Uludağ Üniversitesi Tıp Fakültesi Dergisi
Journal of Uludağ University Medical Faculty
51 (2) 209-215, 2025
DOI: https://doi.org/10.32708/uutfd.1641884

ORIGINAL RESEARCH

In Vitro Study of the Effect of 1.0% Sodium Hyaluronate on Bacterial Strains and Antibiotics*

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ABSTRACT

During anterior segment eye surgeries, ophthalmic viscosurgical devices (OVDs), primarily containing hyaluronic acid, protect the corneal endothelium and help maintain the anterior chamber with reduced trauma. We aimed to investigate the interaction of sodium hyaluronate 1.0% with Gram-positive and Gram-negative bacteria, and its interactions with prophylactic intracameral antibiotics moxifloxacin and cefuroxime. Four quality control bacterial strains were used in vitro to conduct five experiments using either cefuroxime or moxifloxacin. Our experiment included five stages: 1. Testing the ability of OVD to retain bacteria before antibiotic exposure. 2. Examining antibiotic-bacteria interactions in the presence of OVD. 3. Simulating aqueous humor circulation. 4. Evaluating the effect of OVD residuals on antibiotic retention. 5. Analyzing the interaction of bacteria and antibiotics within the OVD. Results showed a significant decrease in bacterial counts ($p<0.001$) between the initial stage and subsequent groups, with moxifloxacin consistently demonstrating lower bacterial counts and greater effectiveness compared to cefuroxime ($p<0.001$). Further in vivo studies are recommended to validate these results.

Key words: Sodium hyaluronate 1.0%. Cefuroxime. Moxifloxacin. Ophthalmic viscosurgical devices.

%1.0 Sodyum Hyaluronatın Bakteriler ve Antibiyotikler Üzerindeki Etkisinin İn Vitro Çalışması

ÖZET

Ön segment göz ameliyatları sırasında, öncelikli olarak hyaluronik asit içeren oftalmik viskocerrahi cihazlar (OVD'ler), kornea endotelini korur ve ön bölmenin daha az travma ile korunmasına yardımcı olur. Çalışmamızda %1.0 Sodyum hyaluronat içeren OVD'nin Gram pozitif ve Gram negatif bakterilerle etkileşimini ve profilaktik olarak kullanılan intrakamaral moksifloksasin ve sefuroksim ile etkileşimlerini araştırmayı amaçladık. Sefuroksim veya moksifloksasin kullanılarak beş deney yürütmek için dört kalite kontrol bakteri suşu in vitro kullanıldı. Deneyimiz beş aşamadan oluşmaktadır; 1. Antibiyotik maruziyetinden önce OVD'nin bakterileri tutma yeteneğini test etme, 2. OVD varlığında antibiyotik-bakteri etkileşimlerini inceleme, 3. Humor aköz dolaşımını simüle etme, 4. OVD kalıntılarının antibiyotik tutması üzerindeki etkisini değerlendirme, 5. OVD içindeki bakteri ve antibiyotik etkileşimini analiz etme. İlk deney grubundaki bakteri sayısı ve sonraki aşamalar arasındaki bakteri sayılarında önemli bir azalma olduğu ($p<0,001$) saptandı. Moksifloksasin, sefuroksim ile karşılaştırıldığında daha fazla etkinlik gösterdi ($p<0,001$). Çalışmamız invitro bir çalışma olup, sonuçları doğrulamak için daha fazla in vivo çalışma önerilmektedir.

Anahtar Kelimeler: %1 Sodyum hyaluronat. Sefuroksim. Moksifloksasin. Oftalmik viskocerrahi cihaz.

Date Received: 25.February.2025
Date Accepted: 2.July.2025

* Presented as an oral presentation at the "40th Congress of the European Society of Cataract & Refractive Surgeons" (16-20 September 2022, Milan, Italy).

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Hyaluronic acid (HA) is a linear polysaccharide composed of alternating β-D (1→3) glucuronic acid and β-D (1→4) N-acetyl-β-D-glucosamine units. HA, a biodegradable and biocompatible carbohydrate polymer, is present throughout the eye[1,2]. Sodium hyaluronate accelerates wound healing by promoting intercellular interaction, cell-matrix adhesion, cell motility, and extracellular organization[3]. In the 1980s, the US Food &Drug Administration (FDA) approved the first ophthalmic medical device containing HA. HA is primarily produced through the fermentation of *Streptococcus zooepidemicus* rather than being extracted from rooster combs. This method ensures minimal contaminants in the final product, such as proteins, pathogens, or endotoxins. CD44 is a primary cell surface receptor for HA and is responsible for internalizing HA-coated nanoparticles to the cornea and conjunctiva. HA is highly susceptible to degradation through enzymatic, chemical, and physical pathways[1,2]. Ophthalmic viscosurgical devices (OVD)primarily contain HA andprotect the corneal endothelium and maintain the anterior chamber during anterior segment eye surgeries, with less trauma[1,2].

Infection is an uncommon but severe complication that may occur after cataract surgery. One of the most critical complications is post-operative endophthalmitis, which can result in irreversible blindness or even loss of the eye. The reported incidence rates of post-operative endophthalmitis vary significantly across medical centers worldwide, ranging from 0.28 to 1.6 per 1000 cataract surgeries[4]. Many cases of sporadic endophthalmitis are caused by pathogens from a patient's eyelid and periocular flora. *Staphylococcus epidermidis* is the most commonly identified organism in such cases. Patients who have a compromised immune system may be more susceptible to developing infections from endogenous pathogens. Intraocular surgery, which includes cataract surgery, is a possible means of transmitting external pathogens. A cluster of multiple cases of post-operative endophthalmitis in the same surgical center is a significant cause for concern. It can often be traced back to transmitting pathogens from external sources such as surgical instruments, contaminated fluid solutions, and the surgical environment[4]. Therefore, administering antibiotics during the perioperative period is a reasonable strategy for reducing the occurrence of post-operative endophthalmitis. In daily practice, various antibiotics have been used to prevent endophthalmitis and different antibiotic administration routes have been proposed accordingly. However, the effectiveness of antibiotic use has not been established until recently[5].

In the current study we created a non-surgical simulation environment to showcase how a commercial product containing sodium hyaluronate 1.0% (an OVD) interacts with bacteria and antibiotics because of its polysaccharide structure. Our objective was to demonstrate how this device interacts with gram-positive and gram-negative bacteria and interacts with moxifloxacin and cefuroxime, commonly used intracameral antibiotics as prophylactics.

Material and Method

We conducted an in vitro laboratory study consisting of five experimental steps (Figure 1). *Staphylococcus aureus* (ATCC 25923), two strains of *S. epidermidis* (ATCC 12228 and ATCC 35984), and *Pseudomonas aeruginosa* (ATCC 27853) were used in this study. Two antibiotics, cefuroxime (Cefeye, Deva, Istanbul, Turkey) and moxifloxacin (Moxai %0.5, Abdi İbrahim, Istanbul, Turkey), were also used.

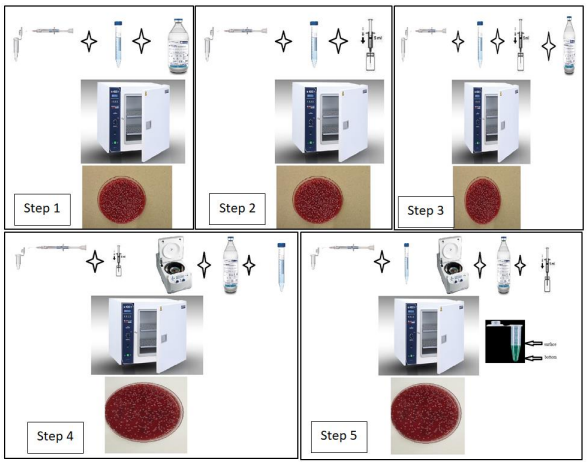

Figure 1.
The design of the experimental process

Sterile Eppendorf tubes (1.5 milliliters) represented the eye's anterior chamber. After every experimental step, the number of bacteria in the Eppendorf tubes was determined. To do this, 5% sheep blood agar was streaked and incubated at 35°C for 16-18 hours. To ensure even distribution across the entire plate in the colony counting process, we took 10 µl of the solutions created in each experimental step, diluted it with 990 µl of physiological saline, and spread the mixture onto a 5% sheep blood agar plate, making sure to wet the entire surface evenly. Each experimental step was repeated five times, and the average bacterial colony numbers per milliliter were calculated. The sodium hyaluronate 1.0% was studied in five experimental steps, and all procedures were repeated for both antibiotics using four quality control strains. When evaluating bacterial counts calculated by the colony counting method, percentage reduction and logarithmic reduction formulas were used.

1.0% Sodium Hyaluronate

Before conducting the experiments, we performed antibiotic susceptibility testing for each bacterium using the disc diffusion method with the antibiotics we intended to use. The results were evaluated based on the Clinical and Laboratory Standards Institute (CLSI) criteria[6]. We used antibiotic concentrations of 4 µg/ml for moxifloxacin and 16 µg/ml for cefuroxime in staphylococci, and 8 µg/ml for moxifloxacin and 64 µg/ml for cefuroxime in *P. aeruginosa*. CLSI criteria determine these concentrations.

Experimental steps

The initial experiment aimed to assess the ability of OVD (Healon Pro - sodium hyaluronate 1.0%) to retain bacteria prior to antibiotic exposure. The experiment also aimed to determine the impact of antibiotics on other stages where they were used. To begin, 500 µl of bacterial solution with a density of 1/10000 McFarland was added to a drop of viscoelastic material in an Eppendorf tube. As antibiotics were not used in this stage, 500 µl of sterile irrigation fluid (BSS Ocrosol-Polifarma) (SIF) was added to maintain a constant bacterial concentration. After an hour of incubation at 37°C, the mixture was streaked onto 5% sheep blood agar using the colony count method (Figure 1- step 1).

In the second stage of the experiment, the objective was to showcase the interaction between antibiotics and bacteria in the presence of OVD. Initially, a drop of OVD was added to an Eppendorf tube, followed by 500 µl of antibiotic. The mixture was then incubated at 35°C for an hour. After that, bacterial solution at 1/10000 McFarland density was added to the mixture. The tube was then incubated again at 35°C for another hour. Finally, the colony count method was used to determine bacterial count (Figure 1- step 2).

During the third experimental stage, an additional step was taken in addition to the second stage. The mixture was washed with SIF to simulate aqueous humor circulation before spreading in the medium. To prevent the removal of OVD during the washing process, 500 µl of liquid was taken from the surface of the mixture in an Eppendorf tube and replaced with 500 µl of SIF. This mixture was gently shaken by hand and incubated for 15 minutes. The process was repeated eight times, and the colony count method was used (Figure 1- step 3).

During the fourth experimental step, we performed a centrifugation and washing step. The aim was to evaluate the antibiotic retention effect of the OVD left at the bottom of the tube. We incubated the antibiotics with the OVD in this step, as in the second step. Next, we centrifuged the Eppendorf at 1000 rpm for 10 seconds to ensure the precipitation of the OVD. After centrifugation, we discarded 300 µl of the supernatant remaining on the surface and added 300 µl of SIF instead. We repeated this cycle three times. Then, we added 500 µl of bacterial solution with a density of 1/10000 McFarland and incubated it for 1 hour at 35°C. Finally, the colony count method was used (Figure 1- step 4).

In the fifth experimental step, we applied the centrifugation process at different stages to evaluate the antibiotic and bacteria-retaining effect of OVD. We also examined the interaction of bacteria and antibiotics within the OVD. This step demonstrates the effectiveness of post-operative antibiotics in preventing surgical site infections caused by contamination during surgery in patients who did not receive preoperative prophylaxis. To perform this step, we added 500 µl of bacterial solution at 1/10000 McFarland density onto a drop of OVD added to the Eppendorf tube. We then incubated it for 1 hour at 35°C. After incubation with the bacterial solution, we repeated the centrifuge and washing cycle described in the fourth experimental step three more times. Then, we added 500 µl of antibiotic and incubated it for another 1 hour. After the second incubation, we centrifuged the OVD at 1000 rpm for 10 seconds to ensure precipitation of OVD. Next, we discarded 500 µl of the supernatant remaining on the surface and added 500 µl of SIF instead. We repeated this cycle four times. After the fourth centrifuge, we made surface and bottom inoculations separately on 5% sheep blood agar without washing. We left them for incubation for 16-18 hours at 35°C and evaluated them by the colony count method. With the first centrifuge-washing process in this step, the supernatant was removed, and the OVD and the bacteria precipitated and remained mainly at the bottom of the Eppendorf. During the incubation phase with antibiotics, the antibiotic was expected to affect the bacteria present with OVD. With the centrifuge washing process in the last stage, we removed the supernatant and the antibiotics. This step helps us understand how OVD interacts with bacteria and antibiotics and evaluate the antibiotic and bacteria-retaining effect of OVD (Figure 1- step 5).

The design of the experimental process is summarized below, with Figure 1 for visualization:

1. OVD+bacteria+SIF; incubation; cultivation

2. OVD+antibiotic; incubation; +bacteria; incubation; cultivation

3. OVD+antibiotic; incubation; +bacteria; incubation; irrigation; cultivation

4. OVD+antibiotic; incubation; centrifugation; +bacteria; incubation; cultivation

5. OVD+bacteria; incubation; centrifugation; + antibiotic; incubation; centrifugation; cultivation (deep and supernatant)

Statistical analysis

The statistical data analysis was conducted using IBM SPSS 28.0 (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp.) software. The Shapiro-Wilk test was employed to determine whether the data exhibited a normal distribution. Descriptive statistics were presented as mean, standard deviation, or median (interquartile range) for quantitative data. For data that showed normal distribution, a one-way analysis of variance was used to compare more than two groups. At the same time, the Kruskal-Wallis test was employed for non-normal distribution. In the case of significance, one of the multiple comparison tests, the Bonferroni test, was used. The level of significance was set at p=0.05.

Results

Before conducting the experiments, we performed antibiotic susceptibility testing for each bacterium using the disk diffusion method. The antibiotics we used were evaluated according to CLSI criteria. We found that *S. aureus* ATCC 25923 and *S. epidermidis* ATCC 12228 were sensitive (S) to cefuroxime and moxifloxacin. However, *S. epidermidis* ATCC 35984 and *P. aeruginosa* ATCC 27853 were resistant (R) to cefuroxime. Because no CLSI data were available to evaluate *P. aeruginosa* with moxifloxacin, we evaluated it according to levofloxacin. We found that it was sensitive at high doses (I).

Tables I and II show the logarithmic and percentage reductions in the number of bacteria for each quality control bacterium tested with moxifloxacin and cefuroxime, respectively, compared to the initial step.

A significant difference ($p<0.001$) was observed between step 1 and the subsequent steps when comparing moxifloxacin and cefuroxime against all bacteria (Table III). In step 1, bacteria were incubated solely with OVD. It was noted that when OVD was exposed to antibiotics in any of the following steps, there was a significant reduction in the number of bacteria.

The moxifloxacin group showed a lower bacterial count at all stages compared to the cefuroxime group. However, there were statistically significant differences ($p<0.001$) in bacterial counts, specifically at step 2 and step 4 (see Table III).

During step 3 of the experiment, the circulation was utilized to simulate aqueous humor. Step 2 demonstrated static conditions, while step 3 involved dynamic conditions. The number of bacteria in the *P. aeruginosa* group also decreased during step 3; however, this decrease was not statistically significant when moxifloxacin was used. It was observed that the number of bacteria decreased significantly ($p < 0.001$) in all other groups.

Table I. The logarithmic and percentage reduction in the number of bacteria for moxifloxacin

MOXIFLOXACIN								
	S. aureus		*S. epidermidis* 35984		*S. epidermidis* 12228		*P. aeruginosa*	
	%	*log*	*%*	*log*	*%*	*log*	*%*	*log*
Second step	-72.93	-0.57	-76.98	-0.64	-59.25	-0.39	-98.01	-1.70
Third step	-98.77	-1.91	-95.79	-1.38	-92.00	-1.10	-99.97	-3.54
Fourth step	-57.96	-0.38	-46.95	-0.28	-54.29	-0.34	-99.30	-2.16
Fifth step supernatant	-99.73	-2.56	-99.23	-2.12	-97.87	-1.67	-99.99	-4.01
Fifth step deep	-99.44	-2.25	-98.60	-1.85	-95.28	-1.33	-99.78	-2.65

Table II. The logarithmic and percentage reduction in the number of bacteria for cefuroxime

CEFUROXIME								
	S. aureus		*S. epidermidis* 35984		*S. epidermidis* 12228		*P. aeruginosa*	
	%	*log*	*%*	*log*	*%*	*log*	*%*	*log*
Second step	-41.87	-0.24	-1.71	-0.01	-5.91	-0.03	-36.66	-0.20
Third step	-95.43	-1.34	-90.82	-1.04	-89.95	-1.00	-97.53	-1.61
Fourth step	-39.82	-0.22	-32.92	-0.17	-39.41	-0.22	-36.95	-0.20
Fifth step supernatant	-99.22	-2.11	-99.15	-2.07	-98.51	-1.83	-99.53	-2.33
Fifth step deep	-97.62	-1.62	-98.77	-1.91	-97.05	-1.53	-98.26	-1.76

1.0% Sodium Hyaluronate

Table III. The average number of bacteria colonies observed in the experimental steps

	S. aureus (ATCC 25923)		*S. epidermidis* (ATCC 35984)		*S. epidermidis* (ATCC 12228)		*P. aureginosa* (ATCC 27853)	
	Moxifloxacin	Cefuroxime	Moxifloxacin	Cefuroxime	Moxifloxacin	Cefuroxime	Moxifloxacin	Cefuroxime
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
First step	205040±12969.5	205040±12969.5	91240±5781.7	91240±5781.7	92760±5485.25	92760±5485.25	206200±19976.86	206200±19976.86
Second step	55500±3708.1	119200±5761.94	21000±1421.27	89680±5655.71	37800±1923.54	87280±3048.28	4100±1208.3	130600±17854.97
Third step	2520±676.02	9380±957.6	3840±981.33	8380±1961.38	7420±641.87	9320±370.14	60±89.44	5100±234.52
Fourth step	86200±1254.99	123400±5549.77	48400±5140.53	61200±1104.54	42400±1557.24	56200±3053.69	1440±512.84	130000±5000
Fifth step supernatant	560±461.52	1600±696.42	700±187.08	780±44.72	1980±83.67	1380±311.45	20±44.72	960±638.75
Fifth step deep	1140±260.77	4880±216.79	1280±334.66	1120±130.38	4380±258.84	2740±384.71	460±114.02	3580±676.02

In Step 4, we measured the number of bacteria remaining at the bottom of the Eppendorf after exposure to antibiotics using OVD. This was done by discarding the surface layer following centrifugation. This step aimed to simulate the effects of prophylactic antibiotics administered before surgery. In Step 1, only the bacteria were incubated with OVD. In Step 4, we observed a significant decrease in bacteria ($p<0.001$) across all tested microorganisms compared to Step 1. Additionally, moxifloxacin proved more effective than cefuroxime ($p<0.001$).

Step 5 simulated the adhesive effect of antibiotics and bacteria on OVD, and deep cultivation was conducted to test for potential infections due to residual OVD in the environment after surgery. This step aimed to evaluate the effectiveness of antibiotics following surgery involving contaminated OVD. The results showed a significant decrease ($p<0.001$) in the number of bacteria observed in the deep cultivation during Step 5 compared to Step 1 for both antibiotics across all tested bacteria.

Staphylococcus epidermidis (ATCC 35984) and *P. aureginosa* (ATCC 27853) were resistant to cefuroxime. Although moxifloxacin led to a significant decrease ($p<0.001$) in the number of bacteria in all steps compared to the first step, cefuroxime resistance prevented any significant decrease from being observed in the second step.

Discussion and Conclusion

During cataract surgery, OVDs are used to coat surgical instruments. The primary purpose of these devices is to minimize the risk of damage to intraocular tissue. They also help to create space, maintain stability in the anterior chamber, and protect the endothelium against fluid turbulence, free radicals, air bubbles, and lens fragmentation. OVDs are well-established and commonly used during cataract surgery[7]. One of the serious but uncommon complications that can occur during cataract surgery is a surgical site infection. This type of infection can lead to bacterial endophthalmitis, which can cause significant damage to the eye. Bacterial endophthalmitis progresses quickly and can affect the retina, leading to vision loss[8]. The purpose of this study was to gain a better understanding of how OVD interacts with bacteria and antibiotics. Specifically, we investigated how 1% sodium hyaluronate interacts with the bacteria that most commonly cause endophthalmitis and the antibiotics most frequently used to prevent it. To achieve this, we conducted five separate experimental steps.

One of the most concerning issues after cataract surgery is the increased risk of developing post-operative endophthalmitis. This condition often begins during surgery when a corneal incision is made in the anterior chamber of the eye to remove the cataract lens. This incision allows ocular surface fluid containing bacteria to enter the eye[9]. Bacteria mainly come from the conjunctiva and are inoculated into the eye during ocular surgery, but can also come from the skin[10]. Different types of eye surgeries are associated with various bacterial strains, but most are Gram-positive. Two studies, the Endophthalmitis Vitrectomy Study and the French Institutional Endophthalmitis Study, discovered that Gram-positive bacteria caused 94% of acute cases following cataract surgery. Among these bacteria, 70% were coagulase-negative staphylococci (CoNS), normal bacteria in the body's commensal flora[11,12]. CoNS is the most frequently identified pathogen, followed by *S. aureus* and *Streptococcus spp*. About 20% of infections are caused by Gram-negative microorganisms[13]. Therefore, we chose CoNS, *S. aureus* and *P. aureginosa*.

Post-operative endophthalmitis refers to severe inflammation in both the anterior and posterior segments of the eye following intraocular surgery[14]. According to a 2014 survey by the American Society of Cataract and Refractive Surgery (ASCRS),

approximately 90% of respondents reported using antibiotics regularly during the peri-operative period. However, there is no universally agreed-upon regimen for administering these antibiotics. According to the ASCRS survey, the most commonly used medication was a fourth-generation fluoroquinolone, such as moxifloxacin or gatifloxacin[15]. Moxifloxacin has a broad spectrum of activity and is effective against Gram-positive and Gram-negative bacteria, including *P. aeruginosa*[14]. In 2005, the European Society of Cataract and Refractive Surgeons (ESCRS) conducted a significant randomized clinical trial to evaluate the routine use of topical and intracameral antibiotics during cataract surgery. The study revealed that prophylactic intracameral injections of cefuroxime significantly reduced the incidence of post-operative endophthalmitis (POE) by almost five times, decreasing the rate from 0.33% to 0.07%. Enterococci are resistant to cefuroxime, and cefuroxime's narrow spectrum of activity is not ideal for treating infections caused by Staphylococcus species. In Sweden, routine use of intracameral cefuroxime has led to an increase in cases of Enterococci endophthalmitis, and its use has also been associated with an increase in fungal endophthalmitis cases[14]. The occurrence of endophthalmitis was found to be significantly lower in patients who were administered intracameral cefuroxime (5/6836; 0.07%) as compared to those who did not receive the same (23/6862; 0.33%) in a single randomized clinical trial by the ESCRS in 2007. However, the incidence of endophthalmitis was not significantly different between patients who received levofloxacin eye drops (12/6852; 0.18%) and those who did not receive them (16/6846; 0.23%)[16]. In our laboratory study, we found that moxifloxacin was effective against all tested strains, while cefuroxime showed resistance in *S. epidermidis* ATCC 35984 and *P. aeruginosa*. Throughout the experiments, the bacterial counts for moxifloxacin were consistently lower than those for cefuroxime across all steps and bacterial types. Notably, the differences observed were statistically significant ($p<0.001$) in steps 2 and 4 (see Table III). Based on these findings, moxifloxacin is considered to be more effective than cefuroxime in addressing both Gram-positive and Gram-negative bacterial contamination.

The aqueous humor is a fluid that comprises organic and inorganic ions, carbohydrates, amino acids, glutathione, carbon dioxide, oxygen, and water. Its primary function is to supply nutrients and oxygen to the avascular tissues of the eye, such as the cornea and the lens. Additionally, it helps remove waste products, blood, macrophages, and other debris from the anterior lens and posterior cornea. It also helps to maintain the shape of the eyeball shape and intraocular pressure[17]. Astafurov et al.[18] found that patients with glaucoma had a higher oral bacterial load compared to those without glaucoma. Moreover, the immune system successfully eliminates a low amount of bacteria. The number of bacteria in the aqueous humor is reduced by the circulation of aqueous humor and the immune system. In step 3, even though we could not simulate the immune system, we saw that the number of bacteria was reduced by stimulating the circulation of the aqueous humor.

A meta-analysis indicated that the rates of post-operative endophthalmitis using intracameral cefuroxime, moxifloxacin, and vancomycin were 0.0332%, 0.0153%, and 0.0106%, respectively. Moxifloxacin provides a wider range of bacterial coverage than cefuroxime and vancomycin[19]. During the fourth step, the number of bacteria decreased significantly ($p<0.001$) in all microorganisms compared to the first. Furthermore, moxifloxacin proved more effective than cefuroxime ($p<0.001$). These findings highlight the significance of prophylactic antibiotics in case of endogenous or exogenous contamination during surgery. In step 5 of the study, the effectiveness of antibiotics was checked after surgery involving contaminated OVD. The results showed a significant decrease ($p<0.001$) in the number of bacteria during step 5 deep cultivation as compared to step 1 for both antibiotics in all bacteria. This indicates that OVD, which can remain as a residue for days after the surgery, is less likely to cause an infection.

Staphylococcus epidermidis (ATCC 35984) and *P. aureginosa* (ATCC 27853) were resistant to cefuroxime. Moxifloxacin significantly reduced the number of bacteria ($p<0.001$) at all steps when compared to the first. Despite cefuroxime resistance, there was no significant reduction in the second step. However, a decrease in the number of bacteria was observed in other steps due to the implementation of washing procedures in the cefuroxime group. It is worth noting that ATCC 35984 is a biofilm-forming strain. If extracellular polymeric substances do not protect the bacteria, they can be removed by the circulation of body fluids or through irrigation during surgery. Unfortunately, cefuroxime is not effective in eliminating this particular strain of bacteria.

It is important to recognize some limitations of this study. First, it is an in vitro study, meaning an accurate anterior chamber simulation may not have been achieved at all stages.

In conclusion, we found that moxifloxacin is more effective than cefuroxime against Gram-positive or Gram-negative bacterial contamination. Additionally, we found that it is unlikely that contaminated OVD may cause an infection when antibiotics are present. These findings emphasize the importance of using prophylactic or post-operative antibiotics in endogenous or exogenous contamination cases. Further, in vivo studies should support our results.

1.0% Sodium Hyaluronate

Researcher Contribution Statement:
Idea and design: N.U.T., M.B., E.S.S., T.T., K.E., G.Ö. and C.O.; Data collection and processing: N.U.T., T.T. and K.E.; Analysis and interpretation of data: G.Ö.; Writing of significant parts of the article: N.U.T., M.B., E.S.S., T.T., K.E., G.Ö. and C.O.
Support and Acknowledgement Statement:
none
Conflict of Interest Statement:
The authors of the article have no conflict of interest declarations.
Ethics Committee Approval Information:
No human or animal was used in this study. This is experimental study that does not require ethics committee approval.

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