Research Article / Araştırma Makalesi
doi: 10.18678/dtfd.1612612

Duzce Med J, 2025;27(2):118-122
Düzce Tıp Fak Derg, 2025;27(2):118-122

Effect of Taurine on Experimental Facial Paralysis and Dry Eye in Rats

Taurinin Sıçanlarda Deneysel Fasyal Paralizi ve Kuru Göz Üzerine Etkisi

Hacı KOÇ[1]
0000-0002-5446-8456
İbrahim KOÇAK[2]
0000-0003-4683-8346
Mehmet TOKMAK[3]
0000-0003-1367-1121
Saim KALE[3]
0000-0003-1044-947X
Ali GÖK[4]
0000-0003-4103-9537
Şerif DEMİR[5]
0000-0002-0305-5758

[1]Has passed away while working at the Department of Ophthalmology, Düzce University Faculty of Medicine, Düzce, Türkiye

[2]Department of Ophthalmology, University of Health Sciences, İstanbul, Türkiye

[3]Department of Neurosurgery, Medical Park Kocaeli Hospital, Kocaeli, Türkiye

[4]Experimental Animals Application and Research Center, Düzce University, Düzce, Türkiye

[5]Department of Physiology, Düzce University Faculty of Medicine, Düzce, Türkiye

Corresponding Author
Sorumlu Yazar
Şerif DEMİR
serifdemir19@hotmail.com

Received / Geliş Tarihi : 03.01.2025
Accepted / Kabul Tarihi : 02.05.2025
Available Online / Çevrimiçi Yayın Tarihi : 05.06.2025

ABSTRACT

Aim: This study aimed to evaluate dry eye development and the efficacy of taurine for dry eye treatment in a rat model with facial paralysis.
Material and Methods: Thirty-two rats were divided into four groups with eight rats in each. The rats in groups 2, 3, and 4 underwent facial paralysis surgically, while the rats in group 1 remained as controls. The rats in group 2 did not receive any treatment. Group 3 was treated with 0.2% sodium hyaluronate, and group 4 was treated with 0.2% sodium hyaluronate and 0.5% taurine. The results of the first and last Schirmer's tests were compared.
Results: When the Schirmer's tests were performed in rats with facial paralysis under general anesthesia to detect dry eye, the scores were low, indicating that general anesthesia increased dry eye in all groups. Thus, Schirmer's tests were performed without general anesthesia. The final test results were significantly different between groups (p=0.001). Pairwise comparisons revealed that there was a significant decrease in groups 2 (p=0.001) and 3 (p=0.002) compared to the control group. Group 4 was similar to the control group (p=0.304) and had a significant improvement compared to group 2 (p=0.037). No statistically significant difference was found between groups 2 and 4 (p=0.566).
Conclusion: Taurine seems to have the potential to be effective in relieving dry eye symptoms. This could be related to the dominantly antioxidant effect of taurine. These results warrant further studies with larger sample size to determine the effectiveness of taurine for dry eye treatment.
Keywords: Dry eye; facial paralysis; Schirmer's test; taurine.

ÖZ

Amaç: Bu çalışmanın amacı fasiyal paralizili sıçan modelinde kuru göz gelişimini ve kuru göz tedavisinde taurinin etkinliğini değerlendirmektir.
Gereç ve Yöntemler: Otuz iki sıçan her birinde sekiz sıçan olacak şekilde dört gruba ayrıldı. Grup 2, 3 ve 4'teki sıçanlara cerrahi olarak fasiyal paralizi uygulanırken, grup 1'deki sıçanlar kontrol grubu olarak bırakıldı. Grup 2'deki sıçanlara herhangi bir tedavi uygulanmadı. Grup 3 %0,2'lik sodyum hiyaluronat ile tedavi edildi ve grup 4 ise %0,2'lik sodyum hiyaluronat ve %0,5'lik taurin ile tedavi edildi. İlk ve son Schirmer testinin sonuçları karşılaştırıldı.
Bulgular: Fasiyal paralizi olan sıçanlarda kuru göz hastalığını tespit etmek amacıyla genel anestezi altında Schirmer testleri yapıldığında skorların düşük çıkması, genel anestezinin tüm gruplarda kuru gözü arttırdığını gösterdi. Bu nedenle Schirmer testleri genel anestezi olmadan gerçekleştirildi. Son test sonuçları gruplar arasında önemli ölçüde farklıydı (p=0.001). İkili karşılaştırmalar grup 2'de (p=0,001) ve 3'te (p=0,002) kontrol grubuna kıyasla anlamlı bir azalma olduğunu gösterdi. Grup 4 ise kontrol grubuna benzerlik göstermekteydi (p=0,304) ve grup 2 ile karşılaştırıldığında belirgin bir düzelme vardı (p=0,037). Grup 2 ile 4 arasında ise istatistiksel olarak anlamlı bir fark bulunmadı (p=0,566).
Sonuç: Taurinin kuru göz semptomlarını hafifletmede etkili olma potansiyeli olduğu görünmektedir. Bu, taurinin baskın antioksidan etkisi ile ilişkili olabilir. Bu sonuçlar, taurinin kuru göz tedavisindeki etkinliğini belirlemek için daha büyük bir örneklemde daha fazla çalışmayı gerektirmektedir.
Anahtar kelimeler: Kuru göz; fasyal paralizi; Schirmer testi; taurine.

INTRODUCTION

The facial nerve controls the muscles that allow facial movement. Facial nerve pathology causes facial asymmetry, decreased emotional contact, and temporary or permanent paralysis (1). Facial paralysis has a psychological, social, and physiological impact (2), which affects all races and ages (3).

Facial nerve paralysis results from supranuclear, nuclear, and infranuclear lesions of the nerve. Facial nerve paralysis can occur from various reasons. The most common causes include Bell's paralysis, Ramsay-Hunt syndrome, trauma, and surgical interventions (3). Facial nerve trauma is often difficult to treat, since spontaneous recovery is unpredictable, and results without intervention are often unsatisfactory (1). Facial nerve paralysis can be classified as idiopathic, infectious, or neoplastic. Although vascular diseases are commonly involved in the etiology, demyelination and tumors may also be attributed to it (3).

In patients with facial paralysis, prioritizing the ocular presentation and addressing the related physiological findings are crucial (2). Comprehensive scanning of the ocular surface and the surrounding tissues is important for treatment planning (4). Facial nerve paralysis that involves the eyes and eyelids may adversely affect vision. Facial nerve paralysis may result in dry eye, due to difficulty in closing the eyelid as well as decreased tearing.

Dry eye disease is a condition affecting the ocular surface due to various causes (5). While its features are common with those of autoimmune diseases (6), dry eye syndrome is characterized by qualitative and quantitative abnormalities of the tear film (7). The main lacrimal gland, ocular surface, meibomian glands, and innervation between them constitute a network related to the lacrimation of the eye; these structures could be affected by dry eye disease. Moreover, increased tear osmolarity and inflammation on the ocular surface are observed (5), which cause tear film instability, ocular discomfort, and visual impairment.

Taurine (TAU) is an amino acid that is abundant in tears, the iris, the ciliary body, the cornea, and the retina (8). Low TAU levels have been reported in ocular diseases, such as dry eye disease, glaucoma, retinitis pigmentosa, cataracts, and hereditary retinal eye diseases (9-13). TAU is an antioxidant, anti-inflammatory, and an osmoprotectant, which can aid in the treatment of dry eye diseases (8).

This study aimed to evaluate the development of dry eyes in a rat model of surgically induced facial paralysis and subsequently evaluated the effectiveness of TAU for the treatment of dry eye in this model.

MATERIAL AND METHODS

This study was conducted at the Düzce University Experimental Animals Application and Research Center and approved by the Düzce University Local Ethics Committee on Animal Experiments (12.01.2022, 01/04). The study adhered to the Guidelines for Ethical Conduct in the Care and Use of Animals of the NIH or similar.

The rats included in this study were obtained from the Bolu Abant İzzet Baysal University Experimental Animals Application and Research Center. Wistar albino female rats (n=32), aged 2.5-3 months, weighing 250±30 g, were maintained in the laboratory at an ambient temperature of 23°C, 60±5% humidity, and 12 h/12 h light/dark cycle, with free food and water intake. Rats were randomly and equally divided into four groups: group 1 (control group, n=8), group 2 (facial paralysis group, n=8), group 3 (facial paralysis+atropine+0.2% sodium hyaluronate (SH) group, n=8), and group 4 (facial paralysis+atropine+0.2% SH+0.5% TAU group, n=8). A standard surgical procedure was performed by the same surgeon to induce facial nerve paralysis (Figure 1).

The surgical procedure was applied as previously reported in the literature (14-17). The rats were anesthetized with intraperitoneal xylazine (10 mg/kg; Bayer, Istanbul, Turkey) and ketamine hydrochloride (60 mg/kg; Parke-Davis) before surgery. They were then placed in the prone position on mushroom blocks, and the right facial nerve traces of the animals were shaved and disinfected with povidone iodine. A horizontal incision of approximately 2 cm was made, extending from the front of the external auditory canal to the mustache level at the corner of the mouth. The right facial nerve trunk of each rat was exposed under general anesthesia. A nerve cut was performed between the exit point of the stylomastoid foramen and the first bifurcation point. Following hemostasis, the layers were closed, and the rats were awakened at an appropriate ambient temperature (24°C). The rats were fed standard rat chow in a separate cage that was in a heated section, where the temperature was maintained at around 24°C.

The amount of tears produced by each rat was measured using the Schirmer's test at specified times. In this study, the Schirmer's test was slightly modified. The filters were cut into 1-mm-wide pieces. A 1-mm piece at the end of the Schirmer's strip was folded and then placed on the outer third of the lower eyelid. After 5 min, the tear-soaked sections on the strip were measured. Schirmer's tests were first conducted under general anesthesia (Figure 2), which resulted in adverse effects as all rats developed dry eyes. Therefore, Schirmer's tests were again performed but under more challenging conditions without general anesthesia (Figure 3) as discussed in detail in the discussion section.



Figure 1. The stage of surgically inducing facial paralysis under general anesthesia

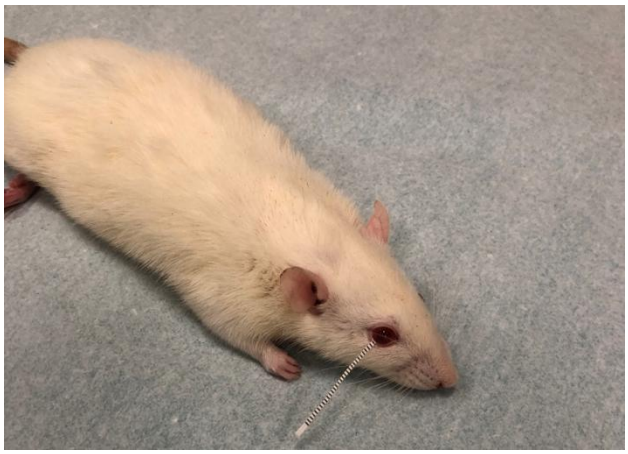


Figure 2. Schirmer's test under general anesthesia

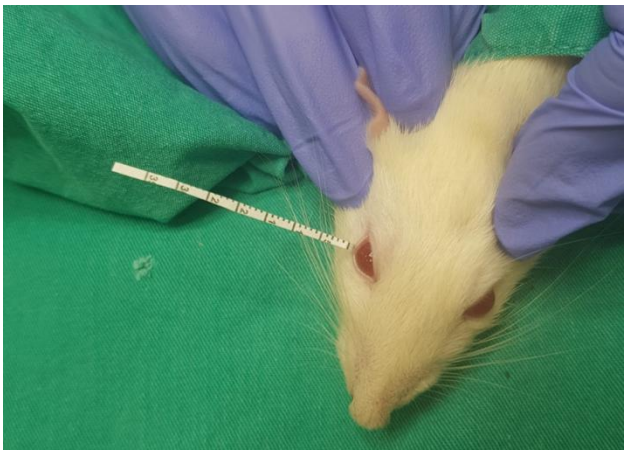


Figure 3. Schirmer's test without general anesthesia

Schirmer's test was performed in rats that underwent surgery before and after surgery, and in those in the control group on the first and last days. The rats in group 1 did not undergo any procedure; only the amount of tears was measured using the Schirmer's test. In group 2, facial paralysis was surgically induced, and only the Schirmer's test was applied, without any treatment. In group 3, one drop of 0.2% SH was administered, four times a day between the 7th and 14th days after the facial paralysis surgery. In group 4, 0.2% SH + 0.5% TAU was administered as one drop, four times a day between the 7th and 14th days after the surgery. The rats in groups 3 and 4 were administered 1 % atropine sulfate to induce dry eyes to evaluate the effectiveness of SH and TAU. One day before the final Schirmer's tests, one drop of 1% atropine sulfate was administered four times, at 2-h intervals, to induce dry eyes. Fifteen minutes after applying each drop of 1% atropine sulfate, 0.2% SH was applied to group 3, and 0.2% SH and 0.5% TAU were applied to group 4. The final Schirmer's test was performed 1 day after the last drop. All rats were delivered to the laboratory without sacrifice 2 days after the last Schirmer's test.

Statistical Analysis

The Number Cruncher Statistical System (NCSS) 2007 program (Kaysville, Utah, USA) was used for statistical analysis. Descriptive statistics (mean, standard deviation, median, minimum, and maximum) were used to evaluate study data. The normality assumption was evaluated using the Shapiro-Wilk test. The Kruskal-Wallis test was used for comparisons of non-normally distributed variables among the groups, and the Bonferroni-Dunn test was used for pairwise comparisons. The Wilcoxon signed-rank test was used to compare non-normally distributed results of the first- and post-test measurements. Results were considered statistically significant at $p<0.05$.

RESULTS

The results of the first Schirmer's test were not significantly different between groups (p=0.669). A statistically significant difference was observed in the final Schirmer's test results between the groups (p=0.001). Pairwise comparisons for the final Schirmer's test results demonstrated that the measurements in group 2 (p=0.001) and group 3 (p=0.002) were significantly lower than in group 1. The measurements in group 4 were significantly higher than those of group 2 (p=0.037), while there was no significant difference between group 3 and 4 (p=0.566) in the final Schirmer's test results (Table 1, Figure 4).

In group 1, the change in the final test compared to the first test was not statistically significant (p=0.558). In group 2, a mean decrease of 10.88±2.59 mm in the final test was observed compared to the first test (p=0.011). In group 3, there was a mean decrease of 10.50±1.85 mm in the final test as compared to the first test (p=0.011). In group 4, there was a mean decrease of 7.13±2.10 mm in the final test compared to the first test (p=0.012).

Table 1. Evaluation of Schirmer test results by groups

		Group 1	Group 2	Group 3	Group 4	p[1]
First Test	Mean±SD	19.88±2.23	18.75±2.12	19.88±1.96	19.38±1.85	
	Median	20	18.5	20	19.5	0.669
	Min–Max	16 – 23	16 – 22	17 – 23	16 – 22	
Final Test	Mean±SD	20.25±1.91[a]	7.88±1.46[c]	9.38±1.41[bc]	12.25±1.83[ab]	
	Median	20.5	8	9.5	12.5	**0.001**
	Min–Max	17 – 23	6 – 10	7 – 11	9 – 14	
	p[2]	0.558	**0.011**	**0.011**	**0.012**	
Difference	Mean±SD	0.38±1.60[a]	-10.88±2.59[b]	-10.50±1.85[b]	-7.13±2.10[ab]	
	Median	1	-11	-9.5	-6.5	**0.001**
	Min–Max	-2 – 3	-16 – -7	-13 – -9	-11 – -5	

SD: standard deviation, p[1]: Kruskal-Wallis test, p[2]: Wilcoxon signed ranks test, [a,b,c]: different superscript letters denote significant differences between the groups according to the Bonferroni-Dunn post hoc test results; for final test: Group1 vs Group2: p=0.001, Group1 vs Group3: p=0.002, Group1 vs Group4: p=0.304; Group2 vs Group3: p>0.999; Group2 vs Group4: p=0.037; Group3 vs Group4: p=0.566; for difference: Group1 vs Group2: p=0.001, Group1 vs Group3: p=0.001, Group1 vs Group4: p=0.212; Group2 vs Group3: p>0.999; Group2 vs Group4: p=0.234; Group3 vs Group4: p=0.332

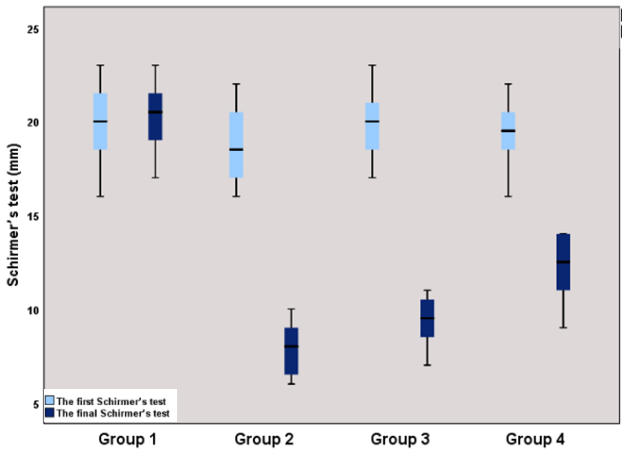


Figure 4. Schirmer's test results according to the groups

The changes in the Schirmer's test results also differed significantly among the groups (p=0.001). Based on the pairwise comparisons, the decrease in group 2 (p=0.001) and group 3 (p=0.001) was significantly higher than that in group 1. While the decrease in group 4 was statistically similar to the other groups, there was a remarkable improvement compared to group 2 and group 3 (Table 1).

DISCUSSION

In this study, a rat model of dry eye induced with facial paralysis was created to investigate the efficacy of TAU in the treatment of dry eye. Our results showed that rats with facial paralysis developed dry eyes and that those treated with SH and TAU were able to produce more tears than those without TAU treatment.

Bucolo et al. (8) stated the antioxidant effect of TAU in a rabbit eye model. They reported that TAU reduces matrix metalloproteinase 9 tear level in rabbit corneal epithelial cells subjected to oxidative stress. They also found that TAU and SH had recovered the break-up time and Schirmer's test results in atropine induced dry eyes of rabbits more than SH eye drop alone. Although the animals used in the study were different, these findings are convenient with the present study and support the hypothesis. This dry eye relieving attribute of TAU may be related to its antioxidant effect. Seen and Tong (17), in their review article, pointed out the additive effect of oxidative stress in dry eye and the futuristic treatment options with antioxidant agents such as L-carnitine, pterostilbene, alpha-lipoic acid, and selenoprotein P (17).

TAU has many bioactive functions, including osmoregulation, protein stabilization, growth factor regulation, and cytoprotective activity against a significant number of toxic agents. TAU also protects tissues against oxidative stress (8).

The Schirmer's test was applied 15 days following surgically induced facial paralysis. The test results were significantly lower than those obtained in the pre-surgical period only in the rats that underwent facial paralysis. It was found that SH and TAU increased the tear levels in Schirmer's tests. Among the treated groups, only the group treated with 0.2% SH and 0.5% TAU showed significantly higher Schirmer's test results than the group with untreated dry eye with facial paralysis. Moreover, although the differences were not found statistically significant, the Schirmer's test results of the group treated with 0.5% TAU and 0.2% SH were higher than those of the group treated with 0.2% SH only. These findings imply the probable efficacy of TAU in dry eye.

When the Schirmer's test in rats was applied under general anesthesia, the results were approximately 3-4 mm in all rats. After general anesthesia, it was noticed that the eyes of the rats became slightly proptotic and their ocular surfaces were dry. Thus, it was noticed that the Schirmer's test results would not be objective under these conditions, and despite the difficulty, the Schirmer's tests were performed without administering general anesthesia to the rats. There are similar reports that general anesthesia reduces tear level (18). The Schirmer's test scores in the present study were higher than those reported in previous studies (19,20). This may be because the rats in the previous studies were administered general anesthesia prior to the Schirmer's test.

The small number of rats included in this study is one of the limitations of the study. Particularly in terms of establishing the effectiveness of 0.5% TAU, it seems necessary to include more rats to achieve more accurate results. Additionally, it would be useful to determine the long-term effects of 0.5% TAU on dry eye. The lack of a standard for the test filters used in the rats poses a challenge for comparison across other studies. The absence of histological evaluation of ocular tissues, and the tear break-up time test could not be performed since the general anesthesia caused exaggerated dry eye and affected the test results. Further studies included additional tests, such as fluorescein staining, tear film osmolarity measurements, or inflammatory marker analysis, may be planned to comprehensively evaluate the dry eye.

CONCLUSION

Combination of 0.2% SH and 0.5% TAU increased the tear levels in rats with dry eye. TAU seems to be effective in relieving dry eye symptoms. This could be related to dominantly antioxidant effect of TAU. It would be beneficial to conduct further studies in a larger sample to determine the effectiveness of TAU as a treatment option for dry eye more conclusively.

Ethics Committee Approval: The study was approved by the Local Ethics Committee on Animal Experiment of Düzce University (12.01.2022, 01/04).

Conflict of Interest: None declared by the authors.

Financial Disclosure: None declared by the authors.

Acknowledgments: None declared by the authors.

Author Contributions: Idea/Concept: HK, MT, ŞD; Design: HK, İK, MT, ŞD; Data Collection/Processing: HK, İK, MT, SK, ŞD; Analysis/Interpretation: HK, İK, MT, SK, AG, ŞD; Literature Review: HK, İK, MT, AG, ŞD; Drafting/Writing: HK, İK, MT, SK, ŞD; Critical Review: HK, İK, MT, SK, AG, ŞD.

REFERENCES

1. Tekdemir E, Tatlipinar A, Özbeyli D, Tekdemir Ö, Kınal E. The effects of lipoic acid and methylprednisolone on nerve healing in rats with facial paralysis. Acta Oto-Laryngol. 2018;138(6):537-41.
2. Chi JJ. Management of the eye in facial paralysis. Facial Plast Surg Clin N Am. 2016;24(1):21-8.
3. Portelinha J, Passarinho MP, Costa JM. Neuro-ophthalmological approach to facial nerve palsy. Saudi J Ophthalmol. 2015;29(1):39-47.
4. Homer N, Fay A. Management of long-standing flaccid facial palsy: Periocular considerations. Otolaryngol Clin North Am. 2015;51(6):1107-18.
5. Huang JF, Zhang Y, Rittenhouse KD, Pickering EH, McDowell MT. Evaluations of tear protein markers in dry eye disease: repeatability of measurement and correlation with disease. Invest Ophthalmol Vis Sci. 2012;53(8):4556-64.
6. Messmer EM. The pathophysiology, diagnosis and treatment of dry eye disease. Dtsch Arztebl Int. 2015;112(5):71-82.
7. Ohashi Y, Ishida R, Kojima T, Goto E, Matsumoto Y, Watanebe K, et al. Abnormal protein profiles in tears with dry eye syndrome. Am J Ophthalmol. 2003;136(2):291-9.
8. Bucolo C, Fidilio A, Platania CBM, Geraci F, Lazzara F, Drago F. Antioxidant and osmoprotecting activity of taurine in dry eye models. J Ocul Pharmacol Ther. 2018;34(1-2):188-94.
9. Madl JE, McIlnay TR, Powell CC, Gionfriddo JR. Depletion of taurine and glutamate from damaged photoreceptors in the retinas of dogs with primary glaucoma. Am J Vet Res. 2005;66(5):791-9.
10. Pasantes-Morales H, Quiroz H, Quesada O. Treatment with taurine, diltiazem, and vitamin E retards the progressive visual field reduction in retinitis pigmentosa: a 3-year follow-up study. Metab Brain Dis. 2002;17(3):183-97.
11. Malone JI, Lowitt S, Cook WR. Nonosmotic diabetic cataracts. Pediatr Res. 1990;27(3):293-6.
12. Berson EL, Schmidt SY, Rabin AR. Plasma amino-acids in hereditary retinal disease. Ornithine, lysine, and taurine. Br J Ophthalmol. 1976;60(2):142-7.
13. ChenZhuo L, Murube J, Latorre A, Martin del Rio R. Different concentrations of amino acids in tears of normal and human dry eyes. Adv Exp Med Biol. 2002;506:617-21.
14. Henstrom D, Hadlock T, Lindsay R, Knox CJ, Malo J, Vakharia KT, et al. The convergence of facial nerve branches providing whisker pad motor supply in rats: implications for facial reanimation study. Muscle Nerve. 2012;45(5):692-7.
15. Hohman MH, Kleiss IJ, Knox CJ, Weinberg JS, Heaton JT, Hadlock TA, et al. Functional recovery after facial nerve cable grafting in a rodent model. JAMA Facial Plast Surg. 2014;16(1):20-4.
16. De Faria SD, Testa JRG, Borin A, Toledo RN. Standardization of techniques used in facial nerve section and facial movement evaluation in rats. Braz J Otorhinolaryngol. 2006;72(3):341-7.
17. Seen S, Tong L. Dry eye disease and oxidative stress. Acta Ophthalmol. 2018;96(4):412-20.
18. Nemet A, Belkin M, Rosner M. Transplantation of newborn lacrimal gland cells in a rat model of reduced tear secretion. Isr Med Assoc J. 2007;9(2):94-8.
19. Zagon IS, Campbell AM, Sassani JW, McLaughlin PJ. Spontaneous episodic decreased tear secretion in rats is related to opioidergic signaling pathways. Invest Ophthalmol Vis Sci. 2012;53(6):3234-40.
20. Zernii EY, Baksheev VE Kabanova EI, Tiulina VV, Golovastova MO, Gancharova OS, et al. Effect of general anesthesia duration on recovery of secretion and biochemical properties of tear fluid in the post-anesthetic period. Bull Exp Biol Med. 2018;165(2):269-71.