HYDROCORTISONE OR DEXAMETHASONE

DECISION GUIDE

Théa

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Inflammation is the immune system's response to different insults and aims to overcome the harmful effects and initiate the healing process. It is ubiquitous in ocular diseases, and may affect all the structures of the eye, starting with ocular surface, and including anterior and posterior chambers, vitreous, uvea retina and/or the optic nerve.

Corticosteroids are amongst the most potent and effective anti-inflammatory medications and they are widely prescribed for the management of various ocular diseases. Corticosteroids used in ophthalmology can be administered through several possible routes, each with their respective advantages and disadvantages. They can also be used for multiple indications with variable levels of evidence, though they have always shown high efficacy in clinical practice.

Topical steroids (as drops) are used to treat inflammation of the conjunctiva, cornea and the anterior segment. In certain circumstances they can also be useful in treating posterior segment for example uveitic or postoperative macular oedema. Penetration into the aqueous humour occurs by diffusion across the cornea. However, the efficacy of each preparation depends not only on the drug's intrinsic potency, but its penetration and durability.

This decision guide aims to present the main differences between hydrocortisone and dexamethasone and the right indication.

We hope this leaflet will be useful in your practices.

Enjoy your reading!

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1. COMPARTMENTS OF THE EYE

The human eye is composed of 3 compartments: the ocular surface, the anterior chamber filled with aqueous humor and the posterior chamber bordered by the vitreous body. Each of these compartments has characteristics that can promote or limit the action of eye drops. Pre-corneal factors such as the palpebral blink, lacrimal secretion and nasolacrimal drainage change the concentration of the active ingredients and/or accelerate their evacuation from the conjunctival cul de sac[1]. The water component of the tear film constitutes a barrier for lipophilic substances. Then, to penetrate the cornea, the drug must cross 3 specific barriers: the epithelium, the stroma and the endothelium.

The tight junctions of the epithelium make it the most difficult barrier to cross. The transport of molecules is transcellular or paracellular. Lipophilic substances are transported transcellularly and only hydrophilic drugs are transported paracellularly, despite the limited capacity of this transport pathway. The stroma, composed of 78% water, therefore water soluble substances distribute easily. The monocellular layer of the endothelium facilitates the penetration of drugs via active transport mechanisms[1].

In total, because of the strong hydrophilicity of the cornea and the existence of cellular barriers rich in membrane lipids, penetration into the cornea is optimal for substances both hydrophilic and lipophilic. However, even under optimal conditions, these barriers prevent the cornea from absorbing more than 1 to 10% of the applied active substance[1].

The conjunctiva and sclera, lacking tight junctions, are more permeable to hydrophilic drugs than the epithelium of the cornea. The active ingredients that pass through the arterial networks of the conjunctiva and sclera thus reach the uvea (which includes the iris, ciliary body and choroid) directly. The active ingredients therefore reach this site of action in higher concentration than if they enter through the cornea[1].

The active ingredient is then distributed to nearby tissue structures such as the iris, the ciliary body, the lens and the vitreous.
The vitreous body occupies 80% of the ocular volume, but receives only a small amount of active substances from the aqueous humor. This is mainly due to its gelatinous consistency, associated with a low diffusion rate. In addition, three processes can impede distribution to the vitreous body. Melanin in the iris and ciliary body may bind the drug and participate in storage followed by release of the drug into the aqueous humor. Moreover, binding to the proteins of the aqueous humor or the vitreous body also constitutes a limitation to the diffusion of the product in the posterior chamber. Finally, there is a rapid elimination due to the high rate of renewal of the aqueous humor, whose flow (from the ciliary body towards the anterior chamber of the eye) opposes the diffusion of the drug towards the posterior chamber[1].

In conclusion, medications are not equal regarding ocular penetration. Their physicochemical characteristics condition their penetration into the cornea and the anterior chamber. The very low penetration of eye drops into the posterior chamber makes them unsuitable for treatments targeting this compartment.

2. INFLAMMATION OF THE EYE

Inflammation is the immune system's response to different insults and aims to overcome the harmful effects and initiate the healing process.
Inflammation is therefore a defensive mechanism that is vital to health, including eye health[2].
The inflammatory response shows variations depending on the nature of the initial stimulus and its location in the body, but there are common mechanisms:
1) Cell surface pattern receptors recognize detrimental stimuli;
2) Inflammatory pathways are activated;
3) Inflammatory markers are released; and
4) Inflammatory cells are recruited[2].

Usually, during acute inflammatory responses, cellular and molecular events and interactions efficiently minimize impending injury or infection. This mitigation process contributes to restoration of tissue homeostasis and resolution of the acute inflammation. However, uncontrolled acute inflammation may become chronic, contributing to a variety of chronic inflammatory diseases[2].

Chronic inflammation is characterized by a low-grade persistent inflammatory response that frequently is not clinically evident, but can be detected by the presence of increased levels of cytokines, chemokines, prostaglandins, nitric oxide, proteases, and other inflammatory mediators both at the tissue and plasma levels[3].

Various pathogenic factors can induce inflammation followed by tissue damage. Those most commonly include infections (bacterial, viral, fungal, parasital), physical or chemical injuries, or internal (endogenic) processes[2].

Inflammation is ubiquitous in ocular diseases, and may affect all the structures of the eye, starting with ocular surface, and including anterior and posterior chambers, vitreous, uvea (iris, ciliary body, choroid) retina and/or the optic nerve, through various immunological pathways and with different intensities and time-lines.

Indeed, beside the "inflammatory" diseases, a classic example of which is uveitis, it has been recognized that processes that had once been believed to be purely degenerative, such as age-related macular degeneration (AMD[4]), diabetic[5] retinopathy and glaucoma[6], also involve inflammatory and immune elements[7] . While dry eye disease (DED) has been traditionally described as a deficiency in tears component (aqueous or lipidic), or as an excessive evaporation, inflammation is currently known to be the starter and the mainstay of all DED clinical manifestations[8].

3. CORTICOSTEROIDS AND OCULAR INFLAMMATION

Corticosteroids are amongst the most potent and effective anti-inflammatory medications[9].

The anti-inflammatory effect of steroids is caused by inhibiting the transcription of inflammatory and immune genes. These actions block the release of arachidonic acid and its subsequent eicosanoids (prostaglandins, thromboxanes, prostacyclins and leukotrienes).

This affects the blood-retinal barrier with a reduction in fibroblast proliferation, collagen and scar formation, tissue oedema, fibrin deposition, capillary leakage, intraretinal migration of inflammatory cells and levels of vascular endothelial growth factor (VEGF)[10].

All corticosteroid drugs act by modulating the gene expression of a number of proteins involved in the inflammatory reaction. They can regulate the expression of target genes by 3 distinct mechanisms of action[11]:

>> Direct transcriptional action: binding of the glucocorticoid receptor to a nucleotide DNA sequence called the Glucocorticoid Response Element (GRE), which exerts an activation of transcription. This results in an increase in the production of anti-inflammatory proteins such as lipocortin-1 (or annexin-1), interleukin[10] or IkB protein[9,11].

>> Indirect transcriptional action: interaction between the glucocorticoid receptor and transcription factors NF-kappa B, NF-IL6, AP-1 and STATS, leading to inhibition of these factors and thus to repression of target genes. This interaction constitutes the main mechanism responsible for the effects of glucocorticoids, by controlling the expression of multiple inflammation genes as well as those of many cytokines (activation or inhibition of their transcription)[9,11].

>> Action on chromosome structure: modification of chromatin structure, reducing access of transcription factors to their binding sites and inhibiting the expression of the genes concerned[11].

Cortisteroids also exert non-genomic effects, responsible for their rapid effects, through membrane actions, post-transcriptional actions on mRNAs, proteins[11]. The nongenomic mechanism exerts rapid effects on immune cells and regulates cell adhesion and involves the inhibition of dilatation of the blood vessels, vascular permeability, and leukocyte migration through the inhibition of phospholipase A2[9].

LOCAL OCULAR EFFECTS

Anti-inflammatory
- **↓Lymphocyte circulation/proliferation**
- **↓Leukocyte differentiation/reactions**
- **↓T-lymphocyte mediated cytotoxicity**
- **↓Monocyte/macrophage circulation & function**
- **↓Circulating neutrophils & eosinophils**

Anti-angiogenesis
- **↓Proliferation/migration of vascularendothelial cells**
- **↓VEGF expression**

Local ocular effects of corticosteroids (from Fung et al[10])

4. CORTICOSTEROIDS IN OPHTHALMOLOGY

Corticosteroids are widely prescribed for the management of various ocular diseases. The routes of application include: topical (on ocular surface), periocular, intraocular or systemic with lots of pharmacological modifications[10]. Considering the compartmentalization, the routes can be divided into two main groups[9].

APPLICATION INTO ANTERIOR SEGMENT

(drops, inserts, subconjunctival injections and intracameral applications).

Those are addressing diseases affecting the anterior segment of the eye :

- inflammation caused by surgery, injury, or other conditions,
- conjunctivitis,
- dry eye,
- uveitis,
- corneal allograft rejection,
- scleritis, and episcleritis etc.

APPLICATION INTO POSTERIOR SEGMENT

(sub-tenon/retro-bulbar injections, intra-vitreal applications and systemic intake).

Diseases affecting the posterior segment of the eye treated by corticosteroids are:

- diabetic macular edema (DME),
- diabetic retinopathy (DR),
- noninfectious posterior segment uveitis,
- macular edema following branched/ central retinal vein occlusion,
- age-related macular degeneration (AMD),
- postoperative macular edema.

Topical

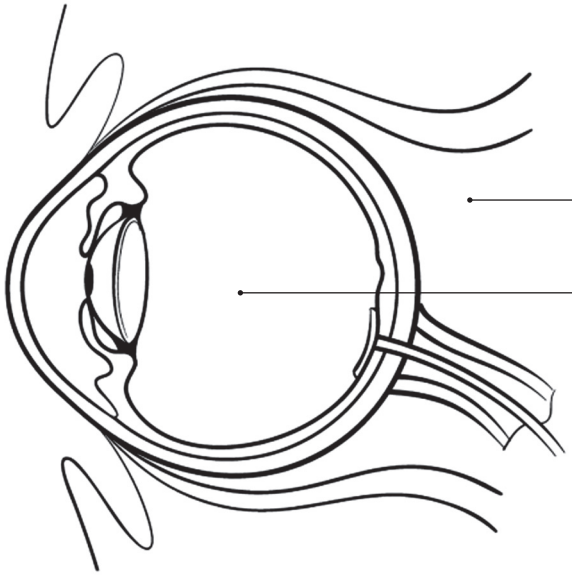
- Fluorometholone acetate
- Loteprednol etabonate

Prednisolone acetate

- Hydrocortisone acetate

Subconjunctival, Sub-tenon & Orbital floor

- Triamcinolone
- Dexamethasone
- Betamethasone



Adnexal & Periorbital

- Triamciinolone acetate

Methylprednisolone acetate

Intravitreal

- Triamcinolone acetate
- Dexamethasone
- Dexamethasone implant
- Fluocinolone implant

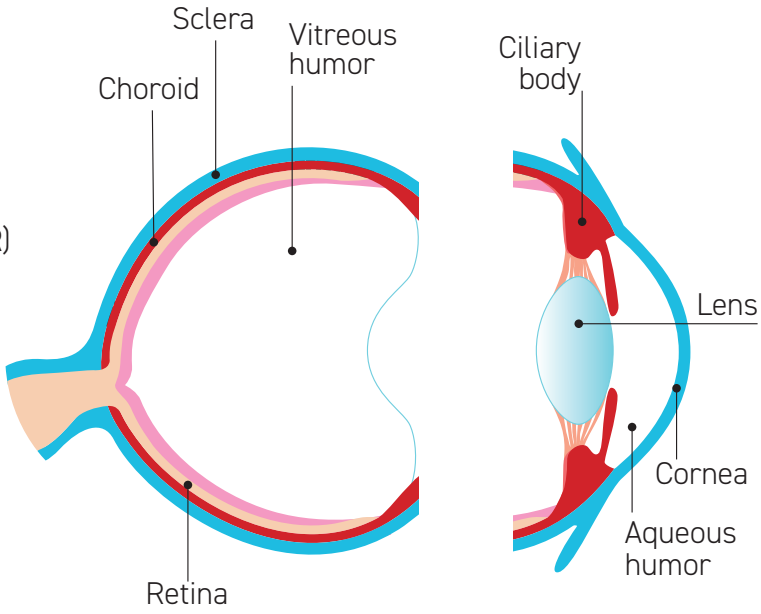
Ocular routes for administration of different corticosteroid preparations (from Fung et al.[10])

POSTERIOR SEGMENT

Diseases of the posterior segment of the eye

- Diabetic retinopathy (DR)
- Diabetic macular edema (DME)
- Age-related macular degeneration (AMD)
- Choroid neovascularization
- Posterior uveitis (retina and choiroid)

Can be treated with more invasive techniques like intravitreal and periocular injections



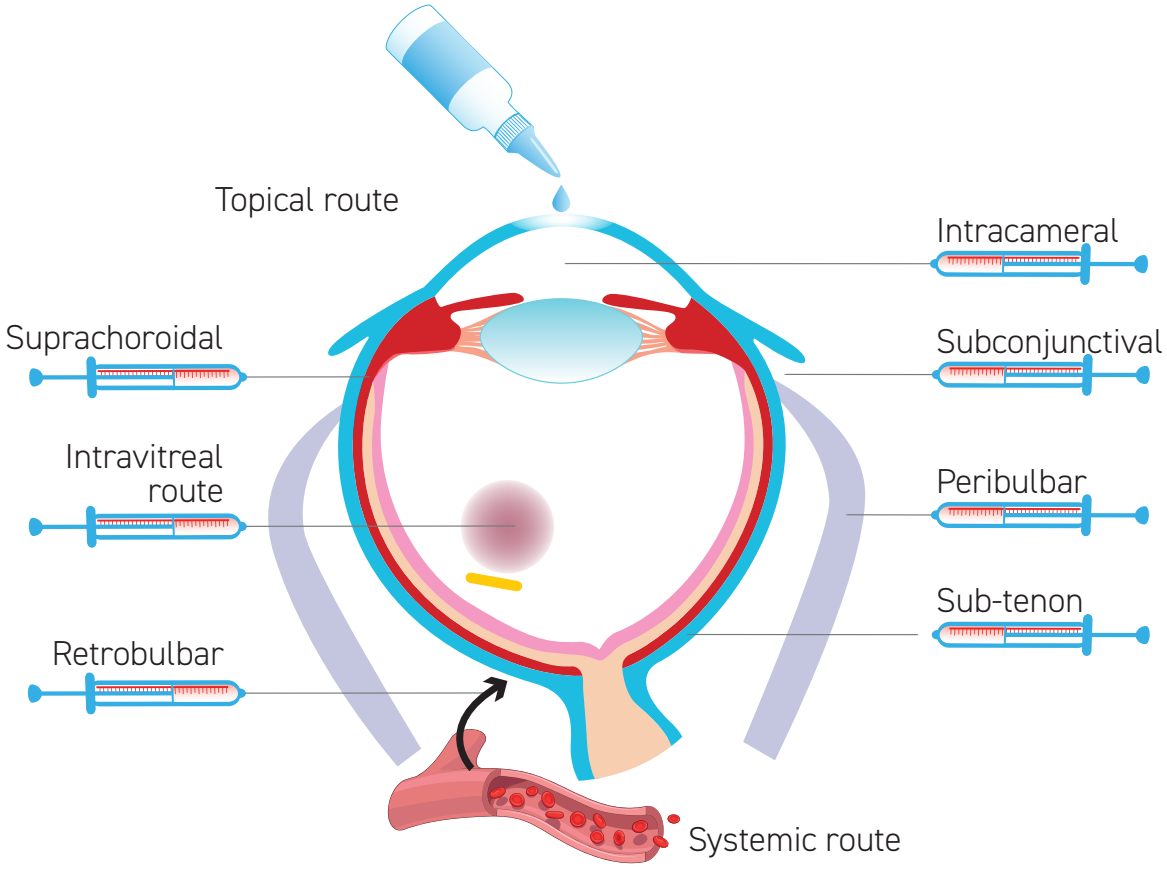
Various ocular surface, anterior and posterior eye diseases potentially treated with corticosteroids (from Gaballa et al.[9])

ANTERIOR SEGMENT

Diseases of the surface of the eye and the anterior segment of the eye

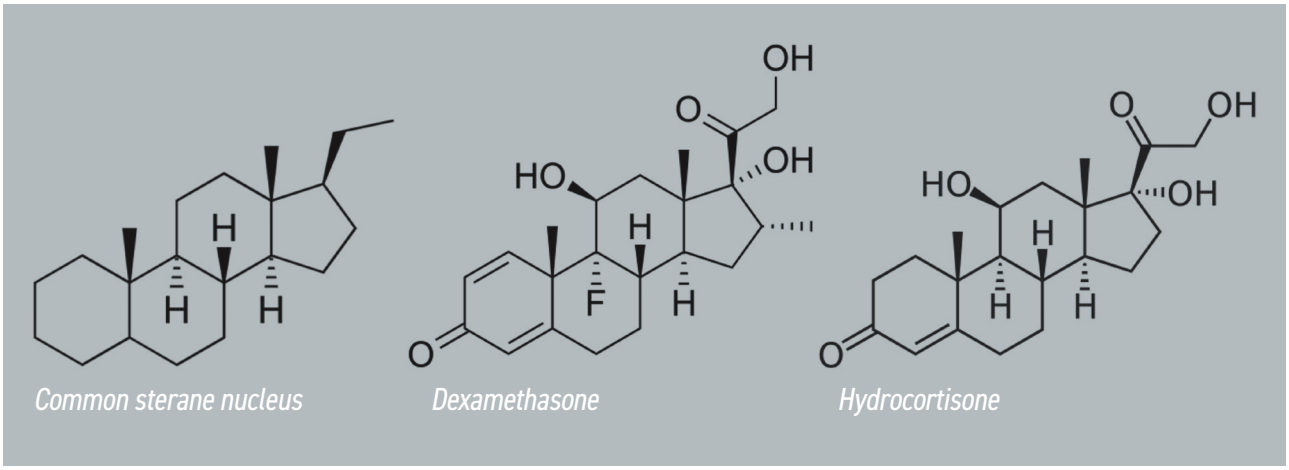
- Keratoconjunctivitis sicca (dry eye)
- Conjunctivitis
- Keratitis
- Scleritis
- Episcleritiss
- Anterior Uveitis

Can be treated by tropical corticosteroid formulations



Routes of administration for ocular delivery of corticosteroids (from Gaballa et al.[9])

5. CORTICOSTEROIDS: THE DIFFERENCE BETWEEN HYDROCORTISONE AND DEXAMETHASONE



Common sterane nucleus *Dexamethasone* *Hydrocortisone*

All corticosteroids share a basic sterane (steroid nucleus) structure with 21 carbon atoms and four rings[9].

Hydrocortisone is the pharmacotherapeutic denomination of the natural molecule "cortisol" synthetized by the adrenal glands. It's used therapeutically, along with other synthetic corticosteroids derived from hydrocortisone, which have been developed to offer longer duration of action, greater anti-inflammatory activity, and lesser mineralocorticoid properties compared to the parent compound[11].

Dexamethasone was developed in 1957 and its nucleus is similar to other corticosteroids. However it is fluorinated at position 9[12], which increases its potency and biological half-life. Unfortunately, this characteristic also confers a greater potential for side effects[13].

COMPARISON OF POTENCY AND EFFICACY

Molecule	Biological half-life	Anti-inflammatory potency
Hydrocortisone	8 - 12 H	1
Dexamethasone	36 - 54 H	30

Half-life and potency of hydrocortisone and dexamethasone (from Samuel et al.[14])

Corticosteroids can be classified according to their anti-inflammatory potency and half-life. The anti-inflammatory potency has, by convention, been set at 1 for hydrocortisone, the reference molecule, and is expressed as a multiple of this reference potency for the other molecules.

But independently of their anti-inflammatory potency, the clinical efficacy of topically applied corticosteroids depends on many parameters[10,15].

- the corneal penetration capacity,
- the concentration,
- the duration of action in the cornea, aqueous humor or posterior chamber,
- and the frequency of instillation, although beyond a certain frequency, a threshold effect is observed.

The corneal penetration varies according to the hydrophilic and lipophilic profile of the molecule and, for the same molecule, according to the salt considered and the excipient : alcoholic formulations and acetate salts, which are more lipophilic, have a better penetration through the lipid layer of the tear film than phosphate salts [15,16]. Hydrocortisone is available as a phosphate salt dosed at 3.35 mg/ml. Dexamethasone is available as an alcohol or phosphate derivative in the form of a 0.1%-0.2% ophthalmic suspension or solution. It is also formulated as dexamethasone sodium phosphate ointment, 0.05%-0.2%[17].

Studies have shown that hydrocortisone acetate achieves good concentrations into the conjunctiva and the cornea, and to a lesser degree into the sclera, but has very low penetration into the anterior chamber: after topical administration, the drug is found for 60 to 85% into the conjunctiva (depending on the frequency of administration), for 1 to 20% into the cornea and for 1 to 8% into the aqueous humor[18]. Dexamethasone is considered to have a medium intraocular penetration , but its absolute bioavailability into the aqueous humor is actually rather low (<2%)[20] . A study in rabbits showed that for a concentration of the drug of 4.8 +/- 1.1 micrograms/g into the cornea, it was only 0.8 +/- 0.12 microgram/ml into the aqueous humor[21].
Solutions with preservatives also have greater penetrance than those without, as the preservative disrupts tight junctions between corneal epithelial cells[10]. Dexamethasone is mostly available with preservatives, and dexamethasone and hydrocortisone are both available preservative-free in some countries.

The duration of action has not been specifically studied in the eye, but it has been shown that the suppression of endogenous cortisol synthesis after oral administration varies considerably, depending upon the amount of time since the therapeutic dose. Dexamethasone was 52 times as potent as hydrocortisone 8 h after the steroid dose, but 154 times 8 and 14h after the steroid dose[22]. The enzymatic degradation of the steroid can affect the duration of its effect : ocular tissues may be particularly active in the metabolism of steroids[22].

A "A" ring reduction (primarily by the liver) accounts for the inactivation of circulating steroids, and ocular tissues also appear to possess degradative enzymes. The iris-ciliary body and cornea show high levels of "A" ring reductase activity, Some corticosteroids are more protected from "A" ring reductions than hydrocortisone, especially synthetic steroids, such as dexamethasone, which are considerably more resistant to these degradative pathways[22].

COMPARISON OF SIDE EFFECTS

The main ocular side effects of corticosteroid eye drops are ocular hypertension and potential steroid-induced glaucoma. Aside patient-related factors, the risk depends on the molecule penetration into the aqueous humour and its potency[9,16,19]. The concentration, formulation, frequency of administration and duration of treatment also play major roles[9,16, 23,24]. Therefore, the most potent steroids tend to produce corticosteroid-induced hypertonia more often than less potent molecules[16, 22].

The less potent agents require a longer duration of therapy to produce increased IOP and the elevation is not as high as those induced by more potent agents[9]. Available data suggest that dexamethasone is more likely than other steroids to result in clinically significant increase in IOP, particularly in steroid responders[17], and it has been demonstrated that the IOP rise is much higher with dexamethasone compared to hydrocortisone[23,25]. Factors contributing to the reduced propensity of some steroids to raise IOP could include their lower intraocular bioavailability, shorter pharmacokinetic half-life and greater susceptibility compared to dexamethasone[26].

Corticosteroid	Final IOP	Rise IOP
	(Mean nm Hg ± SE)	
Dexamethasone 0.1 %	45.1 ± 2.7	22.0 ± 2.9
Hydrocortisone 0.5 %	26.3 ± 1.5	3.2 ± 1.0

Intraocular pressure response to topically applied corticosteroids in the same patients. (from Cantrill et al.[23])

However, the ocular hypertension is not only a result of corticosteroid applications, as genetic factors also play a significant role[19]. Interestingly, most of the cases result only from local therapy and the reaction is relatively early after the instillation of the first drops. In long term therapies, there is a high risk of glaucoma, therefore this is probably the most serious complication of steroid therapy.

Among other side effects are subcapsular cataract (which is associated with local as well as systemic therapy[9]), delay in wound healing and activation of different infections[16].

Steroid-induced cataract occurs after prolonged administration of corticosteroids, on average 1 year. Its occurrence depends mainly on the cumulative dose, but also on the route of administration, the dose, the duration of treatment, the extent of ocular inflammation and the age of the patient[9,26]. The risk of developing a steroid-induced cataract also depends on the intraocular penetration of the steroid. However, even molecules with low intraocular penetration have been reported to cause iatrogenic cataracts after several months of administration[16]. Here again, the individual susceptibility to corticosteroids seems to be an important factor regarding the risk of steroid-induced cataract[26].

There is evidence for delayed corneal wound healing associated with steroid topical administration. However, whether such delayed healing has detrimental clinical implications is still being debated[16,27]. No data currently allows to distinguish the effect of different steroids in that matter.
The risk of reactivation of latent infections with steroid therapy is related to their immunosuppressive effect. No data currently allows to distinguish the effect of different steroids in that matter.

THERAPEUTIC REGIMEN

Rules for the use of topical corticosteroids for ocular surface diseases[28]

- The type and location of inflammation determine the appropriate route of administration.
- The anti-inflammatory potency of the corticosteroid must be adapted to the pathology being treated.
- The frequency of instillation should be frequently reassessed.
- The duration of corticosteroid treatment for mild ocular surface disorders should not exceed 3 to 4 weeks.
- Corticosteroids should not be discontinued abruptly.
- The minimum effective doses should be used for the shortest possible time.
- Each patient should be treated according to the degree of inflammation.
- Follow-up should be regular and close to assess the tolerance and efficacy of the treatment.
- Patient compliance should be regularly assessed.
- The presence of a history of ocular herpes must be systematically sought.

The frequency of instillation modulates the total dosage and local concentration of the steroid. It depends on the severity of the damage, with increased frequency of instillation, of up to one drop every hour, for the most severe situations[29].

The duration should be limited (for example, to less than 1 month for mild pathologies of the ocular surface)[29].
The slow decrease of the drug is necessary for treatment duration over a few days, to prevent the inflammatory rebound phenomena[29].

In case of dependence to steroids, a progressive decrease with molecules of decreasing potency may be a beneficial strategy[30].

SUMMARY

An ideal steroid treatment for external eye inflammation would ensure the presence of the anti-inflammatory agent at ocular surface with minimal penetration into the eye, and therefore reduced risks of ocular hypertension and cataract[18]. The anti-inflammatory potency must be adapted according to the pathology and damage, giving preference to low potency molecules for conjunctival damage (hydrocortisone) and more potent ones (dexamethasone) for corneal and scleral damage[29].

Conversely, to target intraocular inflammation, the anti-inflammatory drug must be able to penetrate the cornea to reach the internal structures of the eye at sufficient concentration. In any cases, vitreous concentrations remain low with topically applied steroids, and oral corticosteroids or preferably injectable administration are needed to reach significant concentrations into the retina and the choroid.

Respective characteristics of topical hydrocortisone and dexamethasone suggest that, as a short-acting, mildly potent steroid with limited intraocular penetration, hydrocortisone is better fitted for ocular surface therapy in case of mild to moderate inflammation, such as chronic low-grade inflammation observed in dry eye disease. Furthermore, with a low propensity to rise the IOP[17], hydrocortisone may be used for longer periods than dexamethasone.

Dexamethasone is a long-acting, highly potent steroid, with medium penetration into the anterior chamber and a greater susceptibility to IOP rise. It seems suitable for moderate to severe inflammation of the ocular surface or the anterior chamber, in short treatment courses.

	Hydrocortisone	Dexamethasone
Salt	Phosphate	Phosphate, acetate, alcohol
Preservative	-	+ and -
Anterior chamber penetration	Low[18]	Medium[19]
Potency[14]	1	30
Enzymatic degradation in the eye[22]	Susceptible	Resistant
Biological half-life[14]	8 - 12 H	36 - 54 H
Risk of IOP rise	Low[23]	High[22]

NOTES

NOTES

REFERENCES

1. Bänninger PB & Becht CN.
Comment un médicament atteint-il son site d'action dans l'œil? *Forum Med Suisse 2011;11(11):192–5*

2. Chen L et al.
Inflammatory responses and inflammation-associated diseases in organs.
Oncotarget, 2018; 9(6) : 7204-18

3. Ferreira Mendès A et al.
Editorial: The Physiology of Inflammation—The Final CommonPathway to Disease.
Front. *Physiol. 2018; 9:1741.*

4. Kauppinen A et al.
Inflammation and its role in age-related macular degeneration.
Cell. Mol. Life Sci. 2016; 73:1765–86

5. Rübsam A et al.
Role of Inflammation in Diabetic Retinopathy.
Int. J. Mol. Sci. 2018; 19 : 942;

6. Baudouin C et al.
Inflammation in Glaucoma: From the back to the front of the eye, and beyond.
Progress in Retinal and Eye Research 2021; 83 : 100916

7. Perez VL & Caspi RR.
Immune Mechanisms in Inflammatory and Degenerative Eye Disease.
Trends Immunol. 2015 June ; 36(6): 354–63

8. Periman LM et al.
The Immunological Basis of Dry Eye Disease and Current Topical Treatment Options
J Ocul Pharmacol Ther. 2020; 36(3): 137–46

9. Gaballa SA et al.
Corticosteroids in ophthalmology: drug delivery innovations, pharmacology, clinical applications, and future perspectives.
Drug Deliv Transl Res. 2021 Jun;11(3):866-893.

10. Fung AT et al.
Local delivery of corticosteroids in clinical ophthalmology: A review.
Clin Experiment Ophthalmol. 2020;48:366 – 401.

11. Corticoides : Les points essentiels.
PHARMACOMédicale.org (Collège National de Pharmacologie Médicale)
https://pharmacomedicale.org/medicaments/par-specialites/item/corticoides-les-points-essentiels

12. National Library of Medicine.
https://pubchem.ncbi.nlm.nih.gov/compound/Dexamethasone

13. Abelson MB & Butrus S.
Corticosteroids in Ophthalmic Practice.
Chapter 25. In: Albert DM et al., eds. Albert & Jakobiec's Principles and Practice of Ophthalmology, *3rd ed. Philadelphia: Saunders Elsevier; 2008.*

14. Samuel S et al.
Pharmacologic Characteristics of Corticosteroids.
J Neurocrit Care 2017;10(2):53-9

15. Offret H et al.
Chapitre 7 : traitement des maladies inflammatoires.
In : Thérapeutiques médicamenteuses en ophtalmologie. *Ed : Masson 2002*

16. Mc Ghee CNJ et al.
Locally administered corticosteroids.
Benefits and risks. Drug Saf. 2002;25(1):33-55

17. Cutolo RA et al.
The Use of Topical Corticosteroids for Treatment of Dry Eye Syndrome.
Ocular Immunology and Inflammation 2019, 27:2, 266-75

18. Longwell AM et al.
The relationship between hydrocortisone acetate distribution and efficacy in inflamed eyes: continuous versus intermittent delivery.
Ann Ophthalmol. *1976 May;8(5):600-8*

19. Bremer F.
Origine de la corticosensibilité.
Bull. Soc. belge Ophtalmol., 2007 ;304, 111-6

20. Naageshwaran V et al.
Topical pharmacokinetics of dexamethasone suspensions in the rabbit eye: Bioavailability comparison. *Int J Pharm. 2022 Mar 5;615:121515*

21. McDermott ML et al.
The intraocular penetration of dexamethasone after photorefractive keratectomy.
Ophthalmic Surg Lasers. 1998 Oct;29(10):839-41.

22. Polansky JR & Weinreb RN.
Anti-inflammatory agents. Steroids as anti-inflammatory agents.(1984).
Handbook of Experimental Pharmacology.
M. Sears. 69: 459-538.

23. Cantrill HL et al.
Comparison of in vitro potency of corticosteroids with ability to raise intraocular pressure.
Am J Ophthalmol 1975;79(6): 1012-7.

24. Podos SM et al.
Topically administered cosrticosteroid preparations. Comparison of intraocular pressure effect.
Arch Ophthalmol. 1971 Sep;86(3):251-4.

25. Razeghinejad MR & Katz JL.
Steroid induced iatrogenic glaucoma.
Ophthalmic Res 2012; 47:66-80.

26. Jaanus SD et al.
Anti-inflammatory Drugs. Clinical ocular pharmacology. *B. JD, J. SD., E. K. E. Blahoet al. Boston, Butterworth-Heinemann. 2001; 12: 265-298*

27. Lepore D et al.
Effect of topical antiinflammatory drugs on mechanical behavior of rabbit cornea.
J Appl Biomater Funct Mater 2017; 15(2): e142-e148

28. Rapport SFO Surface Oculaire.
Thérapeutiques chapitre 16.
https://www.em-consulte.com/em/SFO/2015/html/file_100029.html

29. Stephan S & Doan S.
Quand faut-il prescrire des corticoïdes en cas d'inflammation de la surface oculaire ?
Réalités Ophtalmologiques – n° 278_Février 2021 – Cahier 1

30. Turpin C & Weber M.
Anti-inflammatoires en ophtalmologie: quand ? pour qui ? comment ?
Réalités Cardiologiques – Juin 2011

Théa
let's open our eyes

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