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RESEARCH ARTICLE

The Effects of Different Mydriatics on Intraocular Pressure and Central Corneal Thickness in New Zealand White Rabbits [1]

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Abstract

This study was aimed to compare the effect of 1% atropine, 1% cyclopentolate, 0.5% tropicamide, and 10% phenylephrine eye drops on intraocular pressure (IOP) and central corneal thickness (CCT) in New Zealand White rabbits. Adult male, eight, New Zealand White rabbits were randomly received each of four mydriatic eye drops separately on left eye at a one-week washout period. Each rabbit received all of five different treatments (sterile saline solution, four mydriatic drugs) on the left eye, whereas no measurements were performed on the right eyes during the experiment. The IOP and CCT recordings of rabbits were performed until the pupil returned to normal diameter. The mean CCT values of sterile saline, 1% atropine, 0.5% tropicamide, 1% cyclopentolate, and 10% phenylephrine were 370±15, 368±17, 372±15, 364±18, and 360±17 µm, respectively, and no statistically significant differences (P>0.05) were observed among groups. The mean IOP values of control (sterile saline), 1% atropine, 0.5% tropicamide, 1% cyclopentolate, and 10% phenylephrine as, 9.7±2.1, 10.4±1.8, 10.3±2.1, 11.0±2.1, and 10±1.8 mmHg, respectively, and these were not statistically significant among groups (P>0.05). In conclusion, topical 1% atropine, 0.5% tropicamide 1% cyclopentolate, and 10% phenylephrine do not have significantly effect on IOP and CCT in New Zealand white rabbits.

Keywords: *Central corneal thickness, Intraocular pressure, Mydriatic, New Zealand white rabbit, Tropicamide*

Beyaz Yeni Zelanda Tavşanlarında Farklı Midriyatiklerin Göz İçi Basıncı ve Merkezi Kornea Kalınlığı Üzerine Etkileri

Öz

Bu çalışma, Beyaz Yeni Zelanda tavşanlarında %1 atropin, %1 siklopentolat, %0.5 tropikamid ve %10 fenilefrin göz damlasının göz içi basıncı (GİB) ve merkezi kornea kalınlığı (MKK) üzerindeki etkilerini karşılaştırmayı amaçladı. Sekiz, yetişkin erkek Beyaz Yeni Zelanda tavşanının sol gözüne dört ayrı midriyatik göz damlası bir haftalık arınma periyoduyla rastgele uygulandı. Her tavşanın sol gözüne beş farklı tedavinin (steril serum fizyolojik, dört midriyatik ilaç) tamamı uygulanırken, sağ gözlerde ise deney boyunca ölçüm yapılmadı. Tavşanların GİB ve MKK verileri pupil normal çapa dönene kadar alındı. Steril salin, %1 atropin, %0.5 tropikamid, %1 siklopentolat ve %10 fenilefrinin ortalama MKK değerleri sırasıyla 370±15, 368±17, 372±15, 364±18 ve 360±17 µm idi ve gruplar arasında istatistiksel olarak anlamlı farklılık (P>0.05) gözlenmedi. Kontrol (steril salin), %1 atropin, %0.5 tropikamid, %1 siklopentolat ve %10 fenilefrinin ortalama GİB değerleri sırasıyla 9.7±2.1, 10.4±1.8, 10.3±2.1, 11.0±2.1 ve 10±1.8 mmHg'idi ve gruplar arasında istatistiksel olarak önem yoktu (P>0.05). Sonuç olarak, Beyaz Yeni Zelanda tavşanlarında topikal %1 atropin, %0.5 tropikamid, %1 siklopentolat ve %10 fenilefrinin GİB ve MKK üzerinde anlamlı bir etkisi yoktur.

Anahtar sözcükler: *Beyaz Yeni Zelanda tavşanı, Göz içi basıncı, Merkezi kornea kalınlığı, Midriatik, Tropikamid*

INTRODUCTION

Mydriatics are commonly used in human and veterinary ophthalmology to examine the posterior segment and treat uveitis and corneal ulceration by providing pupil dilation [1,2].

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Mydriatics may alter the intraocular pressure (IOP) by obstructing the iridocorneal angle [3] or decreasing traction on trabecular meshwork that effects aqueous outflow drainage or widening on anterior chamber angle [4]. So many researches have been conducted to find the relationship between mydriatics and IOP in different species such as sheep [3], monkeys [5], horses [6], goats [7], dogs [1,8], cats [1,9] and rabbits [10].

Measuring the central corneal thickness (CCT) is important for laser corneal refractive surgery for the maximum safety of performance [11]. Mydriatic drugs are commonly used for ocular surgery and they may elevate the CCT because of the impairment of corneal physiological metabolism or function of epithelial barrier [12] Several studies have investigated the relationship between IOP and CCT in humans [13,14], cats [15] and dogs [16]. It has been reported that low CCT may lead to underestimation of IOP [17].

This study was aimed to compare the effects of 1% atropine, 1% cyclopentolate, 0.5% tropicamide, and 10% phenylephrine on CCT and IOP values of New Zealand White rabbits.

Material and Methods

Ethical Statement

Atatürk University Local Board of Ethics Committee for Animal Experiments has approved the study protocol of this research (HADYEK decision no: 2021/22).

Animals

Eight, adult New Zealand white rabbits with average weights of 2.9 kg were used. The animals were housed in individual cages (60x50x60 cm height) without bedding material and received water and a standard pellet diet *ad libitum*. The humidity ranged between 40 and 60%. A uniform temperature of 22±2°C was maintained throughout with a 12:12 h light: dark cycle.

Study Design

The rabbits were checked for pre-existing ocular disorders by measuring the IOP (Tonovet®, Icare, Finland), Schirmer tear test - I (STT-1; Eye Care Product Manufacturing LLC, Tucson, USA), fluorescein staining (Flu-Glo® ophthalmic strips USP 1.0 mg, Akorn, USA), and indirect ophthalmoscopy (Aesculap AC-635 C, Braun, Germany).

The treatment procedure was randomized, and each animal received all of five treatments on the left eye (sterile saline solution, four mydriatic drugs) with a minimum one-week washout period. No measurements were performed on the right eyes during the experiment.

The treatment protocols were one drop of sterile saline solution, 1% atropine ophthalmic solution (Atrosol® %1, Sanovel, Turkey), 0.5% tropicamide ophthalmic solution (Mydriaticum Stulln® 0.5%, Pharma Stulln GmbH, Germany), 1% cyclopentolate ophthalmic solution (Sikloplejin® %1, Abdi Ibrahim, Turkey), and 10% phenylephrine ophthalmic solution (Fenilefrin® 10%, Sanovel, Turkey). All mydriatics were administered by the same person who was unaware of the experimental design.

During the each IOP measurement, the rabbits were gently handled to prevent any pressure on the animal's neck which might effect IOP [18]. All measurements were recorded at predefined time points [9]. No anesthetic eye drops were used throughout the experiment. Before the experiment, the rabbits were adapted to the study for two weeks period to prevent false recordings.

Measurement

Intraocular pressure and CCT measurements were discontinued until the two independent researchers were not able to examine posterior segment of the eye by direct ophthalmoscopy. The IOP and CCT measurements were recorded in an examination room with the same light circumstances. The IOP and CCT recordings were collected by rebound tonometer (Tonovet, Icare, Vantaa, Finland) and ultrasound pachymetry (Ipac, Reichert, NY, USA), respectively.

All IOP and CCT measurements were performed by the same person at the predefined time points (32 h for 1% atropine, 14 h for 0.5% tropicamide, 40 h for 1% cyclopentolate, 6 h for 10% phenylephrine, 40 h for saline group. IOP and CCT measurements of sterile saline, 1% atropine, 0.5% tropicamide, 1% cyclopentolate and 10% phenylephrine were recorded 19, 17, 12, 19 and 8 times, respectively. On the first day, IOP and CCT were measured at 8 a.m., 8.30 a.m., 9 a.m., 9. 30 a.m., 10 a.m., 11 a.m., 12 p.m., 2 p.m., 4 p.m., 6 p.m., 8p.m., 10 p.m., 12 a.m. On the second day, IOP and CCT were measured at 4 a.m., 8 a.m., 12 p.m., 4 p.m., 8 p.m., 12 a.m. The time point of 30 min after mydriatic administration was chosen based on the previous study [9].

Statistical Analysis

All data were analyzed using the SPSS 19.0 (IBM, SPSS Inc, USA, 2010) statistical package. Data are reported as mean±standard deviation. To evaluate the differences in IOP levels among groups, a Repeated Measures-ANOVA followed by Bonferroni multiple comparisons Post-Hoc test was performed. A P-value of <0.05 was considered statistically significant.

Results

No signs of ocular irritation or pain were encountered during the experiment. The mean CCT values of sterile saline, 1% atropine, 0.5% tropicamide, 1% cyclopentolate, and 10% phenylephrine were 370±15, 368±17, 372±15,

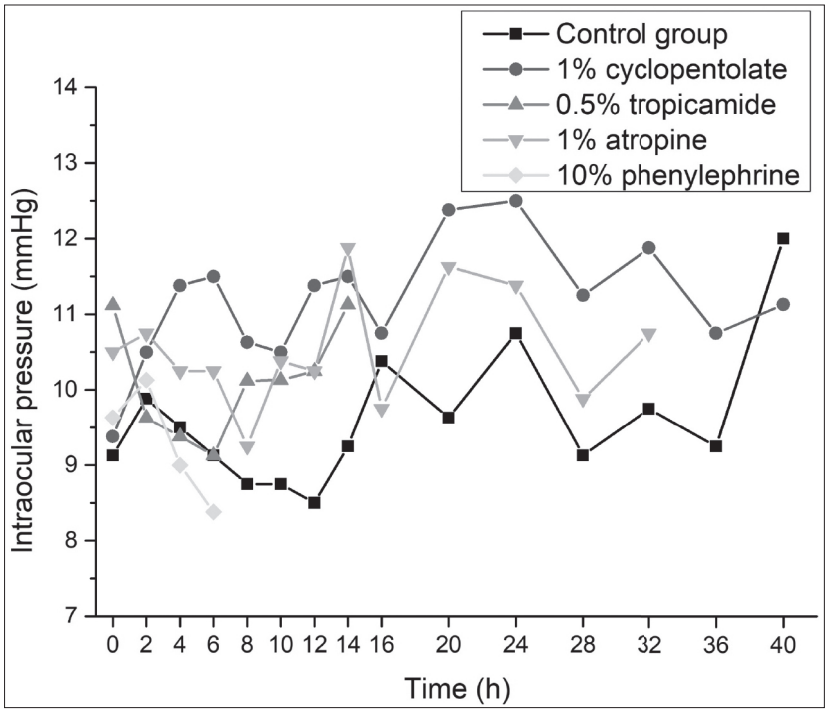
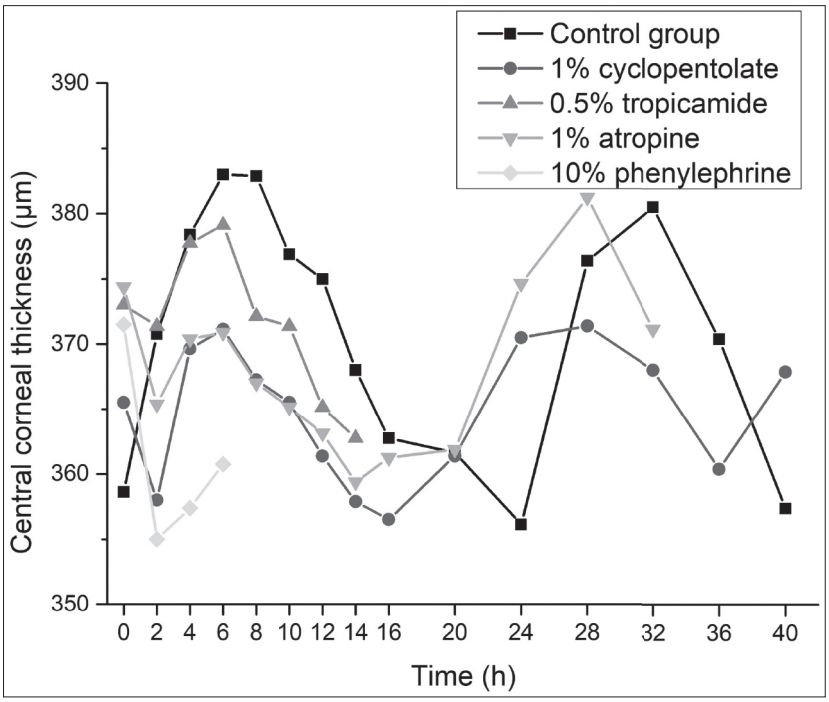


Fig 1. The effect of mean central corneal thickness values during the predefined time points after the topical sterile saline, 1% atropine, 0.5% tropicamide 1%, cyclopentolate, and 10% phenylephrine administrations

Fig 2. The effect of mean intraocular pressure values during the predefined time points after the topical sterile saline, 1% atropine, 0.5% tropicamide 1%, cyclopentolate, and 10% phenylephrine administrations



364±18, and 360±17 µm, respectively, and no statistically significant differences (P>0.05) were observed among groups *(Fig. 1)*.

The mean values of IOP in sterile saline, 1% atropine, 0.5% tropicamide, 1% cyclopentolate, and 10% phenylephrine as, 9.7±2.1, 10.4±1.8, 10.3±2.1, 11.0 2.1, and 10±1.8 mmHg, respectively and no significant differences (P>0.05) were observed among groups. No significant differences were observed on IOP levels in all groups at all-time intervals except for at the 4th h and 20th h *(Fig. 2)*. The IOP level was significantly increased (P<0.05) in 1% cyclopentolate group (11.4±1.8 mmHg) at 4th h compared to the 10% phenylephrine (9±1.2 mmHg). And also, 1% cyclopentolate (12.4±2.0 mmHg) resulted with a significant increase in IOP at 20th h compared to the control group (9.6±1.7 mmHg, P<0.05).

Discussion

Mydriatics are regularly administered to the eye to assist the clinician in the routine evaluation of ocular structures

located in the posterior segment of the eye [19,20]. In our study, 1% atropine, 0.5% tropicamide, 1% cyclopentolate and 10% phenylephrine were used for mydriatic effect. Atropine, tropicamide, and cyclopentolate are a parasympatolitic agents that have anti-muscarinic activity, which causes pupillary dilatation followed by ciliary paralysis [21]. However, phenylephrine shows its mydriatic effect by activating sympathetic receptors on the iris dilator muscle by inhibiting iris sphincter muscle action [22]. A previous study has reported that 1% atropine ointment may reduce the IOP in horses, possibly due to the large capacity of aqueous humor outflow [6]. However, in this study, 1% atropine did not cause any significant effect on IOP and CCT values of New Zealand white rabbits. Similar results were previously reported in sheep [3] and horses [23]. In the current study, no significant differences were observed in IOP and CCT levels between cyclopentolate and atropine groups. This may occur due to similar pharmacological effect of both drugs [1,8]. We observed an increase in IOP levels at some time points in the 1% cyclopentolate group compared to the saline and phenylephrine group. This finding was consistent with a previous report [10]. Therefore, 1% cyclopentolate must be used carefully in rabbits especially when the higher IOP levels are suspected.

Tropicamide is a commonly used ophthalmic solution to inhibit the action of acetylcholine on the iris sphincter [24]. It has been stated that tropicamide-induced mydriasis may cause an increase in IOP recordings of dogs [1] cats [9] and humans [4]. We observed an insignificant increase in IOP level after the 0.5% tropicamide application compared to the saline group, however, this was clinically acceptable. Because phenylephrine is sympathomimetic drug that causes less humor aqueous production and thereby lower IOP levels. However, in this study phenylephrine did not cause a significant effect on IOP. Similar results were also reported in cats [9], monkeys [25], and humans [26].

In this experiment, no topical anesthetics were used, which may affect the IOP [27] and CCT [28,29]. The IOP is dynamic so it changes during the day [30,31]. Environmental changes and stress-related factors may increase IOP [32]. Based on these premises, IOP and CCT measurements of the current study were recorded at the same time of the day with two weeks acclimation period. In our study, we did not serve the right eyes as a control because previous studies have shown that unilateral application of mydriatic drugs may affect both eyes [9].

Intraocular pressure values of healthy rabbit with Tonovet is ranged between 9.51±2.62 mmHg [32]. In the current study, the mean IOP recordings of the saline group were within the reference values. CCT measurements were easily obtained from rabbits' eyes' using an ultrasound pachymeter; however, it involves contact with the surface of the cornea epithelium [33]. Chan et al.[34] reported that CCT values of New Zealand white rabbits with ultrasound pachymeters were 407±20 µm. In this study, the mean CCT value was 370±15 µm, and the results were consistent with Wang et al.[35]'s report, which used optical coherence tomography for measuring the CCT.

In conclusion, topical application of 1% atropine, 0.5% tropicamide, 1% cyclopentolate, and 10% phenylephrine do not have a significant effect on IOP and CCT values of New Zealand white rabbits. 10% phenylephrine is less likely to affect IOP in rabbits among the mydriatics used in this study. Moreover, future studies that focus on the relationship between CCT and IOP levels of glaucomatous eyes may reveal the possible interactions of both parameters.

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Conflict of Interest

The authors declared that there is no conflict of interest.

Author Contributions

LEY, SO, UE, MGS, ED, ZO: Study design. LEY, SO, UE, MGS, ED, ZO: Data collections. MGS: Data analysis. LEY, SO: Writing the manuscript.

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