Pathogenetic treatment for neurotrophic keratopathy

T. B. Gaidamaka, Dr. Sc. (Med.); **T. A. Veliksar,** Postgraduate Student; **G. I. Drozhzhyna,** Dr. Sc. (Med.); **T. M. Serebrina,** Cand. Sc. (Med.)

Filatov Institute of Eye Diseases and Tissue Therapy;
Odessa (Ukraine)

E-mail: tveliksar@gmail.com

Introduction. *Continuous soft contact lens (SCL) wearing can result in development of neurotrophic keratopathy. Treatment of this pathology is long-term and, in general, symptomatic: tear-substitute, epithelizing, vitaminous, antibacterial, anti-inflammatory therapy.*

Purpose. *To improve a correction method for metabolic alterations in corneal tissues in continuous-SCL-wear-associated neurotrophic keratopathy through using transorbital electrophoresis with 1% thiotriazoline.*

Material and Methods. *We developed a method of treatment for neurotrophic keratopathy which includes a 10 day course of daily transorbital electrophoresis with 1% thiotriazoline as a part of complex therapy. We applied for approval of Author's certificate (application No U 201710621 dated 01 November 2017).*

Results. *Clinical cases of treatment of stage 1 neurotrophic keratopathy are reported.*

Conclusion. *The proposed treatment enables in a short term to significantly decrease pathological changes in corneal tissues in stage 1 neurotrophic keratopathy, to increase comfort in the eyes, to prevent severe complications of neurotrophic keratopathy and soft contact lens wearing.*

Key-words:

neurotrophic keratopathy, contact lenses, thiotriazoline, electrophoresis

Introduction

Every year, approximately 0.5% of persons are reported to refuse to wear soft contact lenses (SCL) for intolerance and discomfort with various corneal complications registered in 5.2-15 % of cases [1].

Wearing contact lenses can lead to development of severe complications. Annually, one of 2 500 daily SCL wearers and one of 500 SCL users with continuous wear are diagnosed with infectious keratitis [2, 3,4].

Causes of corneal complication associated with soft contact lens wearing can be different: microtrauma, infection, decrease of tear production and tear fluid quality, irritant and toxic action of contact lens cleaning solutions. One of the leading causes is metabolic disorders in corneal tissues which are mainly associated with chronic hypoxia.

It is known that two-hour SCL wearing already induces a shift toward anaerobic metabolism in the cornea, which speaks for the increased lactate dehydrogenase activity in tear and the presence of hypoxic corneal swelling caused by the enzymatic dysfunction of the endothelial pumps [5].

Continuous SCL wearing can result in development of neurotrophic keratopathy of stage 1 [6]. Treatment of this pathology is long-term and, in general, symptomatic: tear-substitute, epithelizing, vitaminous, antibacterial, anti-inflammatory therapy [7].

Neurotrophic keratopathy (NK) is clinically classified with three stages. Stage 1 NK is characterized by the presence of superficial punctuate keratitis, corneal edema, superficial neovascularization, stromal scarring, conjunctival epithelium damage, and a decrease in the breakup time. Stage 2 NK is characterized by recurrent or persistent epithelial defects with edematous and opaque epithelium at the edge that can spontaneously detach because of poor adherence; there can be Descemet's membrane folds and stromal edema. Stage 3 is characterized by corneal ulcer with a tendency to stromal melting and corneal perforation; sometimes, there can be an inflammatory reaction in the anterior chamber associated with sterile hypopyon [7].

Thiotriazoline as a synthetic hepatoprotective and cardioprotective drug with an anti-ischemic, membrane-stabilizing, antioxidant, and immunomodulatory action was registered in 1994 (Order No 85 of Ministry of Health of Ukraine dated May, 31, 1994; Reg. No 94/85/1) and approved for mass production and clinical use. The same order (No 94/85/3) registered 1% thiotriazoline solution for injections.

Thiotriazoline is an indirect antioxidant that acts at initial stages of lipid peroxidation (LPO), reactivates the antioxidant complex, inhibits the excessive LPO production in pathologically altered tissues and, thereby, provides protection for the structural and functional

integrity of cell biomembranes [8]. The drug improves blood circulation in ischemic areas of the eye, reduces the intensity of inflammatory and neurotrophic processes. Thiotriazolin stimulates reparative processes and restores sensitivity of the cornea.

In the modern pharmacological industry and practical medicine there is a tendency to use methods which are least traumatic and unpleasant for the patient; that is why, creation of prolonged-action drugs and their non-injectable administration are of relevance.

Features of electrophoresis in medicine are conditioned by a combined effect of both a medicinal product (MP) applied and an electric current.

Electrophoresis enables to prolong the action of MP with a dose less than that which is commonly used in parenteral administration. Besides, the cornea serves as an ideal semipermeable membrane through which ions penetrate into the eye. The increased permeability of the blood–ocular barrier under galvanization contributes to a greater penetration of MP inside the eye compared to injection administration of MP into eye-surrounding tissues. Besides, MP is accumulated in the tissues, which enables the prolonged effect of MP on the pathologically altered tissues. A medicinal product being in the state of electrical activity has a more pronounced pharmacological action. Electrophoresis is also accompanied by elimination of products of inflammation and pathological metabolism. Influenced by electric current, metabolism and blood circulation in tissues are accelerated [9].

Electrophoresis with 0.25% quinine as well as with aloe extract is a well-known treatment for neurogenic keratitis [9].

Thiotriazoline instillations have been used in pharmacotherapy for anterior eye dystrophic diseases. As a part of complex treatment, two drops of 1% thiotriazoline was instilled into a patient's eye 4-5 times per day [10].

Development of treatment for neurotrophic keratopathy which would shorten the duration and increase the efficacy of complex therapy is of great relevance and importance in the ophthalmic practice.

The purpose. To improve a correction method for metabolic alterations in corneal tissues in continuous-SCL-wear-associated neurotrophic keratopathy through using transorbital electrophoresis with 1% thiotriazoline.

Material and methods

We developed a method of treatment for neurotrophic keratopathy which includes a 10 day course of daily transorbital electrophoresis with 1% thiotriazoline as a part of complex therapy. We applied for approval of Author's certificate (application No U 201710621 dated 01 November 2017).

Patients were prescribed disinfectant (2% aqueous boronic acid, 0.02% aqueous chlorhexidine), tear-substituent (0.21% optinol, hylo care), and epithelializing (corneregel) therapy. In addition, they underwent daily transorbital electrophoresis with 1% thiotriazoline and thiotriazoline instillations for 10 days.

An active electrode (anode) in the form of a bath, on the bottom of which 2-3 ml of 2% calcium chloride was placed, followed by 10 ml of 1% thiotriazoline and 2% calcium chloride to fill the bath. Current strength and duration of the procedure was steadily increasing from 0.3 to 0.5, 0.8 and 1 mA and from 3 min to 5 min, 8 min, and 10 min, respectively. Maximal dosage was 1 mA, 15 min. The indifferent electrode with a hydrophilic gasket was placed in the collar area.

Clinical studies were performed at Corneal Pathology Department in the Filatov Institute of Eye Diseases and Tissue Therapy of NAMS of Ukraine.

Results

Clinical example No1. A 32 y/o patient had used SCLs for 11 years. Diagnosis in both eyes: moderate myopia, stage 1 NK, corneal haze, and dry eye syndrome. The patient complained of visual impairment, foreign body sensation in the eye, blurring, redness, strong discomfort-associated inability to wear contact lenses. Visual acuity: OD 0.04 cc – 5.5 d = 0.2; OS 0.02 cc – 6.0 d = 0.5. Objectively in both eyes: conjunctival hyperemia; 360-degree limbal vascularization; pronounced pannus in the upper half of the cornea; cloudy, punctuate, jerk-shaped corneal opacities (a greater amount was on the left) were fluorescein stained; expressed epitheliopathy in the entire cornea; significantly decreased sensitivity of the cornea. In addition to therapy using disinfectant, tear- substituent, and reparative agents, the patient underwent a 10 day course of daily transorbital electrophoresis with 1% thiotriazoline. Moreover, the patient was recommended thiotriazoline instillations four times per day. On the second day, we noted a decrease in haze intensity and the presence of bloodless corneal vessels. Visual acuity after treatment: OD: 0.05 cc – 5.5 d = 0.4; OS: 0.08 cc – 6.0 d = 0.85. A clinical picture of both eyes: conjunctival hyperemia decreased; corneal surface was epithelialized; the pronouncement of limbal vascularization and vascular pannus of the cornea significantly decreased; there was a tendency to vessel bloodlessness; corneal opacities decreased in number and intensity. Subjectively, the patient noted the disappearance of discomfort in the eyes. One month later, the patient successfully continued wearing soft contact lenses.

Clinical example No2. A 39 y/o patient had used SCLs for 20 years. Visual acuity: OD: 0.02 cc – 5.25 d = 0.9-1.0; OS: 0.02 cc – 5.75 d = 0.9-1.0. Diagnosis in both eyes: moderate myopia, stage 1 NK, and dry eye syndrome; corneal haze in the right eye. The patient complained of dryness in the eye, more extensive on the right; periodic redness; strong discomfort when wearing lenses, which made it difficult to wear them. Objectively in both eyes: significantly decreased sensitivity of the cornea; moderate conjunctival injection; 360-degree limbal vascularization; pannus in the upper cornea; the cornea fluorescein staining was punctated in the entire surface, more extensively in the lower half of the cornea; to the right, at 10-11 o'clock, there were two paracentral round corneal opacities. The complex treatment was supplemented with thiotriazoline

instillations four times per day and a 10 day course of daily transorbital electrophoresis with 1% thiotriazoline. At day 3, we noted a decrease of corneal opacities in the right eye. After treatment, the patient noted a decrease of discomfort in the eyes. Visual acuity: OD: 0.02 cc – 5.25 d = 1.0; OS: 0.02 cc – 5.75 d = 1.0. Objectively in both eyes: the conjunctiva was pink; corneal vascularization decreased; bloodless vessels were noted; the corneal surface was smooth, brilliant, not fluorescein stained; the smaller opacity in the right eye dissolved and another became semi-transparent.

Clinical example No3. A 37 y/o patient had used SCLs for over 10 years. Visual acuity: OD: 0.02 cc – 5.75 d = 0.12; OS: 0.02 cc – 5.0 d = 0.25. Diagnosis in both eyes: stage 1 NK, dry eye syndrome, and moderate myopia; corneal haze in the right eye. The patient complained of redness, discomfort, sand sensation in the eyes, more extensively in the left; inability to wear SCLs on the left eye. Objectively in both eyes: corneal sensitivity was moderately decreased in the right eye and significantly decreased in the left; conjunctival injection; 360-degree limbal vascularization; vascular pannus in the upper cornea in the right eye expressed vascular pannus and in the upper and lower halves of the cornea in the left eye; in the area of lower pannus there was semi-transparent corneal opacity; the fluorescein staining of the cornea in the left eye was punctated in the outer half. As a part of complex treatment of neurotrophic keratopathy, the patient underwent a 10 day course of daily transorbital electrophoresis with 1% thiotriazoline and thiotriazoline instillations four times per day. After treatment, the patient noted that comfort in the eye increased. Visual acuity: OD: 0.02 cc -5.75 d = 0.2; OS: 0.02 cc – 5.0 d = 0.3-0.4. A clinical picture of both eyes: the conjunctiva was pink, the cornea was not fluorescein stained; corneal vascularization decreased; pathological vessels were bloodless; in the left eye, corneal opacity was less intensive.

Conclusions

Electrophoresis enables a prolonged stay of active substances in the body and targeted administration of a medicinal product into damaged parts of the eye, which makes it possible to prolong the action of the medical product on pathologically altered tissues. Moreover, electrophoresis requires a smaller dose than it is commonly used in parenteral administration.

Electric current appears to have a positive effect which is accompanied by partial electric elimination of inflammation products and accelerates blood circulation and metabolism in tissues.

The proposed treatment enables in a short term to significantly decrease pathological changes in corneal tissues in stage 1 neurotrophic keratopathy, to increase comfort in the eyes, to prevent severe complications of neurotrophic keratopathy and soft contact lens wearing.

Reference

1. Efron N. Staining of the cornea caused by contact lens wear. Glaz. 2000;1(11): 5-13. Russian.
2. Drozhzhina GI, Ivanova ON, Gaidamaka TB. et al. Severe corneal infections induced by contact lens wearing. J.ophthalmol.(Ukraine).2016;6:38-42.
3. Cavanagh HD, Petroll M, Alizadeh H et al. Clinical and diagnostic use of in vivo confocal microscopy in patients with corneal disease. Ophthalmology. 1993;100(10):1444 – 53.
4. Dart JK, Radford CF, Minassian D, Verma S, Stapleton F. Risk factors for microbial keratitis with contemporary contact lenses: a case-control study. Ophthalmolo gy.2008;115(10):1647-54.
5. Ziadi M, Moiroux P, d'Athis P et al. Assessment of induced corneal hypoxia in diabetic patients. 2002;21(5):453-7.
6. Gaidamaka T, Veliksar T, Drozhzhyna G, Hramenko N. [Condition of tear film, conjunctiva, limbus and cornea in long-term use of siliconehydrogel contact lenses]. Oftalmologiia. Vostochnaia Evropa. 7(3): 289-98. Russian.
7. Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. Clin. Ophthalmol. 2014;8:571−9.
8. Trofimova TS, Briuzgina TS, Chekman IS. [Effect of thiotriazolinum on lipid indices in the liver and the heart of rats in toxic action of doxorubicin]. Zaporozh. med. zhurn. 2005;1:124-6. Ukrainian.
9. Cherikchi LE. [Physiotherapy in ophthalmology]. Kyiv: Zdorovya;1979:3-4;53-4. Russian.
10. Chekman IS, Replianchuk ND. [Use of thiotriazolinum and corneregel in pharmacotherapy of dystrophic diseases of the anterior eye]. [Proceedings of scientific practical conference “Filatov Memorial Lectures – 2013”: 52-3. Ukrainian.