OPHTHALMOLOGICAL
REALITIES

GOOD PRACTICE IN OPHTHALMOLOGY

THE USE OF TOPICAL CORTICOSTEROIDS ON THE OCULAR SURFACE

Théa

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THE USE OF TOPICAL CORTICOSTEROIDS ON THE OCULAR SURFACE

Round table report compiled by

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With the institutional support of Théa.

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The presented data may therefore not have been validated by the French authorities and, in this case, should not be put into practice.

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SUMMARY

GOOD PRACTICE IN OPHTHALMOLOGY

THE USE OF TOPICAL CORTICOSTEROIDS ON THE OCULAR SURFACE

Round table report

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Corticosteroid eye drops are one of the pillars of the ophthalmological pharmacopoeia. They are used in a wide range of indications, in the treatment of obviously inflammatory manifestations, such as scleritis, as well as certain ocular surface pathologies where inflammation is sometimes less evident. They are also essential post-operatively for almost all eye surgeries.
In this round table, conducted with the support of the Laboratoires Théa, we discussed the role of corticosteroid eye drops in several clinical situations, by detailing the prescription methods of the various available molecules.

1

SHORT REMINDERS OF CORTICOSTEROID PHARMACOLOGY

Corticosteroids are steroid hormones secreted by the cortex of the adrenal glands. There are **glucocorticoids (GCs)**, which act mainly on protein and carbohydrate metabolism and have anti-inflammatory properties, and **mineralocorticoids**, which take part in fluid and sodium regulation in the body. Here, we will look at GCs, with cortisol being the only representative present in the body's natural state. All other GCs are synthetic molecules.

In order to act, GCs must first cross the cytoplasmic membrane of the target cells to reach their receptors in the cytoplasm (glucocorticoid receptor or GR). Very schematically, GC–GR complexes translocated into the nucleus induce direct transcriptional regulation, by binding to glucocorticoid response elements (GRE) on target genes, or indirect transcriptional regulation, by binding with other proteins such as NF B. In short, these mechanisms induce the synthesis of anti-inflammatory cytokines and inhibit the synthesis of pro-inflammatory cytokines. At the same time, GCs have a faster non-genomic effect, specifically involving inhibition of phospholipase A2, which in turn decreases the synthesis of arachidonic acid, a key player in the inflammatory reaction [1].

1.1 Glucocorticoid actions

Immunomodulatory

GCs have anti-inflammatory/immunosuppressive/anti-allergic properties [2]. These properties result in inhibition of chemotaxis and activity of cellular actors in the inflammatory/immune response (macrophages, neutrophils, lymphocytes, mast cells).

Antimitotic

In ophthalmology, this action is used, among others, to limit fibrotic reaction and angiogenesis.

Vasoconstrictor

This action, mediated by prostaglandin inhibition, is primarily used to classify topical corticosteroids.

1.2 Classification of glucocorticoids

Classification differs greatly according to the proprietary medicinal products. Corticosteroids are usually classified by dose equivalence to obtain a comparable anti-inflammatory effect [3]. This classification primarily incorporates the bioavailability of molecules and their affinity for binding to GRs.

To classify corticosteroid eye drops, GR binding affinity is of course essential, but so is **biodistribution** into the ocular tissue, which specifically depends on their ability to reach the corneal stroma and aqueous humour, and finally concentration [4].

1.3 Corticosteroids available as eye drops

Currently, three corticosteroids are available as eye drops in France: – a high-potency corticosteroid, which has the highest GR affinity and which, in phosphate form (the most common), effectively penetrates the corneal stroma and reaches the aqueous humour [4]. It is available as a formulation combined with antibiotics or on its own, containing preservatives or as preservative-free single doses. These eye drops are all dosed at 0.1% (i.e., 1 mg/ml); – two low-potency corticosteroids: the first has an intermediate GR affinity and poor penetration of the corneal stroma and aqueous humour. It is available in a vial containing preservatives stored at a concentration of 0.1% [4]. The second has a low GR affinity but satisfactory penetration into the corneal stroma and less into the aqueous humour. It is available as preservative-free single doses at a concentration of 3.35 mg/ml (0.33%).

1.4 Ocular side effects of corticosteroid eye drops

The main ocular side effects of corticosteroid eye drops are, of course, cataracts and hypertonia or even steroid-induced glaucoma. Among other factors, the risk depends on the molecule's penetration into the aqueous humour and its GR affinity (its "potency"). The duration of treatment also plays a major role. For all these reasons, any prescription of corticosteroid eye drops should be preceded by history-taking and a complete examination and should be subject to monitoring.

2

CORTICOSTEROIDS AND ALLERGIES

The vast majority of allergic conditions do not require corticosteroids.

Simple forms

(seasonal and perennial conjunctivitis, **Fig. 1**) generally resolve with standard treatments. These include avoidance of the allergen when possible, eye washes with a cold saline solution, antihistamine eye drops in the acute phases and anti-mast cell degranulation agents as prevention (or multi-action eye drops), and artificial tears.

Corticosteroids usually have no place in these clinical forms. However, some patients have persistent symptoms and sometimes signs despite well-managed treatment. In such cases, short-term treatment with anti-inflammatory (nonsteroidal [NSAID]) eye drops or low-dose corticosteroids may be helpful in breaking the vicious cycle and providing relief to the patient. A preservative-free eye drop should ideally be chosen to avoid further irritation

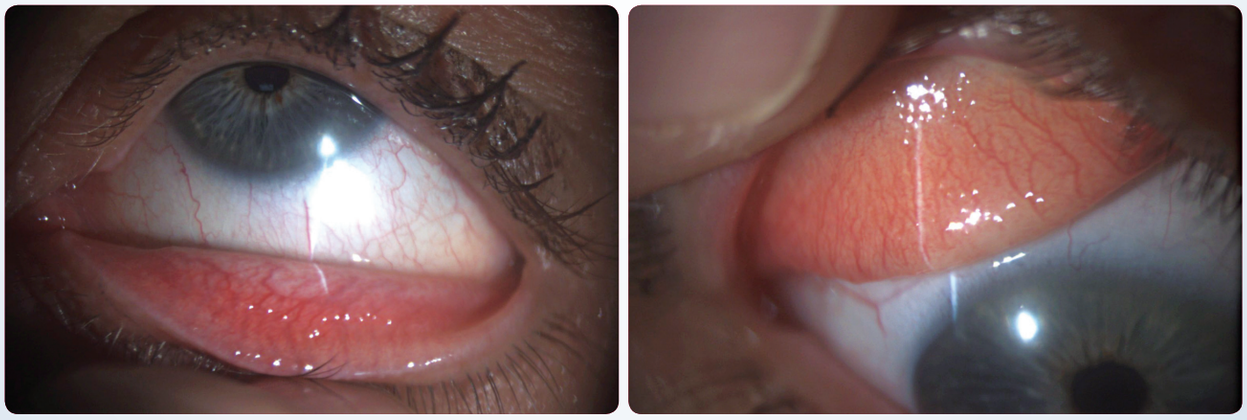

Figure 1: Perennial allergic conjunctivitis: papillae and follicles on the tarsal conjunctiva.

In severe forms

In severe forms (vernal keratoconjunctivitis [VKC] and atopic keratoconjunctivitis), the situation is completely different. In periods of VKC activity, treatment includes the same components as in simple forms, but anti-inflammatory treatment is always required. Corticosteroid eye drops are effective, but corticosteroid dependence and side effects make immunosuppressive eye drops essential for steroid-sparing purposes [5]. However, short courses of corticosteroid eye drops may be a useful adjuvant at the start of treatment, to quickly relieve symptoms and allow time for the immunosuppressant to be fully effective. They are also essential in cases of vernal plaque or ulcer and should be instilled frequently with tapering as quickly as possible, with adjustment in line with monitoring. In both of these situations, the severity of the disease justifies the use of high-potency corticosteroid eye drops, again, ideally preservative-free.

Corticosteroids may also be useful in flares of atopic keratoconjunctivitis, which generally require long-term topical immunosuppressants (applied to the eyelids). In these severe and chronic diseases, the use of corticosteroids should always be very cautious, bearing in mind the major risk of ocular side effects.

3

CORTICOSTEROIDS AND INFLAMMATORY DRY EYE

By "inflammatory" dry eye, we mean dryness related to infiltration of the glands on the ocular surface that ultimately leads to fibrosis followed by lacrimal hyposecretion and major meibomian gland dysfunction (MGD). This type of dryness occurs in the context of autoimmune or related diseases, the most common of which are Sjögren's syndrome, ocular manifestations of chronic graft-versus-host disease (or GvHD, which occurs after allogeneic bone marrow transplantation), and other conditions such as scleroderma.

Although rare, these conditions are not exceptional. In fact, for the record, Sjögren's syndrome is the most common autoimmune disease, with a prevalence of between 0.01 and 3%[6] inclusively, and is accompanied by dry eye in 85% of cases[7]. Similarly, ocular involvement occurs in the majority of patients with chronic GvHD, with the latter occurring in 50 to 75% of allogeneic bone marrow transplant patients (approximately 2,000 patients in France each year)[8].

In these conditions, dry eye is accompanied by dry, often severe, sometimes filamentous keratoconjunctivitis with conjunctival-corneal pitting, that may be confluent **(Fig. 2)**. The free eyelid margin is often inflammatory, with MGD contributing to inflammation of the ocular surface.

In these patients, several treatments are generally combined: long-lasting artificial tears, anti-inflammatory drugs (steroids or immunosuppressants), tear-sparing techniques (punctal plugs), and even scleral lenses to protect the corneal epithelium from the effects of inflammation.

To treat inflammation, immunosuppressive eye drops are most often indicated. In such cases, corticosteroid eye drops can be used at the start of treatment to rapidly reduce inflammation and improve the condition of the ocular surface as quickly as possible. They may also improve tolerance for immunosuppressive eye drops.

All of these measures generally improve the situation, but disease "flares" (sometimes related to environmental factors) may require short courses of corticosteroids in an attempt to space out and decrease the severity of these periods of exacerbation. Depending on the significance of the signs, high or low-dose corticosteroids may be used.

Finally, low-dose corticosteroids may be of interest in treating inflammation of the free eyelid margin that contributes to patient discomfort and, in some cases, intolerance of the scleral lenses.

As we will see later on, caution should be exercised in this circumstance and the patient should be instructed that corticosteroid eye drops should not be instilled while wearing lenses, but before they are put in or after they are removed.

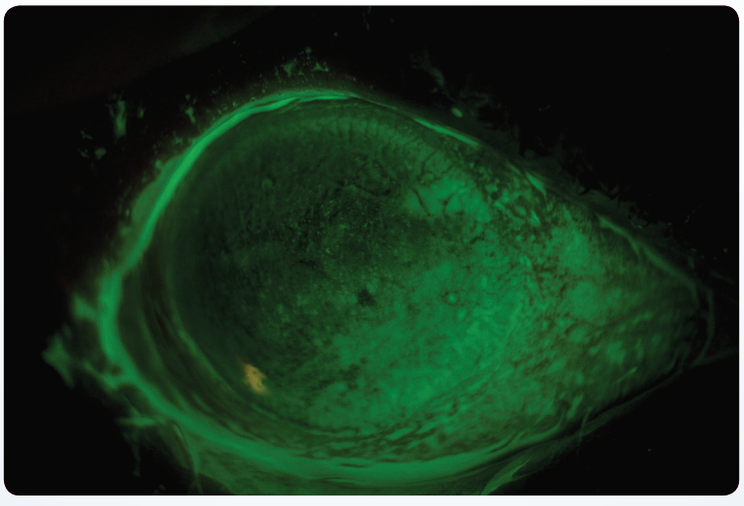

Figure 2: Severe dry keratoconjunctivitis complicating chronic ocular GVHD.

4

CORTICOSTEROIDS AND MEIBOMIAN/DYSFUNCTION ROSACEA

Management of meibomian dysfunction and ocular rosacea was the subject of a consensus conference in 2010 [9], the conclusions of which are broadly included in DEWS II [10]. The role of corticosteroid eye drops is clearly defined in the following situations:

Severe forms with corneal neovascularisation and/or sterile corneal infiltrates

It therefore seems more logical to use high-dose corticosteroids to ensure rapid action and a short treatment period. These forms often warrant long-term immunosuppressive therapy **(Fig. 3A)**.

Phlyctenular keratoconjunctivitis in children/young adults

In these rarer forms, the action to be taken is comparable to that adopted in severe forms (above).

Chalazions

Antibiotic-corticosteroid ointment is readily used in this case, taking care to avoid tetracyclines in children. A combination of eye drops and ointments is not really warranted.

Inflammatory flares/episcleritis

Simple episodes of common redness, where corticosteroids are not indicated (risk of corticosteroid dependence) should be differentiated from severe flares, more marked episcleritis, or even peripheral corneal infiltrates. In these situations, low or high-dose corticosteroids may be used depending on the severity of the presentation.

In all cases, corticosteroids are always combined with other background MGD treatments, namely eyelid hygiene, lubricating eye drops and topical antibiotic therapy.

Corticosteroid eye drops may also be of interest following automated pressure treatment of the meibomian glands. In our experience and although not recommended, a course of corticosteroids of approximately fifteen days in duration and of appropriate potency for post-procedural conjunctival hyperaemia could optimise the functional outcome **(Fig. 3B)**.

The role of corticosteroids after treatment with intense pulsed light remains to be defined. It should be noted that MGD associated with Demodex infestation responds poorly to standard treatments and in particular corticosteroids. Similarly, topical corticosteroids applied to the eyelids can exacerbate the palpebral manifestations of rosacea, particularly when these are associated with demodecidosis [11].

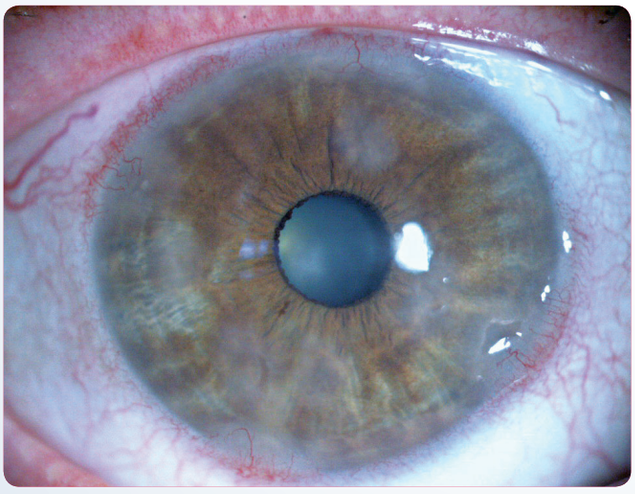

Figure 3A: Severe form of ocular rosacea with corneal complications (paralimbic ulcer, neovascularisation, stromal opacities and Salzmann nodules).

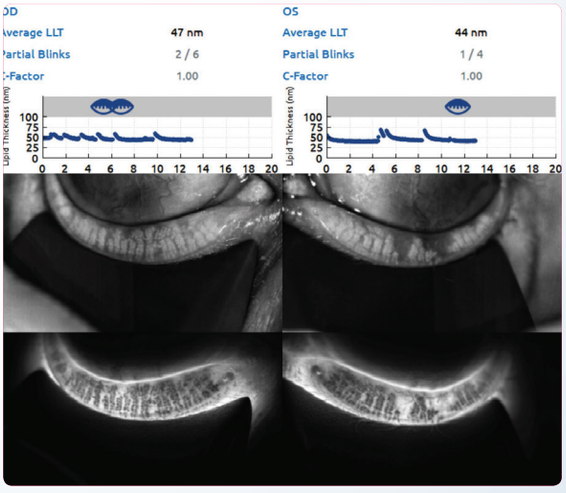

Figure 3B: Blink analysis and infrared meibography.

5

CORTICOSTEROIDS AND EPISCLERITIS/SCLERITIS

5.1 Episcleritis

This generally takes the form of a benign condition affecting the ocular surface, with no underlying systemic aetiology. It is frequently associated with MGD or an ocular allergy and has a spontaneously favourable outcome. For this reason, it is recommended that lubricating eye drops be used as first-line, with efficacy comparable to that of topical NSAIDs [12]. In case of persistent discomfort, an aetiological assessment (similar to that for scleritis) and treatment with low-dose corticosteroid eye drops as first-line [13] and high-dose corticosteroid eye drops in case of failure [14]. In this setting, often associated with dry eye, NSAID eye drops should be used with caution, especially since, as seen above, their efficacy is not demonstrated. Refractory or recurrent forms may warrant oral NSAIDs (in the absence of contraindications) [13, 14].

5.2 Scleritis

The context is completely different: this more severe pathology does not spontaneously heal and is often associated with an underlying systemic disease. Treatment is adjusted to the clinical form. Of course, the following therapeutic considerations assume that an infectious aetiology has been ruled out.

Sectoral or diffuse nodular non-necrotising scleritis

In case of sectoral or diffuse nodular non-necrotising scleritis **(Fig. 4)**, first-line treatment is based on oral NSAIDs. Systemic corticosteroids are used as second-line therapy. In case of corticosteroid dependence, immunosuppressants and/or biotherapies may be necessary. The choice of treatment is based on the possible aetiology and in consultation with an internist or rheumatologist [15]. A conventional immunosuppressant (methotrexate, mycophenolate mofetil, azathioprine) or TNF-inhibitor is usually used in idiopathic forms or forms associated with inflammatory bowel diseases. Rituximab may be considered in scleritis associated with rheumatoid arthritis and necrotising vasculitis [16].

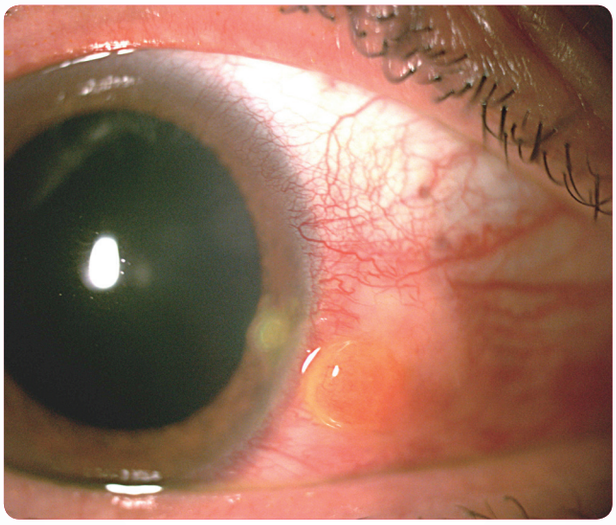

Figure 4: Nodular scleritis.

Corticosteroid eye drops may be useful as adjuvant treatment to reduce total cumulative corticosteroid doses. In this case, it seems more logical to use high-dose corticosteroid eye drops or as prevention if the cause is associated with a disease of the ocular surface (in the long-term, low-dose corticosteroids, or even immunosuppressive eye drops, are preferred).

Necrotising scleritis with or without inflammation

In necrotising scleritis with or without inflammation, treatment is based on systemic corticosteroids. Corticosteroid eye drops are contraindicated due to the risk of ocular perforation. Immunosuppressants and/or biotherapies may be indicated from the outset in severe or systemic disease-associated forms [17].

6

CORTICOSTEROIDS AND INFECTIOUS KERATITIS/KERATOCONJUNCTIVITIS

6.1 Corticosteroids and bacterial keratitis

A large multicentre study has attempted to scientifically answer this difficult question. In the SCUT (Steroid for Corneal Ulcers Trial), 500 patients with microbiologically confirmed bacterial corneal abscess were randomised to receive either prednisone eye drops (tapering over three weeks with an initial dose of four drops per day) or a placebo after at least forty-eight hours of monotherapy with a fourth-generation fluoroquinolone (moxifloxacin, not available in France in eye drop form).

At three months, there was no overall difference between the groups in terms of scar size and/or visual acuity (VA). However, there was a mild but significant improvement in VA in the subgroups with central abscesses and/or a baseline VA less than a "finger count" [18]. Furthermore, patients with a non-Nocardia abscess who were started on corticosteroid therapy early (between forty-eight and seventy-two hours after antibiotics were introduced) had better VA at three months [19].

At twelve months, the overall results were similar with or without corticosteroids. However, visual acuity in non-Nocardia abscess cases that received corticosteroids was found to be one line greater [20].

As a summary, corticosteroids may be indicated if:
- the bacterium is identified, susceptible to prescribed antibiotics and not a Nocardia;

- the clinical presentation initially improved with antibiotics.

In this case, they may potentially improve final VA in patients with an initial central abscess and/or causing a decrease in depth perception [20]. To keep in line with SCUT, high-dose corticosteroids seem logical in this context.

6.2 Amoebic and fungal keratitis

Corticosteroid eye drops are theoretically contraindicated in these two situations where the infectious agent is particularly difficult to eradicate [21, 22]. In amoebic keratitis, their use may be considered to treat inflammatory reactions, only if the infection is controlled by anti-amoebic therapy.

6.3 Herpes and herpes zoster keratitis

As a curative treatment, corticosteroids have a role to play in the treatment of non-necrotic stromal keratitis and endotheliitis **(Fig. 5A)**, combined with maximum-dose systemic antiviral therapy. A potent corticosteroid is needed to be effective in the corneal stroma and sometimes the anterior chamber. Topical corticosteroids are obviously contraindicated in epithelial forms (dendritic and geographic) and neurotrophic ulcers [23].

As prevention, they may be necessary adjuvants in patients with frequent recurrences. They aim to treat the surface inflammation that persists between flares, which itself triggers recurrence. In this case, it is logical to favour low-dose, preservative-free corticosteroids to reduce the risk of side effects. In these patients, immunosuppressive eye drops enable non-negligible corticosteroid sparing [24].

6.4 Adenoviral keratoconjunctivitis

Corticosteroids are reserved for complicated forms of pseudomembranes (acute phase) or subepithelial infiltrates with significant functional discomfort. The choice of molecule (high or low-dose corticosteroid) will depend on the severity of the presentation. In case of epithelial infiltrates **(Fig. 5B)**, corticosteroid dependence is almost routine and generally requires a switch to immunosuppressive eye drops [25].

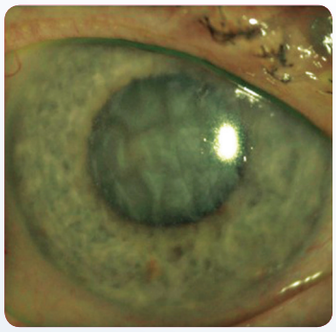

Figure 5A: Diffuse zoster endotheliitis.

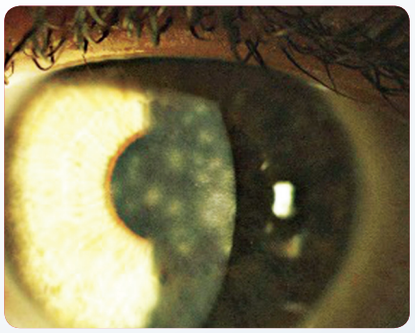

Figure 5B: subepithelial infiltrates following adenoviral keratoconjunctivitis.

7

CORTICOSTEROIDS AND REFRACTIVE SURGERY

7.1 Refractive/therapeutic photokeratectomy (RPK/TPK)

In refractive/therapeutic photokeratectomy (RPK/TPK) although there are no recommendations, corticosteroids are almost routinely prescribed after refractive surface surgery to prevent the onset of postoperative haze, particularly if the myopia was significant[26]. If, however, the haze occurs or does not resolve, it is usual to increase the dosage before considering revision surgery with the application of mitomycin. As a preventive and curative treatment, high-dose corticosteroids are used.

7.2 In LASIK surgery

They prevent the onset of diffuse lamellar keratitis (DLK) and are the cornerstone of curative treatment in case of onset of this rare but severe complication[27, 28]. A high-dose corticosteroid is then instilled every hour with progressive tapering depending on the clinical course. It may be combined with oral corticosteroid therapy in stage 2. Finally, in the most severe forms (stages 3 and 4 without central toxic keratopathy), it can be applied directly into the interface when lifting the cover for rinsing.

7.3 In SMILE surgery

This newer surgical technique is entirely based on a femtosecond cut, which generates less inflammation than the excimer laser [29]. Although current postoperative prescriptions are generally based on those used in LASIK surgery, low-dose corticosteroids could be considered, but studies comparing them objectively to a high-dose corticosteroid are still necessary. Post-SMILE DLK is managed in the same way as post-LASIK DLK. The duration of treatment is usually limited to two weeks. However, in case of a suspected interface fluid syndrome associated with IOH, treatment would consist of discontinuing corticosteroid therapy with reversibility within a week.

7.4 Dry eye post-refractive surgery

This is the most common complication after refractive surgery. This dryness has the peculiarity of having a significant neurotrophic component secondary to the corneal nerve section. For this reason, it occurs more frequently after LASIK surgery.

Fortunately, it generally resolves within a few months. Some authors have demonstrated the benefit of immunosuppressive eye drops either preoperatively in patients with dry eye syndrome or to treat the complication when it occurs [30]. Low-dose (and a fortiori preservative-free) corticosteroids could be a logical option to treat this complication, which is generally temporary, but their role is yet to be assessed.

8

CORTICOSTEROIDS AND CATARACT SURGERY

There are more than 800,000 cataract surgeries per year, with a consistent increase in premium implant placement, associated with an ever-higher level of patient demand. However rapid and successful it is, this surgery causes a rupture of the blood-aqueous barrier and postoperative inflammation (which certainly tends to decrease with new techniques).

8.1 Postoperative corticosteroids

They effectively treat postoperative inflammation, with the beneficial effects of prevention of posterior capsular opacification [31] and cystoid macular oedema [32] plus an analgesic effect. They are prescribed for a prolonged period of time in patients with a history of uveitis, corneal transplant patients or in case of complicated surgery. They are usually combined with NSAID eye drops, except in cases of severe dry eye, specifically related to Sjögren's syndrome, due to the risk of postoperative ulceration in this setting.

A high-potency corticosteroid is most often used in this indication, whether or not it is combined with an antibiotic, and sometimes in single, preservative-free doses, particularly on fragile ocular surfaces.

The main risks inherent in postoperative treatment are corticosteroid-induced hypertonia and corneal herpes recurrence.

8.2 Post cataract dry eye

This is an increasingly common complication [33], often synonymous with postoperative dissatisfaction. Tear film changes related to surgery are multifactorial and the age of cataract candidates itself predisposes to dry eye. Pre-, peri-, and postoperative eye drops, betadine disinfection and the surgical procedure are all traumatic and sources of inflammation for all components of the ocular surface (tear film, tear and meibomian glands, corneal nerves). Under these conditions, there is a clear understanding of how cataract surgery can decompensate a latent/asymptomatic dry syndrome, and hence the importance of preoperative screening through history-taking and a careful clinical examination [34]. In addition, preoperative dry eye can change the implant calculation (including keratometry) and thus decrease the quality of the refractive result [35]. Treatment of postoperative dry eye syndrome is adjusted depending on severity: discontinuation of toxic substances (NSAIDs, preservatives), artificial tears and corticosteroids (low or high-dose, depending on the context) are the first steps. In recalcitrant or chronic cases, the use of punctal plugs, immunosuppressive eye drops, or even scleral lenses may be indicated.

9

CORTICOSTEROIDS AND CORNEAL TRANSPLANTS

9.1 Prevention and treatment of transplant rejection

Corticosteroid eye drops are inseparable from corneal transplantation. Their pharmacological actions are useful for both preventive and curative treatment of transplant rejection. The risk of rejection is not identical in all types of corneal transplantation: it depends first on the type of surgical procedure (highest risk in transfixing keratoplasty, followed by anterior and posterior lamellar keratoplasty), but also the condition that led to the transplantation and the condition of the recipient cornea [36].

"High-dose" corticosteroids are indicated in this case. In this context, their efficacy is based on good intracorneal penetration and effective anti-inflammatory and immunosuppressive properties.

These include inhibition of the synthesis of arachidonic acid, IL1 and IL6 by antigen-presenting cells, and of IL2 and interferon γ by T lymphocytes. Moreover, these molecules inhibit leucocyte chemotaxis and macrophage phagocytosis, decrease the activity of polynuclear cells by stabilising their lysosomal membranes and inhibit neovascularisation.

Calcineurin inhibitor eye drops are useful in combination with or instead of corticosteroids in case of a high risk of rejection or corticosteroid-induced hypertonia, although the data in the literature does not provide any indisputable evidence of their efficacy [37]. This class of molecules inhibits the proliferation and differentiation of T lymphocytes with decreased cytokine production (IL2, 4, 5, interferon γ) [38].

Table I summarises the usual prescription patterns for the prevention and treatment of corneal transplant rejection. It would of course be adapted to each patient and depend on the type of transplant performed.

9.2 Treatment of corneal transplant-associated surface conditions

Low-dose corticosteroids may be useful in the treatment of surface abnormalities (dry eye, MGD) that are often present in patients who have undergone prior transfixing or lamellar keratoplasty.

Table I: Usual prescription patterns for prevention and treatment of corneal transplant rejection.

Clinical situation	Molecule/administration route	Dosage
Preventive treatment		
Standard recipient	High-dose corticosteroid eye drops	4 x/day for 1 month, then 3 x/day for 2 months, then 2 x/day for 3 months, 1 x/day for 3 months, 1 day out of 2 for 3 months and discontinuation.
High-rejection risk recipient	High-dose corticosteroid eye drops Discuss high-dose immunosuppressive eye drops	• Schedule or every two hours from the time of the procedure, then taper, maintain a minimum effective dose in the long-term. • Immunosuppressive eye drops: 1 drop 2 to 3 ×/day in the long term.
Curative treatment		
A) Late, mild rejection	High-dose corticosteroid eye drops and ointment	Schedule or every two hours, then taper, with application of ointment at bedtime in the acute phase
B) Moderately severe late rejection	Same as **A** + high-dose injectable corticosteroid	Same as **A** + subconjunctival injections of 2 mg/day, progressively spaced
C) Early or severe rejection	Same as **A** or **B** + IV bolus ± switch to oral administration	Same as **A** or **B** + IV bolus with switch to oral administration at a tapering dose.

10

CORTICOSTEROIDS AND CONTACT LENSES

10.1 Corticosteroids are contraindicated when contact lenses are in use

Corticosteroids are contraindicated when contact lenses are in use, and contact lens use should be avoided during treatment with eye drops containing corticosteroids. Indeed, contact lenses cause microtraumas, which provide an entry point for any bacteria trapped under the lenses (especially when handling and hygiene rules are not followed). The addition of corticosteroids into this configuration contributes towards the development of infection [39].

10.2 Some clinical entities secondary to the use of contact lenses may make them necessary

Non-infectious "sterile" corneal infiltrates

These are peripheral subepithelial immune infiltrates near the limbus, not to be confused with corneal abscesses. They are secondary to a hypersensitivity reaction to the exotoxins secreted by Gram+ bacteria. In addition to temporary discontinuation of contact lens use, topical corticosteroid therapy (usually with a high-dose corticosteroid) may be proposed to treat the inflammatory reaction, covered by local antibiotic therapy and clinical monitoring [40].

Giant-papillary conjunctivitis (GPC)

The pathophysiology of this entity, specific to contact lens use, is complex and multifactorial. It involves mechanical and immunoallergic components [40]. GPC is more common in certain settings: young, atopic patients, pre-existing MGD. It is also favoured by certain factors related to contact lens use: continuous use, presence of deposits, poor maintenance or insufficiently frequent renewal, large diameter lenses. Treatment combines a change in lens parameters and maintenance procedures, treatment of MGD with eye washes, antihistamine eye drops and anti-mast cell degranulation agents. Corticosteroid therapy can be discussed in refractory cases, but it exposes the patient to the risk of corticosteroid dependence.

Dry eye

In this context, it often exists together with lacrimal hyposecretion and tear instability caused by MGD. In these cases, low-dose corticosteroids can be very useful, of course when the lenses are not in use. Contact lens use should ideally be discontinued or at least temporarily reduced [40].

Infectious keratitis

Contact lenses, particularly soft lenses, are the primary risk factor for infectious keratitis in industrialised countries. Fungal keratitis is rare but serious and exacerbated by corticosteroids. As seen above, corticosteroids (preferably high-dose) may be indicated, but always after identification of the causative organism and clinical improvement with appropriate anti-infective treatment.

11

CORTICOSTEROIDS AND GLAUCOMA

Corticosteroids are used primarily at the time of glaucoma surgery to preoperatively prepare the ocular surface for filtering surgery (within the month prior to surgery) in parallel with withdrawal or reduction of eye drops containing preservatives, which improves the postoperative prognosis [41]. This is an indication of choice for moderate-acting corticosteroids with low intraocular penetration and preservative-free.

The standard postoperative treatment for filtering surgery includes corticosteroids, which are prescribed for a prolonged period of time: they help reduce fibrosis and improve the functional prognosis of the filtration bubble. A mistake that is sometimes made is discontinuing the corticosteroids too early due to postoperative ocular hypertonia (OH) that is incorrectly assumed to be corticosteroid-induced. Indeed, postoperative hypertonia should first point towards a filtration defect, specifically through excessive scarring of the filtration bubble. In the postoperative period, high-dose corticosteroids are usually used.

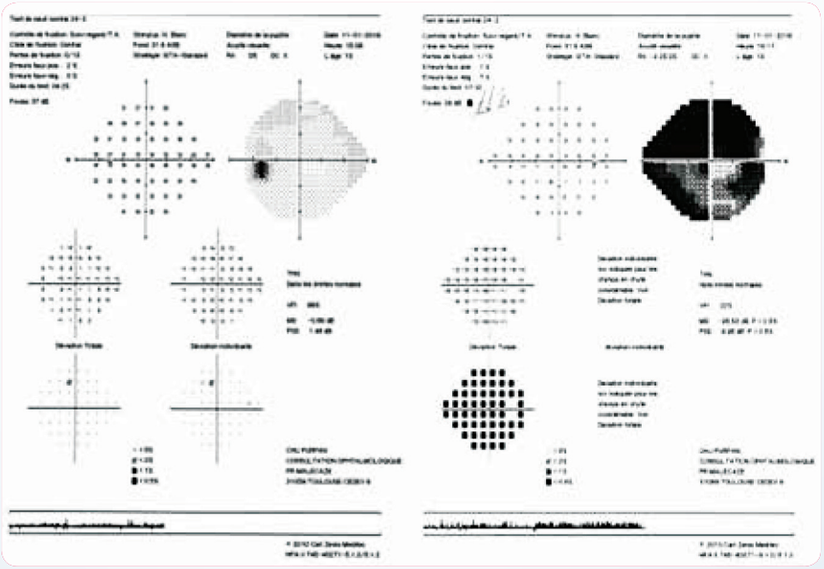

Figure 6: Severe steroid-induced glaucoma following self-medication with antibiotic-corticosteroid ointment for a unilateral chalazion on the right in an adolescent girl.

Corticosteroids for another indication but within a context of hypertonia or glaucoma

Hypertensive uveitis primarily comes to mind: undertreating uveitis to avoid steroid-induced OH is really a false economy because inflammation increases the trabecular damage responsible for resistance to aqueous humour evacuation and thus OH. High-dose corticosteroid eye drops therefore have a role to play. In complex cases, multidisciplinary management is essential: collaboration with internists or rheumatologists enables optimisation of general treatment and thus decreases local corticosteroid use.

Steroid-induced hypertonia

Although it may be secondary to the use of corticosteroids in all their forms (including nasal spray), it is most often secondary to the use of corticosteroid eye drops and appears secondary to the management of inflammatory eye disease. The clinical course of steroid-induced OH is different from that of inflammation. The main risk factors are, of course, a personal or family history of hypertonia or glaucoma [42]. Steroid-induced OH is also more common in melanodermal patients and those with connective tissue diseases and rheumatoid arthritis. In these cases, corticosteroids should be gradually discontinued and low-dose corticosteroids should preferably be used. Special attention is required in the paediatric population, particularly with relation to juvenile idiopathic arthritis-associated uveitis, VKC or chalazions **(Fig. 6)**, as children are more prone to steroid-induced OH than adults [43].

12

CONCLUSION

These different clinical situations demonstrate that knowledge and proper use of corticosteroids are essential if treatment is to be optimised for the most common, the most delicate situations, etc.

A summary of these clinical situations is provided in Table II.

Table II: Summary of clinical situations.

	Low-potency corticosteroid	High-potency corticosteroid
Allergic keratoconjunctivitis		
• Simple form: seasonal and perennial conjunctivitis	– In case of persistent signs and symptoms despite conventional treatments	
• Severe form: vernal and atopic keratoconjunctivitis		– Short treatment, while starting immunosuppressive treatment – In case of vernal plaque or ulcer
• Inflammatory dry eye	– In case of inflammatory flares if non-severe signs – Treatment of inflammation of the free eyelid margin	– While starting immunosuppressive eye drops – In case of inflammatory flares if signs + major
MGD/rosacea		
• Severe form with corneal neovascularisation and/or sterile corneal infiltrates		– Short treatment, to treat a complication or while starting immunosuppressive treatment
• Paediatric/young adult phlyctenular kerato–conjunctivitis		– Short treatment, to treat a complication or while starting immunosuppressive treatment
• Inflammatory flares/ episcleritis	– In severe flares only: depending on severity, use of a low or high-dose corticosteroid – In combination with background MGD therapy	
• Further to automated pressure treatment of the meibomian glands	– Can be offered as a short course if the eye has remained white	– Can be offered as a short course in conjunctival hyperaemia

	Low-potency corticosteroid	High-potency corticosteroid
Episcleritis	– If it persists despite the use of lubricating eye drops	– If low-dose corticosteroid eye drops are ineffective
Scleritis		
• In case of nodular, sectoral or diffuse non-necrotising scleritis	– As a preventive measure when the cause is associated with a condition affecting the ocular surface	– As adjuvant treatment to reduce total doses of oral corticosteroids
• In case of necrotising scleritis with or without inflammation	– Topical corticosteroids are contraindicated due to the risk of ocular perforation – Treatment is based on systemic corticosteroids and/or immuno-suppressants (or biotherapies)	
Infectious keratitis and keratoconjunctivitis		
• Bacterial keratitis		Corticosteroid prescription possible, under supervision, if: – the bacterium is identified, susceptible to prescribed antibiotics and is not a Nocardia – the clinical presentation initially improved with antibiotics
• Amoebic and fungal keratitis	– Corticosteroid eye drops contraindicated (can be discussed after initial improvement in AK)	
• Herpes and herpes zoster keratitis	– Prophylactically, as adjuvant treatment in patients with frequent recurrences	– Curatively, in non-necrotic stromal keratitis and endotheliitis Contraindicated in epithelial forms and neurotrophic ulcers
Infectious keratitis and keratoconjunctivitis		
• Adenoviral keratoconjunctivitis	– Reserved for complicated forms of pseudomembranes or subepithelial infiltrates with functional discomfort.	
Refractive surgery		
• In RPK		– For prevention of the post-operative haze
• In LASIK surgery		– For the prevention of diffuse lamellar keratitis
• In SMILE surgery	– For the prevention of diffuse lamellar keratitis (low-dose corticosteroids may be considered)	
• Post-surgery dry eye	– May be considered	
Cataract surgery	– To treat postoperative dry eye	– Postoperatively with or without an antibiotic
Corneal transplant	– To treat corneal transplant-related surface pathologies (dry eye, MGD)	– Routinely in the prevention and treatment of transplant rejection
Contact lenses	– Contraindicated during use	
Conditions secondary to contact lens use	– Treatment of induced dry eye (after removing lenses)	– Treatment of inflammatory corneal infiltrates (clinical monitoring + local antibiotic therapy)
Glaucoma	– Preoperatively: within the month prior to surgery to prepare the ocular surface	– Postoperatively to limit fibrosis

13

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