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MODERN APPROACH TO THE TREATMENT OF INFLAMMATORY DISEASES OF THE CORNEA USING EYE MEDICINAL COATINGS (literature review)

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ABSTRACT

Over the past few years, the use of biocoatings in ophthalmology in various pathologies has yielded tangible results. However, most of them are covered with muscle mass: tissue connection, graft fixation, intraocular fluid retention. The development in appearance with an antibacterial manifestation is underway, which is important for patients with inflammatory eye lesions. Research in the field of imparting biocoatings with additional properties and functions is promising in ophthalmology.

Scientific research is being carried out around the world to develop effective methods for treating inflammatory eye diseases and optimizing the use of film biocoatings. The development of polycomposite films with methylene blue for the treatment of inflammatory diseases of the cornea, based on hematological, biochemical and pathomorphological changes based on the results of experimental studies in vivo, is important for the scientific substantiation of the results of evaluating the effect of the drug. developed a coating for the processes of regeneration of the cornea based on the results of local and systemic morphological changes. Scientists of Uzbekistan have developed the concept of the optimal composition and properties of the Novacel ophthalmic film. Ziyo "based on a polycomposite polymer material. The film is characterized by biocompatibility, biodegradability, high sorption activity, vapor permeability, elasticity, strength, antimicrobial properties, absence of cytotoxicity, pyrogenic and toxic effects.

Key words: antibacterial action, inflammatory eye diseases, bio-coatings, ophthalmic medical films.

INTRODUCTION

One of the formidable complications of the eyes is infectious keratitis, which causes a sharp deterioration in vision, the degree of which depends on the geographical location and predisposing risk factors [13]. The most common pathogens causing infectious keratitis, from the appearance of: Staphylococcus aureus [1,4], streptococcus pneumonia [5, 6] and fusarium solani [7, 8]. Treatment of infectious keratitis must be prompt in detecting possible destruction of corneal tissue, as well as to limit the area of corneal scarring, which can lead to loss of visual acuity. International standards for the treatment of infectious keratitis include cases of use and systemic antibiotics. [9, 10]. However, to date, the management of patients with infectious keratitis has caused a number of difficulties due to the identification of resistance of pathogenic diseases. The high incidence of pathogenic microbes to antibiotics is due to their rapid reproduction and mutation. There is an acute prospect of searching for alternative acute conditions aimed at weakening resistance in infectious keratitis [11, 12].

There are enough works devoted to evaluating the effectiveness of PDT in malignant eye diseases. Thus, patients with ocular melanoma were irradiated at a dose of 50–100 J/cm^2 [14]. There is also a positive effect of using PDT among patients with initial serous choriortinopathies. Compared with laser photocoagulation, the advantage of PDT was an increased sensitivity of the subretinal fluid (Lim this al. 2011). However, the difference in visual recovery and baseline macular density was not affected. In some cases (2-10%), after the detection of laser photocoagulation, iatrogenic choroidal neovascularization (Reibaldi this al. 2010). Compared with intravitreal injection of diseases that suppress vascular endothelial growth factors, the best results (inflammation of the focus of macular disease, resorption of subretinal fluid) have been reported with PDT. PDT is recognized visually as a treatment for underlying serous chorioretinopathy. (Jinglan, 2014).

PDT has found its application in patients with polypoid-choroidal vasculopathy . In the study of PDT monotherapy , the remission period was within 5 days, which is a relatively high efficiency in the treatment of these diseases. While the use of PDT as a result of intravitreal administration of the drug Ramibizumab achieved a complete cure (Kai Tan , 2014).

In experiments on laboratory rats, in one of the domestic studies, an eye burn was simulated using an EHVCh-2 laser device (60 J, 120 J, 300 J), and bacteriostatic activity was also studied. A 1% solution of methylene blue was taken as a photosensitizer. As a result of irradiation, blood flows in the lateral segments, choroids and posterior poles of the eyes, as well as in the surrounding tissues, were

found in all the observed. Signs of the presence of lacrimal glands were registered in animals with a laser dose of 60 and 120 J (focal dystrophy, accumulation of corneal fragments). There was a bacteriostatic effect against St. hemolytic , St. _ epidermis , St. _ golden . In the comparison groups, a 25% solution of levocetin and a 1% solution of methylene blue were used without the effect of PDT [17].

There are a number of works aimed at studying the antibacterial effects of immunoglobulins and complement in purulent keratitis. In an experimental model in mice under general anesthesia, injuries (1 mm) of the corneal epithelium were made using a needle. Pseudomonas aeruginosa was used as a bacterial flora in the amount of 3×10^5 - 4.5×10^6 CFU per animal. Inflammation of the cornea reached its maximum achievement 48 hours after infection. Evaluation macro scale in the application consisted in the quantitative measurement of pathological processes: the eye does not differ from the intact one - 0 points; slight clouding, partially covering the pupil - 1; intense clouding covering the pupil - 2; active opacification, covering the entire anterior segment - 3; corneal perforation – 4 [16]. To evaluate the results of applying the population count method, histological examination of the eyes.

New Zealand White and Dutch rabbits are the most commonly used to model bacterial keratitis in rabbits. One of the detected cases causing Pseudomonas keratitis in rabbits Pseudomonas in rabbits was developed by Hessburg et al. [18], who proposed the application of an infected silk thread to the corneal stroma. This method was later used to identify the Pseudomonas protease , which causes massive destruction of the cornea and the loss of visual acuity [20], as well as to evaluate the antibacterial effect. Kessler this al . [22] used an intrastromal injection model in which bacteria were introduced into the cornea to determine the degree of proteolytic activity of P. aeruginosa and study the response of rabbit eye tissues. The authors took advantage of the fact that in response to a bacterial injection, not only a massive influx of polymorphonuclear leukocytes is initiated , but also proteolytic enzymes (metalloproteinases), which leads to damage to the cornea. The need for bacterial keratitis in rabbits depends on the detection of increased excitability of cells at injection sites [19].

Iglewski et al. [15,20] injected purified exotoxin A into the cornea of rabbits and observed toxic effects that were neutralized by antitoxin. Thibodeau et al. [21] transformed the genes for two P. aeruginosa virulence factors (elastase and alkaline protease), a species that is non-pathogenic to rabbit eyes, Pseudomonas putid .

Various types of antibiotics and new types of therapy using intrastromal [20, 21] and doses of inoculation [22] have been used in ophthalmology to match

Pseudomonas aeruginosa. Other types of Pseudomonas aeruginosa inoculation with excoriation [23, 24], abrasion [25], and mechanical removal of the corneal epithelium [22]. A method for contaminating contact lenses in rabbits has also been proposed [2, 3, 26].

Beyond antibiotic resistance research, scattered collisions with immunization work. For example, testing a vaccine against specific bacteria or their antigens. Thus, Kroeger et al. [27] immunized rabbits with P. aeruginosa lipopolysaccharides and then infected their corneas with bacteria. Holzer this al. used by Dutch rabbits to study lamellar keratitis after corneal surgery [28–31].

Infection with S. au reus in the experiment cannot be achieved without trauma or increased manipulation, for example, with the use of contaminated contact lenses. there is only a suspension that the population is injected intracorneally. Kupferman And Leibovitz used the intrastromal injection model to study the effectiveness of antitumor therapy in keratitis caused by Staphylococcus aureus [32]. Laboratory studies of the minimum frequency of detection of antibiotics do not always reveal the identification of the picture inside the eye. Moreover, they suggested that not all strains of S. aureus would necessarily have the same sensitivity as the strains used in their study.

Of the significant open areas of affected eyes discovered by S. aureus in the intracorneal model, alpha-toxin was identified as the most influential bacterial virulence factor [33, 34]. This discovery inspired subsequent studies, including immunization with alpha-toxin followed by infection in rabbits [35], as well as cyclic treatment with dextrin, which caused inhibition of alpha-toxin, which greatly reduced the severity of the disease [36].

One study used a rabbit model to achieve efficacy in endophthalmitis and evaluate moxifloxacin bacteria. They were divided into three groups with moxifloxacin induced before and after surgery, only before surgery and only after surgery. As a result of preliminary studies, the quantitative amount of St. golden. Suspended bacterium S. aureus 50 thousand CFU in the amount of 0.025 ml was injected into the anterior chamber during the operation. For a possible day, the eyes are developed with the help of an alkaline lamp. Signs of endophthalmitis were assessed according to a scale (0, 0.5, 1, 2 and 3) in terms of hypopyon, iritis, conjunctivitis, limbal injection, corneal infiltration, blepharitis, red reflection and fibrin. After the animals were removed from the experiment, the degree of infection of the anterior and posterior chambers of the eye was assessed using the standard method of counting colonies [15].

Currently, adhesive coatings in the applied ophthalmology are becoming increasingly popular due to the success achieved in the application of the

frequency of detection of complications. An ideal biocoating should be non-toxic, have high adhesive properties, and have an anti-inflammatory and wound-healing effect. Natural biological and synthetic coatings. Primary synthetic adhesive coatings include: cyanoacrylate adhesives and coatings based on polyethylene glycol (PEG) derivatives. Cyanoacrylate glue has high adhesion values, but after rapid polymerization after contact with a liquid, it can provoke histotoxicity. Fibrin coatings are less traumatic and the time of their polymerization can be pneumonia. However, the adhesive properties of fibrin are much lower than the cyanoacrylate adhesive coating. PEG has advantages in terms of toxicity, mechanical properties, and polymerization time [37].

Cyanoacrylate glue is synthesized by an exothermic reaction between formaldehyde and cyanoacetates [38]. High molecular weight cyanoacrylates (isobutyl, octyl cyanoacrylate) are the most durable and highly sensitive coatings compared to low molecular weight (methyl cyanoacrylates) [39, 40]. Fibrin adhesives are bonded from two components which, when mixed, are water-insoluble adhesives. One outer surface component (Tisseel, USA; Tissucol, USA) self-detection: fibrinogen, coagulation factor XIII and aprotinin. The second component was represented by thrombin and calcium. The mechanism of action is that the reaction of thrombin components stimulates the conversion of fibrinogen into fibrin, which then polymerizes with calcium-stimulated coagulation factor XIII . Aprotinin destroys the destruction of fibrin glue. Known fibrin coatings include various types of combined preparations. For example, Quixil (OMRIX Biopharmaceuticals, New York, USA) detects tranexamic acid instead of aprotinin. Fibrin is a biocompatible and biodegradable property, which increases the risk of toxicity and inflammatory tissue inflammation. Terms of polymerization duration and exacerbation of thrombosis [41, 42]. Evicel is the most durable fibrin coating with the most sensitive mechanical properties [41, 43]. One of the missing fibrin mites is the risk of transmissible infection transmission, since the drug is made from donated blood [44]. Due to possible contamination during collection of autologous blood.

Cyanoacrylate adhesive, due to its low viscosity, is preferable to use during surgical operations in the supine position in patients with possible leakage of the adhesive [45]. The addition of the iofendilate substance slows down the polymerization of the cyanoacrylate adhesive. To reduce the risk of toxicity, the drug applies a very dense mass or uses a sponge impregnated with glue [46]. Application on the cornea of the eye, it is important to pre-dry the surface and surrounding tissues. In this case, the adhesive will not attach to the corneal epithelium [47].

Evicel fibrin coating (USA) is delivered using a nebulizer, which can only be used if the nebulization is accurately predicted. Fibrin Tachosil (USA) is presented in the form of a patch that can be cut to the desired size and placed on the damaged surface [48].

In 1960 Refojo this Al and Webster this For the first time , adhesive coatings were used as a treatment for corneal perforations [49, 50]. Since then, corneal perforations up to 3.0 mm in diameter have been freely treated with cyanoacrylate adhesive [49, 50, 51]. The use of corneas observed in trauma reduces the frequency of enucleations [51].

Cyanoacrylate glue stops the progression of corneal necrosis, inhibition of polymorphonuclear leukocytes due to collagenolytic and proteolytic properties [51, 52]. In 1983, Eiferman and Snyder proved that glue inhibited the growth of Gram-positive organs, inhibited foreign body interests, and selective corneal neovascularization [52, 54]. However, the question of the toxic effect of cyanoacrylate derivatives on the corneal endothelium, which is associated with the formation of iridocorneal and iridolenticular adhesions, remains unresolved [52, 54].

Sharma this Fibrin and N -butyl-2-cyanoacrylate have been found to be effective in corneal perforations up to 3 mm in diameter. It should be noted that healing occurred faster after the use of fibrin glue (within 6 weeks) with the lowest incidence of corneal vascularization compared to cyanoacrylate glue. The primary advantage of fibrin coating is the longest fixation of the coating [49]. As for corneal lesions larger than 3 mm, amniotic membranes or scleral grafts impregnated with cyanoacrylate or fibrin glue are included for their temporary closure [49]. Grau and Duran suggested using more than 3 mm thick amniotic membrane for covering wounded corneas, or a single-layer amniotic membrane with a TachoSil coating layer. [55].

In 1970, Rosenthal performed corneal transplantation in an experiment on rabbits using a platelet -fibrin mixture [56]. In 2003, Kaufman discovered fibrin (Tisseel) for joint keratoplasty in 5 patients. All grafts with a thickness of 200 microns successfully engrafted [57]. In 2007, Duarte and Kim applied the "sandwich" method for lamellar keratoplasty using thrombus and fibrinogen [58]. In the same year, Narendran et al. performed lamellar keratoplasty with suture and fibrin coating. Researchers have found that they cover areas of application for both the donor and the recipient. For more accurate drug delivery in the case of a fibrin glue graft applied with 2 syringes [59].

Fibrin glue has also been successfully used in the preparation of grafts for autonomous endothelial keratoplasty [60].

Meskin, Ritterband and Leung independently used 2-octylcyanoacrylate in humans in cataract surgery [61-63]. Despite the fact that the coating sealed the corneal incision in all manifestations, Meskin noted that in some patients a small foreign body and diffuse conjunctival hyperemia were observed [61]. In 2009, Banitt et al. compared the performance of N -butyl-2-cyanoacrylate, Tisseel fibrin glue, and suture at 3 mm, 4.5 mm, and 6 mm. It was concluded that N -butyl-2-cyanoacrylate is most effective at a 4.5 mm cut, with sizes of 4.5 and 6 mm. In 2012, Kaya et al. demonstrated that N -butyl-2-cyanoacrylate is used more frequently with a 2.5 mm incision [65].

In 1998, Henrik et al. used Tisseel fibrin glue to cover a scleral incision without the use of any expanded surfaces or sutures [66]. Mester et al. demonstrated the use of a Tissucol fibrin coating that compared with a control group of patients with postoperative astigmatism. However, the consequences Alio et al. did not identify a significant group in the use of fibrin glue and the tradition of suturing [66, 68].

In 2007, Hovanesian and Karageozian found that Tisseel fibrin glue has an effect on the effect of intraocular fluid with the absorption of intraocular pressure and significantly increases the pressure required to remove the fluid [67]. In comparative studies in 2009, Banitt et al. found that for lesions up to 3 mm, it is preferable to use fibrin glue, since there is a significant difference in intraocular pressure. For large incisions (4.5–6 mm), suturing is in no way inferior to the use of fibrin coating [50].

Coatings based on PEG derivatives have become very popular in eye cataract surgery. When collecting biocoatings OcuSeal (Beaver - Visitec International), consisting of a powder form of PEG and liquid polyethyleneamine, has the value of increasing the level of intraocular pressure [51]. Kenyon et al. found that OcuSeal showed a risk of postoperative astigmatism and foreign body hypersensitivity compared to suturing [62]. Several case studies have demonstrated the significant efficacy of ReSure coatings in increasing intraocular pressure, the absence of fluid leakage compared with the self-healing of clean cut wounds of the cornea [53-55].

For more than 30 years, fibrin glue, with its success in the surgical preparation of pterygium, indicates a significant safety of gluing the amniotic membrane and conjunctival graft during wound closure. Numerous studies confirm the fact that, compared with the appointment of sutures, the placement of a fibrin coating provides time for surgery, eliminates postoperative discomfort, and reduces the risk of postoperative complications and relapses [66].

A meta-analysis published in 2017 reported a significant efficacy of fibrin glue in fixing conjunctival autographs on pterygium results compared to controls. It was found that in the experimental group with fibrin coating, the frequency of recurrence of diseases within 6 months was revealed in comparison with the imposition of pigs with a non-significant difference in the rates of complications [47]. According to Suzuki et al. Nylon and silk filaments induce immune verification and damage to Langerhans cells in the cornea of the eye [58]. Scientists have found that frequent relapses trigger an inflammatory response.

The use of autologous fibrin glue for fixation of the conjunctival graft is a likely way to detect exacerbation of relapses and postoperative complications. Various fibrin glue application techniques have been applied by Kenyon and others [59]. The traditional method of using fibrin glue has been to alternate fibrinogen and thrombin before applying them to the scleral bed and fixing a conjunctival autograft. Koranyi et al. frequent cases of release and insertion, where the two components of the adhesive were applied separately. Fibrinogen was found on the surface of the graft and thrombin was found on the surface of the sclera [60]. In case of occurrence of cases of rapid formation (30 sec.) of a blood clot after the application of a graft. The fibrin glue sandwich technique was published in 2013 by Fava et al., which made it possible to manipulate the graph prior to fixation. This method consisted of 3 layers: fibrinogen-conjunctival autograft, thrombin. You can apply fibrinogen in the area of the scleral bed, then autograft and thrombin.

Cyanoacrylate glue and fibrin glue are the most widely used for limbal transplantation. Many studies have demonstrated the positive results of using cyanoacrylate glue during the process of dissection and limbal stem cell harvesting [66].

Cyanoacrylate is used to secure the donor corneoscleral rim to the block, which provides absorption that aids plate delamination while minimizing the spread of the limbal epithelium. In addition, fibrin glue fixes keratoballar allografts associated with live conjunctival limbal allograft in people with stem cell deficiency. Stitching can lead to postoperative infection, inflammation, vascularization and provoking graft rejection [67].

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