Knowing CCT and its increase with age is important for diagnosing ocular diseases such as corneal damage and determining the prognosis. In pathological conditions such as hypoxia, keratitis, laceration, corneal thickness goes beyond physiological levels[16]. According to results from the study at different ages it is evident that different corneal thickness. It will be useful to know physiological data in terms of provide animal welfare and preventing economic losses. The presented study will contribute to the literature as it has been conducted on live cattle, unlike other studies on cattle eyes [8,9]. There are studies in literature that have shown a decrease in the density of endothelial cells when an age-related increase is forming in corneal thickness [16,44]. Knowing that corneal thickness increases with age is of diagnostic importance. However, there is a need for further studies to fully clarify the mechanism of age-related increase in thickness.

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