

GUIDELINE & CONSENSUS

Chinese Expert Consensus on Perioperative Medication in Laser Corneal Refractive Surgeries (2019)

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Key words: consensus; corneal refractive surgery; medications; perioperative; ametropia

Abstract Laser corneal refractive surgery has become an important treatment to correct ametropia in recent years. Rational medication in the perioperative period is essential to ensure the success of the surgery and to reduce complications. However, in this area there has been no consistent understanding and unified application guide across the world. Experts in Refractive Surgery Group, Ocular Microcirculation Branch of Chinese Society of Microcirculation who are specialized in keratology and optometry had initiated extensive and rigorous discussions and reached a consensus on appropriate medication before, during and after the refractive surgeries. The consensus covers a broad spectrum of commonly used ophthalmic solutions, provides recommendations of routine and enhanced medication on prevention and management of adverse reactions and complications related to the laser corneal refractive surgeries. We hope the consensus serves as a standard perioperative medication regimen for ophthalmologists, helps to ensure the safety and effectiveness of laser corneal refractive surgeries, and improves the quality and outcome of the refractive surgeries.

THE incidence of myopia is increasing year by year, and the advances of technologies have greatly improved the progresses in the treatment of myopia. Laser corneal refractive surgery has become an important way to correct vision

for patients with ametropia, and the number of this surgery keeps increasing in recent years. Although this surgery is of high safety and efficacy, clinicians should still attach great importance to its complications. In addition to the precise operative skills, the rational use of medicine in the perioperative period is also one of important aspects to ensure the success of surgery and reduce complications.

In clinical practice, laser corneal refractive surgery includes two categories: corneal surface ablation refractive surgery and corneal lamellar refractive surgery. The photo refractive keratectomy (PRK), the

Received January 16, 2020; accepted March 8, 2020; published online March 13, 2020.

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This article was originally published in Chinese on *Chinese Journal of Ophthalmology* 2019; 55(12):896-903.

laser-assisted subepithelial keratomileusis (LASEK), the epipolis laser *in situ* keratomileusis (Epi-LASIK) and the trans-epithelial photorefractive keratectomy (trans-PRK) belong to the laser corneal surface ablation refractive surgery. The laser *in situ* keratomileusis (LASIK), the femtosecond laser assisted laser *in situ* keratomileusis (Fs-LASIK), and the small incision lenticule extraction (SMILE) belong to the laser corneal lamellar refractive surgery.

Regarding the perioperative medication of laser corneal refractive surgery, there is no consistent understanding across the world. We believe the standardization of the perioperative medication for laser corneal refractive surgery can help to ensure the quality and safety of the surgery. Experts in the Refractive Surgery Experts Group, Ocular Microcirculation Branch of Chinese Society of Microcirculation had made extensive and rigorous discussions on this issue, and had reached a consensus based on the status quo of treatment for the post-operative complications in China and the domestic and oversea literatures. Our purposes are to help ophthalmologists in better preventing from adverse reactions and post-operative complications that are related to laser corneal refractive surgeries, and thereby ensure the healthy development of patient care in the specialty.

COMMON MEDICINE USED PERIOPERATIVELY

Antibiotics

The rational application of antibiotics in the perioperative period can effectively sterilize and prevent post-operative infection. However, it should be noted that long-term use of antibiotics may lead to the development of drug-resistant bacteria or even secondary fungal infections. Commonly used antibiotics are listed below.

1. Levofloxacin ophthalmic solution

It is the third-generation fluoroquinolones, commonly used at concentration of 0.5% or 0.3%, and its half-life is 6 h - 8 h. Levofloxacin is a bactericidal antibiotic with strong effect against a broad spectrum of bacteria, including gram-negative bacteria such as *enterobacteriaceae*, *haemophilus influenzae*, *legionella pneumophila*, *neisseria gonorrhoeae*, gram-positive bacteria such as *staphylococcus aureus*, *streptococcus pneumoniae*, *streptococcus pyogenes*, as well as

mycoplasma pneumoniae and *chlamydia pneumoniae*. However, it has poor effect on anaerobes and enterococci. People who are allergic to levofloxacin and other quinolones are prohibited to use this medicine.

2. Gatifloxacin ophthalmic solution

As the fourth-generation fluoroquinolones, gatifloxacin is commonly used at concentration of 0.3%, and its half-life is 7.1 h. It's also a bactericidal antibiotic, inhibiting bacterial DNA replication, transcription and repairing. Apart from the effect against gram-negative bacteria as the third generation fluoroquinolones, it has a strong antibacterial effect against a broad-spectrum of bacteria, which include gram-positive bacteria, anaerobes, mycoplasmas, and chlamydiae. The gram-positive bacteria sensitive to gatifloxacin include *staphylococcus epidermidis*, *staphylococcus aureus*, and *streptococcus pneumoniae* (strains sensitive to penicillin); the gram-negative bacteria sensitive to gatifloxacin include *escherichia coli*, *influenza* and *haemophilus parainfluenzae*, *klebsiella pneumoniae*, *moraxella katamola*, *neisseria gonorrhoeae* and *proteus bizarre*. Gatifloxacin also has good effect on other microorganisms, such as non-tuberculous mycobacteria, *chlamydia pneumoniae*, *legionella pneumophila*, and *mycoplasma pneumoniae*. People who are allergic to gatifloxacin and other quinolones are prohibited to use this medicine.

3. Tobramycin ophthalmic solution

As an aminoglycoside antibiotic, tobramycin is commonly used at concentration of 0.3%, and its half-life is 1.9 h-2.2 h. It's also a bactericidal antibiotic, restraining mRNA from translating into protein. It is mainly effective against gram-negative bacteria, such as *pseudomonas aeruginosa*, *escherichia coli*, *klebsiella*, *enterobacteria*, *proteus* and *citrobacter*. Among gram-positive bacteria, it is effective against *staphylococci*, but not against most group D *streptococci*. People who are allergic to tobramycin and other aminoglycosides are prohibited to use this medicine.

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) mainly inhibit the biosynthesis of prostaglandins. It can stabilize lysosomal enzyme and inhibit its secretion so that take the effects of antipyretic, analgesic, and anti-inflammation. It is contraindicated for patients who have history of asthma, hives or allergic reactions

induced by aspirin or other NSAIDs, as well as patients who are allergic to this drug.

For different types of corneal refractive surgeries, the use of NSAIDs is different. Some NSAIDs can cause corneal epithelial damage by inhibiting corneal epithelial cell proliferation and reducing corneal sensation, and prolong healing time consequently.^[1-2] We recommend, if necessary, change or adjust the administration route and medication time according to the operation method and eye condition. Particularly, NSAIDs should be used with great caution before and after laser photorefractive surgery, because it may delay the healing of corneal epithelium.

1. Diclofenac sodium

The commonly used concentration is 0.1%, and the half-life is 1 h-2 h. Its effect is strong.

2. Bromfenac sodium

The commonly used concentration is 0.1%. It has a strong effect and a long duration, with half-life of 0.5 h-4.0 h.^[3-4]

3. Pranoprofen

As a propionic acid derivative, the commonly used concentration is 0.1%, and its half-life is 1.5 h-3.5 h.

Glucocorticoids

Glucocorticoids can alleviate and prevent inflammatory reactions in tissues by inhibiting aggregation of inflammatory cells, *e.g.*, macrophages and white blood cells, in inflammatory response site, and inhibiting phagocytosis, release of lysosomal enzyme, as well as synthesis and release of inflammatory chemical mediators. Local application of glucocorticoids after laser corneal refractive surgery is usually for the purpose to reduce post-operative inflammatory reactions, such as various kinds of early corneal edema, diffuse lamellar keratitis (DLK) after laser corneal lamellar refractive surgery, subepithelial opacity of the cornea (haze) after laser corneal surface ablation refractive surgery, and other related complications, therefore inhibits scar formation.

Glucocorticoids should not be used in patients with corneal epithelial exfoliation or corneal ulcer, viral keratoconjunctivitis, tuberculous eye diseases, fungal eye diseases, or suppurative eye diseases, for it may cause secondary eye infection, perforation, or healing delay.

In the treatment of infectious inflammatory re-

sponse of eyes, glucocorticoids must be applied in combination with effective antibiotics, and when condition improves, the frequency of administration should be gradually reduced. Abruptly stopping administration should be avoided in order to reduce the risk of recrudescence. Occasionally, elevation of intraocular pressure (IOP) or glaucoma may occur in weeks (or even in days) while continuous administration, so IOP should be checked regularly. Corticosteroids are contraindicated in those being allergic to it.

1. Fluoromethalone eye drop

It is commonly applied at concentration of 0.1%, with a half-life of 54 min. It disappears from eye tissues faster than dexamethasone and prednisolone acetate, and has less effect on IOP than dexamethasone.

2. Dexamethasone eye drop

It is commonly used at concentration of 0.1%, and the half-life is about 190 min. Its effect is stronger than prednisone. As the penetration is strong, it is more likely to affect IOP than flumilone.

3. Prednisolone eye drop

It is commonly used at concentration of 1%, and the half-life is 30 min. It penetrates cornea rapidly, and the concentration in aqueous humor can reach the peak in 30 min - 45 min after administration.

4. Loteprednol eye drop

The commonly used concentration is 0.5% and the half-life is 1 h. It is suitable for treating the inflammatory reaction of the anterior segment.

Antivirals

As viral infection is one of contraindications of laser corneal refractive surgeries, generally antiviral drugs are not routine medications before the laser corneal refractive surgery. For patients suspected for corneal infection by virus after surgery, it is necessary to use antiviral drugs properly according to the pathogen of infection.

1. Ganciclovir eye drop

The half-life is 4.8 h ± 0.9 h. It is a chemically synthesized guanine analog that prevents replication of herpes virus.

2. Acyclovir eye drop

The half-life is 3.0 h-3.5 h. It is a chemical synthesis of purine nucleoside analogues, and inhibits replication of herpes simplex virus type I, II and varicella zoster virus effectively.

3. Recombinant human interferon α -2b eye drop

The half-life is 4 h-12 h. It has a broad-spectrum antiviral function, inhibiting cell proliferation and enhancing immune function.

Artificial tears

The application of artificial tears before and after laser corneal refractive surgery can effectively relieve discomforts such as dry eyes and burning sensation, and can promote the stability and repairing of the tear film. At the same time, using artificial tear medicine after the surgery can help to repair and form a healthy tear film, which is beneficial to the improvement of vision and visual quality.

1. Sodium hyaluronate ophthalmic solution

Sodium hyaluronate binds fibronectin, promotes epithelial cell bonding and extension, and speeds up wound healing. Sodium hyaluronate eye drop is generally used at concentration of 0.1%; in severe case or when the therapeutic effect is not satisfied, it can be used at concentration of 0.3%.

2. Hydroxylsine glycosides ophthalmic solution

It is a compound preparation, mainly composed of dextran (0.1%), hydroxypropyl methylcellulose (0.3%) and glycerin (0.2%). The therapeutic effect is reducing symptoms of dry eyes and stinging pains that caused by insufficient secretion of tears or exposure to the wind and sand, sunlight, or long-time watching screen.

3. Polyvinyl alcohol ophthalmic solution

It is a kind of polymer that is hydrophilic, film-forming, and biocompatible, and can improve symptoms related to dry eyes.

4. Sodium carboxy methyl cellulose ophthalmic solution

It contains 0.5% sodium carboxy methyl cellulose and electrolyte from natural tears, which can replenish electrolytes in tears with long-acting lubrication, and therefore relieve irritation of dry eyes.

5. Hydroxypropyl methyl cellulose ophthalmic solution

It is a semi-synthetic, inactive, viscoelastic polymer, acts as the function of conjunctival mucin, and alleviates the discomforts caused by reduction of mucin in eyes.

6. Vitamin A palmitate ophthalmic gel

It can promote the regeneration and secretion of conjunctival goblet cells and reverse conjunctival epithelial keratinization and squamous metaplasia.^[5]

7. Carbomer ophthalmic gel

This is a kind of lipid gel water which contains carbomer, medium chain triglycerides and water. It can simulate physiological tears, form high viscosity crystal transparent gel and adhere to the corneal surface storing liquid. When the structure of the gel is damaged by salt in tears, it releases water.

IOP-lowering medication

IOP-lowering medicine can be selectively used to control the IOP. Prior to applying, patient's systemic medical history and drug allergy history should be acquired in detail to avoid adverse reactions. Prostaglandin derivatives should be used with extreme caution in reducing IOP.

1. Thiamethoxam bisoprolol (timolol) or carteolol hydrochloride ophthalmic solution

It can be used 2 times daily. Contraindications include bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, II or III degree atrioventricular block, severe heart failure, cardiac shock and being allergic to this drug.

2. Brinzolamide ophthalmic solution

It can be used 2 or 3 times daily, as the sole treatment for patients who have failed to respond or be contraindicated to β -blockers, or as a synergistic treatment with β -blockers. It is contraindicated in patients who are allergic to brinzolamine, with known allergic history to sulfanilamide, or with severe renal insufficiency.

3. Bromomidine tartrate ophthalmic solution

It can be used twice daily. Patients who are allergic to brimonidine tartrate or who are on therapy of monoamine oxidase inhibitors are prohibited to use this medicine.

4. Methazolamide tablets

This medicine can be taken orally at 25 mg twice a day as the initial dose. The dose can be increased to 50 mg twice a day if the effect of lowering IOP is not satisfactory. It is contraindicated for the one with sulfonamide allergy.

Medicine promoting nerve repairing and growth

Laser corneal refractive surgery can cause corneal nerve damage in the processes of incision, making flap, or cutting matrix. The degree of damage may depend on the surgical method, thickness of flap or cap, diameter of light zone, and cutting thickness and depth of matrix.^[6] Poor repair after corneal nerve injury can lead to neurotrophic corneal epithelial lesions, such as patchy erosion of corneal epithelium and positive corneal epithelial staining, which bring symptoms such as dryness and foreign body sensation, and aggravate postoperative discomforts.^[7]

Drugs that promote repair and growth of nerve injuries can accelerate wound healing by promoting proliferation of epithelial cells and fibroblast cells. However, long-term application of these kinds of medicine may cause adverse reactions, such as corneal limbal neovascularization, so it is necessary to follow the indications and monitor changes in eyes during medication.^[8]

1. Deproteinized calf blood extract

It can promote the uptake and utilization of glucose and oxygen of eye tissues and cells, accelerate the energy metabolism of cells, thus improve tissue nutrition and eye microenvironment. When preoperative epithelial abnormality exists, deproteinized extract of calf blood can improve rapid repair of the corneal injury. Early application after the surgery can promote repairing of corneal nerve.^[9]

2. Recombinant bovine basic fibroblast growth factor (rb-bFGF)

It can promote the repair and regeneration of cells derived from mesoderm and ectoderm.^[10] Cautions should be taken when applying in patients with corneal neovascularization.

3. Recombinant human epidermal growth factor (rh-EGF)

It promotes the regeneration of corneal epithelial cells, thus shortens healing time of damaged cornea. It can alleviate symptoms of ocular surface irritation

after corneal refractive surgery, promote repairing of corneal epithelium, and stabilize tear film.^[11]

Anti-eyestrain medication

Visual fatigue is prone to happen early after laser corneal refractive surgery. Studies have suggested that it is related to the post-operative changes in regulating function of eyes. As a representative drug to improve the regulating function of ciliary muscle and treat visual fatigue, Esculin and Digitalisglycosides Eye Drops^[12] is recommended to be administrated since the 3rd to 7th postoperative day because the symptoms of visual fatigue are most obvious in the first post-operative week, and can be used for months.^[13]

PREOPERATIVE MEDICATION

Routine medication

Topical antibiotics are strongly recommended as routine for all patients before the surgery. Applying broad-spectrum antibiotic eye drops for 3 days 4 times a day, or for 2 days 6 times a day, or for 1 day and over 12 times a day.

NSAIDs can be used as appropriate, at 30 min, 15 min and 5 min respectively prior to the cornea surface ablation refractive surgery to relieve postoperative pain.^[14]

Artificial tears can be selectively applied preoperatively for 3 days 4 times a day to promote early postoperative recovery of tear film stability.^[15]

Enhanced medication

For patients requiring surgery immediately, on the premise of informing the related risks, frequent antibiotic eye drops should be administrated preoperatively. The total preoperative usage on the day of surgery should exceed 12 times to achieve the similar effect as the routine preoperative medication.^[16] As ophthalmic gel is characterized by its high bioavailability,^[17] antibiotics in gel can be applied every 2 hours, thus the total administrations can be reduced to 6 times.

INTRAOOPERATIVE MEDICATION

Antibiotics before surgery

Broad-spectrum antimicrobial drugs should be applied 1 h before the surgery, in combination with NSAIDs as appropriate. For conjunctival sac irrigation, normal saline or ringer lactate solution can be routinely used

preoperatively. Antibacterial injections (such as amikacin or tobramycin injection) can be added in the flushing solution, which can inhibit bacteria, prevent from infection, and meanwhile reduce eye irritation and side effects of chemical agents. For some particular cases, lacrimal canal irrigation should be performed. In addition, eyelid margin should be cleaned and disinfected with special attention, which can effectively reduce chances of postoperative infection. The disinfection of cornea before refractive surgery should strictly follow the aseptic disinfection protocols of regular ophthalmic surgeries.

Anesthetics

When performing surface anesthesia of the operating eye, it is recommended to apply anesthetics 2 or 3 times, 1-2 drops/5-10 min. It is suggested not to apply too early and too frequently in order to avoid corneal epithelial peeling. Surface anesthetics should be used with extreme caution in patients with hyperthyroidism or heart diseases, because adverse reactions in these cases, such as damage of cornea, vision loss and delayed wound healing, are prone to occur.

Sodium hyaluronate eye drop

In cases corneal flap is made using a micro corneal knife or femtosecond laser, it is helpful to apply sodium hyaluronate eye drops on the corneal surface to keep the corneal surface moist and smooth, which is conducive to vacuum aspiration .

Rinsing solution

After corneal ablation, rinse thoroughly with balanced saline. In case that ablation is deep, Mitomycin C at concentration under 0.02% can be applied carefully. After ablation, the interface between corneal flap and stromal bed should be thoroughly rinsed with balanced saline before resetting corneal flap *in situ*.

Antibiotics and glucocorticoid early after surgery

Applying eye drops of broad-spectrum antibiotics and glucocorticoids after the operation can reduce the risks of postoperative infections and relieve symptoms such as early postoperative pain. It is worth noting that for corneal surface ablation refractive surgeries, *e.g.* LASEK and trans-PRK, NSAIDs and glucocorticoids are not conducive to corneal epithelial migration, and consequently affect epithelial wound healing, so it is prudent to use these two drugs immediately after the

surgeries.

POSTOPERATIVE MEDICATION AND MANagements FOR ADVERSE REACTIONS AND COMPLICATIONS

For laser corneal lamellar refractive surgery

1. Routine medication

1) After the operation, transparent eye mask or goggles is advised to protect the eyes.

2) Apply antibiotic eye drops continuously 4 times a day for 7-14 days, 1-2 drops each time.

3) Apply glucocorticoid eye drops 4 times a day for 1-2 weeks, 1-2 drops each time. If necessary, prolong the medication time to 1 month, adjusting dosage as appropriate. Alternatively, using non-steroidal anti-inflammatory eye drops 3 or 4 times a day, 1-2 drops each time.

4) Apply artificial tears or eye gel drops to stimulate ocular surface repairation.

5) Regular follow-up in 1 day, 1 week, 1 month, 3 months, 6 months, and 1 year, respectively after the operation.

6) The post-operative medication for synergism operation or re-operation follow the same routine.

2. Managements for adverse reactions and complications

1) Symptoms from inadequate correction or over-correction: for inadequate correction, we suggest to increase the dosage, course or frequency of glucocorticoids, with close monitoring of IOP; for the overcorrection, reduce the dosage of glucocorticoids properly.

2) Diopter regression: symptomatic treatment according to the reason of diopter regression is suggested.

3) Visual disturbance: this includes transient or permanent glare or halo, especially loss of vision at night. For those symptoms severely disturbing life-living early after operation, myotonic drugs, such as low-concentrated pilocarpine eye drops, can be used in the evening.

4) Non-infectious diffuse lamellar keratitis: in this case, glucocorticoids can be used for impact therapy at the early stage according to the principle of firstly high efficiency, high penetration, high concentration, and frequent administration, followed by low efficiency, low concentration and gradually decreasing the dosage. For DLK of grade 3 or above, corneal interla-

minar irrigation should be carried out as appropriate. Dexamethasone and antimicrobial agents, such as amikacin, should be added into the irrigation solution.

5) Dry eyes: when symptoms of dry eyes appear or deteriorate if suffered before operation, apart from routine application of artificial tears, such as sodium hyaluronate eye drops, measurements that can be taken include increasing frequency of dropping, applying bovine blood deprotein-removing extract eye gel, applying two or more kinds of artificial tears or auxiliary lacrimal duct embolization, as well as locally using anti-inflammatory medicines such as low concentrated glucocorticoids. Attention should be paid to the risk of tarsal gland dysfunction and/or inflammatory response.

6) Recurrent corneal epithelial erosion: applying low-concentrated glucocorticoid eye drops. Preservative-free artificial tears, such as sodium hyaluronate, can be used optionally. If available, use bandage contact lens.

7) Recurrence of herpes simplex keratitis: locally or systemically apply antiviral drugs, such as ganciclovir eye gel or oral capsules. For superficial epithelial keratitis at acute phase, locally applying glucocorticoids are contraindicated. For keratitis of prestromal layer or deep layer, antiviral drugs (*e.g.*, ganciclovir eye gel) can be applied locally at its maximum dosage, accompanied by glucocorticoids following the principle of low concentration and low application frequency.^[18]

8) Haze or scar (early or delayed): treatment with glucocorticoids is demonstrated effective. Corneal lamellar opacity may occur after laser corneal lamellar refractive surgery, but the incidence is much lower than that after laser corneal surface ablation refractive surgery. Adjust the concentration and frequency of glucocorticoids according to the degree of haze. Usually, the longer time and higher degree of haze appears, the longer time and higher frequency of glucocorticoids for the treatment. The administration can be started with a high concentration and high frequency, continued with gradual down-regulation. Be alert to glucocorticoid-induced complications, closely monitor IOP, and apply IOP lowering medicine if necessary. Particularly, it is worth noting that: a) the measured value of IOP after surgery is generally low; b) as there is a relatively high proportion of open-angle glaucoma and elevated IOP in patients with high myopia, selecting appropriate surgical methods preoperatively according to the indications is important for reducing chances of postoperative glu-

cocorticoid induced glaucoma or corneal opacity.

9) Corneal infiltration, ulcer, and melting: for these complications, causes should be firstly distinguished between infection and non-infection. Apply anti-infection treatment for infections, and glucocorticoids or NSAIDs in conditions of non-infection.

Corneal infection is an emergent condition after laser corneal refractive surgery. Identifying pathogen and executing effective anti-infection therapy are crucial. In addition to controlling the disease, particular attentions are needed for preservation of vision. The most common pathogens of postoperative infections are gram-positive bacteria, such as atypical *mycobacterium*, *staphylococcus aureus* and *streptococcus*. For infectious keratitis that occur early after operation (within 7 days), the pathogens are usually gram-positive bacteria such as *staphylococcus aureus* and *streptococcus*, and for those occur in the late postoperative period, the pathogens are usually mycobacteria or fungi. If bacterial infection is confirmed, the fourth generation quinolones, such as gatifloxacin eye drops, can be frequently applied locally.^[19, 20] If necessary, inject 2% amikacin under conjunctiva, and perform microbial culturing for further identification of the pathogens. For lamellar infections after laser lamellar refractive surgery, open the corneal flap as soon as possible and do irrigation, while for the SMILE operation, cut off the pouch, open the corneal cap and perform open irrigation as soon as possible; if necessary, use iodine tincture for local cauterization and irrigation afterward. Amikacin is the first choice for irrigation solution. In early stage of acute infection (7-10 days), wash once every other day, with ciliary muscle relaxant eye drops added in the irrigation solution. If the microbial culturing yields fungus, antifungal ophthalmics (*e.g.*, natamycin, or fluconazole) can be jointly applied locally, while glucocorticoids are prohibited in this situation.

For corneal surface ablation refractive surgeries

1. Routine medication

1) Antibiotics: after the operation, applying antibiotics eye drops continuously for 7-14 days. Quinolones are the first choice of antibiotics for the advantages of broad antibacterial spectrum, strong antibacterial power, low drug resistance rate, and not likely to affect corneal epithelial healing. Better anti-infection effects can be achieved if preoperatively apply antibiotics in conjunctival sac. Among fluoroquinolones family, gatifloxacin has been shown the best therapeutic effect

on non-tuberculous mycobacteria infection.^[20] As gatifloxacin has good corneal penetration^[21] and can reach high concentration in cornea,^[17] it has good effect on preventing postoperative infections of corneal interface.

2) Glucocorticoids: glucocorticoids can be used immediately after the operation, and 4 times a day from the second postoperative day for 7-10 days, followed by low-concentration glucocorticoid medicine, such as 0.1% flomicron, for 2-3 months on the principle of decreasing dosage monthly. For patients with elevated IOP or who are likely of loss to follow-up, novel NSAIDs are applicable. For severe haze, flumirone and clotiprenol are preferred in corticosteroid shock therapy, while prednisone and dexamethasone are not recommended. For patients with high myopia and high cutting ratio, glucocorticoids can be applied at a relatively high dosage and for long medication time.

3) NSAIDs: short-term pain and discomfort may occur after operation, where non-steroidal anti-inflammatory eye drops or artificial tears can be a solution. Preservatives free diclofenac sodium eye drops (0.1%) can significantly relieve symptoms of pain and corneal irritation. In the case of delayed epithelial healing, it was shown that early applying preservatives free diclofenac sodium eye drops can promote healing of corneal epithelial, which was faster than applying glucocorticoids.^[22] Free from preservatives avoids its potential damages to stability of tear film, tight connection and mitosis of corneal epithelial cells.^[23] Wearing corneal bandage contact lens after operation can significantly alleviate symptoms related to pains.

4) Artificial tears: artificial tear eye drops are suggested to be applied for 3 months or longer time period after the operation.

2. Managements for adverse reactions and complications

1) Refractive regression: performing enhanced operation. Mitomycin C with concentration under 0.02% can be selectively used during the operation as appropriate. The concentration and timing of the medicine should be carefully and strictly controlled.

2) Haze or scar (early or delayed): once identified, immediately increase the concentration, dosage and frequency of glucocorticoids (e.g., flumilone) locally applied. In the early stage, use high con-

centration with high frequency, and then gradually down-regulate. Be alert to the potential complications induced by glucocorticoids, closely monitor IOP, and apply IOP-lowering medicine if necessary, such as captopril hydrochloride, brimonidine tartrate, etc. Adjust dosage of glucocorticoids according to the degree of refraction correction, the degree of regression and haze. Since UV exposure can increase the probability of haze and scar, it is important to enhance compliance education in patients who are receiving the treatment.

3) Delayed healing of corneal epithelium and filamentous keratitis: it is suggested to locally apply medicines that promote corneal epithelial repair, such as epithelial growth factor, deproteinized calf blood extract, sodium hyaluronate eye drops, and vitamin A palmitate eye gel. The specific medication scheme can refer to the *Expert Consensus on the Clinical Diagnosis and Treatment of Corneal Epithelial Injury in China* (2016).^[7] After the operation, patients are suggested to wear bandage contact lens routinely for 3-10 days. Occasionally, focal epithelial hypertrophy, or focal dotty/patchy cloudiness may occur, which usually recover after removing or replacing the bandage contact lens. Early application of deproteinized calf blood extract eye gel after LASEK can promote corneal nerve repairing and perceptual restoration, thus improve postoperative visual quality.^[24]

4) Other adverse reactions and complications: the management is basically the same as that for the laser lamellar refractive surgery.

SUMMARY

As laser corneal refractive surgeries are performed on relatively healthy eyes, appropriate perioperative medication not only ensures a smooth process of the operation, reduces or prevents chances of various intraoperative accidents, but also is an important prerequisite to prevent and reduce risks of postoperative complications, or effectively control it once occurred. Application of antibiotics in the perioperative period, especially in the preoperative period, is one of the necessities for a successful operation. Fluke minds are not acceptable, for it may cause serious and irreversible visual damage. Therefore, the rational application of medicines in the perioperative period is a paramount base to guarantee the safety and effectiveness of laser corneal refractive surgeries.

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Article information

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There is a Chinese version of this article on *Chinese Journal of Ophthalmology* 2019; 55(12):896-903. Authorization has been acquired for the second publication in English.

Conflict of Interests Statement

All authors declared that they had no economic interests in the production and marketing of mentioned medicines in this article. No conflicting interest disclosed.

Acknowledgement

We acknowledge the work of Dr. Ruijue Ma at Tianjin Eye Hospital on collecting and collating experts' opinions, and the work of Dr. Di Chen at Peking Union Medical College Hospital on language translation of this article. Appreciations are also given to Dr. Yang Jiang for her additional contributions to translation, coordination and documentation of this work.

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