

Corticosteroids and cataract surgery

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ABSTRACT

Many inflammatory events associated with cataract surgery can be controlled through the use of corticosteroids, thereby improving their prognosis. However, the use of corticosteroids may trigger other adverse events, which may occur with any route of administration and with all ophthalmological corticosteroid formulations currently in the market. With this important review of the topic, the Brazilian Society for Cataract and Refractive Surgery offers the most recent information on the use of corticosteroids in patients who have undergone cataract surgery.

RESUMO

Com a utilização dos corticosteroides oftálmicos é possível controlar vários eventos inflamatórios associados à cirurgia de catarata e melhorar o seu prognóstico. No entanto, o uso dos corticosteroides pode desencadear outros eventos adversos que podem ocorrer com todas as vias de administração e com todas as preparações oftálmicas disponíveis no momento. A Sociedade Brasileira de Cirurgia Refrativa e Catarata (ABCCR/ BRASCS) com esta importante revisão sobre o tema oferece o que há de mais atual a respeito do uso de corticosteroides em pacientes submetidos à cirurgia de catarata.

RESUMEN

Con la utilización de los corticosteroides oftálmicos es posible controlar varios eventos inflamatorios asociados a la cirugía de catarata y mejorar su pronóstico. Sin embargo, el uso de los corticosteroides puede desencadenar otros eventos adversos, que pueden ocurrir con todas las vías de administración y con todas las preparaciones oftálmicas disponibles en el momento. La Sociedad Brasileña de Cirugía Refractiva y Catarata (ABCCR/ BRASCS), con esta importante revisión sobre el tema, ofrece lo que hay de más actual respecto al uso de corticosteroides en pacientes sometidos a la cirugía de catarata.

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Cataract, phacoemulsification;
Adrenal Cortex Hormones/ administration & dosage;
Adrenal Cortex Hormones/ toxicity.

Palavras-Chave:

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INTRODUCTION

Cataract surgery is one of the most commonly performed elective surgeries in the world. As is the case with all surgeries, it induces an inflammatory response. Poor control of this inflammation may lead to undesirable consequences, such as synechiae, uveitis, and secondary glaucoma.¹

Two drug classes are used for the management of inflammation induced by surgery: steroidal (corticosteroids) and non-steroidal anti-inflammatory drugs (NSAIDs).¹

One of the concerns regarding the use of corticosteroids through any route of administration is the risk of increased intraocular pressure (IOP). Steroids are known to cause changes to the trabecular meshwork, reducing the flow of the aqueous humor and possibly increasing IOP.^{2,3}

The concept of dropless surgery, which refers to a postoperative period without the need for antibiotic or anti-inflammatory drops, is being researched with increasing frequency.² The posology of current postoperative medications and the amount of patient compliance required often interfere with the efficacy of these topical treatments. Furthermore, corneal absorption and changes in the eyedrop concentrations that reach the aqueous humor may hinder the control of inflammation.^{4,5} Many routes of drug administration are being studied, and the results have been found to be promising.

In patients with a history of uveitis, cataract surgery increases the risk of perioperative complications. The surgical prognosis is worse overall. Patients with active inflammation in the eyes within 3 months preoperatively tend to exhibit more macular edema.⁶

This session will address the current information on the use of steroids in cataract surgery.

Topical Steroids and NSAIDs

Many ophthalmology centers both in Brazil and abroad routinely prescribe combined antibiotic and steroidal eyedrops in the postoperative period following cataract surgery, along with a topical NSAID.

Both steroids and NSAIDs act on the inflammatory cascade, which is presumed to be one of the causes of postoperative cystoid macular edema (CME).⁷

There is evidence that the combination of NSAIDs and corticosteroids creates better outcomes in terms of controlling inflammation, particularly in the prevention and control of CME, than the use of corticosteroids alone. This has been found to be true in both routine cataract surgeries and more complicated cataract surgeries because NSAIDs are more effective in controlling CME.^{1,7,8}

Studies with low and moderate qualities of evidence have shown that the use of NSAIDs alone as an anti-inflammatory in the postoperative period may be as effective as the use of NSAIDs combined with steroidal anti-inflammatory drugs when considering outcomes, such as flare, CME, IOP, and endothelial cell counts.^{7,9} When flare is considered alone, there seems to be no significant differences between the use of NSAIDs alone, steroids alone, or a combination of the two up to 3 months postoperatively. Some authors have also argued that steroids are not absolutely necessary in the postoperative period following cataract surgery and that the use of NSAIDs alone as an anti-inflammatory reduces the risks of the side effects of corticosteroids, such as increased IOP and susceptibility to infections due to their immunosuppressant mechanism.⁹ The topical use of 1% dexamethasone for 4–6 weeks is known to cause ocular hypertension in 40% of patients with non-glaucomatous eyes and in almost 100% of patients with open-angle glaucoma or normal-tension glaucoma.³ Despite this evidence, the total replacement of corticosteroids by NSAIDs is not a routine that most surgeons follow because of the proven benefits of the combination of the two drug classes.^{7,8,10}

Steroids and the Corneal Endothelium

Corticosteroids have been found to be safe for the corneal endothelium during the standard period of use after cataract surgery, regardless of the route of administration,^{11,12,13} and even in cases of intensive topical use (every hour) in the first week.¹³ Preservative-free corticosteroids must be used when administered through an intracameral route.¹⁴

In an *in vitro* study, triamcinolone was found to be toxic to the endothelium when the solution included benzyl alcohol as a preservative.¹² In a study on rabbit eyes, 4 mg/0.1 ml of intracameral triamcinolone reduced microvilli, but neither endothelial cell counts nor central corneal thickness significantly differed.¹¹

Steroids and Meibomian Gland Dysfunction

In a study comparing preservative-free eyedrops with 0.1% fluorometholone to eyedrops with 0.1% sodium hyaluronate used after cataract surgery in patients with meibomian gland dysfunction, preservative-free eyedrops were found to improve the signs and symptoms of dry eye after cataract surgery. This finding is likely because of the anti-inflammatory and antioxidant properties that preservative-free fluorometholone has on the precorneal film.¹⁴

Topical and Systemic Steroids

Patients with uveitis and/or pre-existing systemic inflammatory diseases have a greater chance of developing more extensive inflammation in the postoperative period than those without these comorbidities.^{6,15}

In cataract surgeries in patients with a history of non-infectious uveitis, the intensive use of topical steroids in the first postoperative week (1% prednisolone once every hour) seems to produce the same incidence of disease recurrence as the oral use of this medication in the same regimen. Changes in IOP, visual acuity, and central macular thickness were also similar.¹⁶ It can, therefore, be concluded that orally administered steroids do not provide additional benefits to these patients in the postoperative period. However, because the risk of increased IOP is dose-dependent,^{3,17} the intensive use of corticosteroids may increase IOP to dangerous levels.

In patients with recently active uveitis, short courses of oral corticosteroids (2 days preoperatively) tend to reduce the incidence of macular edema.⁶ The systemic use of corticosteroids seems to be less effective in controlling inflammation than administration via intracameral or subconjunctival route.¹⁵

It is recommended to postpone cataract surgery until the patient's uveitis has been inactive for at least 3 months and to briefly treat patients using systemic corticosteroids preoperatively, as well as for a short period postoperatively. The surgical approach used, the intracapsular position of the intraocular lens (IOL), non-silicone IOL materials, and no recent cases of uveitis are factors that have been found to be associated with a better surgical prognosis.⁶

Intracameral Steroids

If intracameral drugs are used, they should not contain preservatives.^{6,14} The intracameral use of antibiotics has been widely discussed in the literature, and some centers (particularly in Europe) have discontinued the postoperative use of topical antibiotics in cataract surgeries, choosing the intracameral route alone. This would contribute to reduce the selection of more resistant strains of bacteria in the ocular surface, as topical antibiotics could generate.¹⁸

Intracameral corticosteroids have been commonly used in pediatric cataract surgery and in complex cataract surgeries in adults, in which a more substantial inflammatory reaction is expected.^{19,20,21} However, the use of these drugs is questioned in uncomplicated procedures in adults without comorbidities because topical anti-inflammatory drugs are effective in controlling postoperative inflammation.¹

Ophthalmologists are hesitant to use intracameral corticosteroids, such as triamcinolone, because of the risk of increased IOP in the postoperative period, a risk that has been well documented when this drug is administered via other routes, both in short- and medium-term periods.²² Therefore, some researchers have begun to study the effects of dexamethasone administered via the intracameral route.¹¹ However, many studies have found minimal-to-no effects of corticosteroids on IOP when used at low concentrations or administered through the intracameral route,^{15,19,20,23,24} even in patients with glaucoma.⁴

Dexamethasone or triamcinolone intracamerally administered has been associated with better postoperative control of inflammation.²³ Intracapsular implants of dexamethasone have also shown to produce good outcomes in this respect,²⁵ however, the technical difficulty in positioning the implant and the lack of studies on the topic limit their use.

Dexamethasone is a steroid with rapid turnover and a short half-life, both of which help to minimize the risk of increased IOP and the effects on the cornea that occur with the prolonged use of topical corticosteroids. This drug has been tested at a concentration of 0.4 mg/0.1 ml through the intracameral route. When injected at the end of surgery, it significantly reduced inflammation on the first postoperative day and seemed to be safe for patients with glaucomatous eyes.^{4,11,26} The intracameral use of 0.4 mg/0.1 mg dexamethasone was found to be safe for the endothelium when compared to its subconjunctival use at a concentration of 2 mg/0.5 ml.

²⁶

Triamcinolone has anti-inflammatory properties similar to those of topical prednisolone.²⁷ It acts upon the anterior vitreous and may be used to aid in vitreous removal in patients with posterior capsular tear or zonular dehiscence.^{11,21} In these complicated surgeries, triamcinolone has been found to be safe for the long-term control of CME and increased IOP.²¹ Because of this property of acting upon the vitreous, the patient might complain of floaters or blurred vision in the first postoperative week, even when there are no surgical complications, because of the transzonular route.² The intracameral use of triamcinolone at concentrations of 0.04 mg/0.1 ml for preventing inflammation in the immediate postoperative period³ and at concentrations of 2–4 mg/0.1 ml²⁸ in children^{19,20,11} to replace topical steroids has been described in the literature.¹⁷

In pediatric cataract surgeries, routine posterior capsulotomy and anterior vitrectomy are indicated. In addition to aiding in visualization and the complete removal of the vitreous, thereby minimizing postoperative complications, triamcinolone has been found to provide benefits, such as reduced anterior chamber inflammation and fewer pigment deposits on IOL, in these patients.^{19,20} The use of triamcinolone was found to be fundamental in a recent study on traumatic cataracts in children.²⁸ In that study, no cases of posterior synechiae, fibrin deposition, or opacity of the visual field were found in the group that used this corticosteroid compared with the control group, in which there was a significant difference.

In the case of post-uveitis cataracts, some studies have shown that intracameral use of triamcinolone is more effective in controlling postoperative inflammation than the systemic use of methylprednisolone or the subconjunctival use of steroids. Intracameral use of triamcinolone produces the lowest increases in IOP and provides the best control of CME.¹⁵

Subconjunctival and Subtenon Steroids

Both topical and subconjunctival steroids are widely used to prevent postoperative inflammation. However, subconjunctival applications may be painful in cases of topical anesthesia and may also cause hyposphagma and chemosis.¹¹

The prolonged action of subtenon corticosteroids may limit the safety and IOP control in patients with glaucomatous eyes. Such patients must be rigorously monitored. There are several reports of increased IOP that does not respond to treatment after subconjunctival injection of triamcinolone.⁴

In routine cataract surgeries with no complications and in patients with no comorbidities, some researchers have reported no significant differences in inflammation, CME, or IOP between the subconjunctival use of methylprednisolone and the standard regimen of topical prednisolone in the postoperative period.²⁹ The same findings have been reported for subconjunctival triamcinolone⁷ and subtenon triamcinolone.²⁷

In patients with a previous history of anterior uveitis, subconjunctival betamethasone combined with the conventional topical treatment produced a significant reduction in inflammation of the anterior segment in the initial postoperative period.⁴

Intravitreal Steroids

Intravitreal steroids are primarily used to prevent or treat macular edema. All intravitreal steroids may increase IOP, but most cases can be controlled with antiglaucomatous drugs.^{3,22}

The intravitreal injection of 4 mg triamcinolone has become an established treatment for many conditions that cause macular edema, but the postoperative increase in IOP is now recognized as a common occurrence²² because of its prolonged action and the fact that concentrations are detected up to 3 months postoperatively.^{3,4} In approximately 50% of patients, IOP may increase by 30% of the baseline value, and in 12% of patients, IOP reaches 35 mmHg. This increase generally occurs in the first 2 months after the intravitreal injection of triamcinolone.²²

In a multicenter study analyzing the use of steroids in the treatment of uveitis, which was published in *Ophthalmology* in 2016, the preoperative intravitreal implantation of 0.59 mg of fluocinolone (Retisert[®], Bausch & Lomb, Rochester, NY, USA) was analyzed in cataract surgery. This steroid slowly releases controlled levels of the ocular corticosteroid for 3 years or more. The cataract surgeries performed in this study resulted in substantial and sustained improvements in vision after both the fluocinolone implant and the standard systemic treatment (oral immunosuppressants and steroids) in patients with intermediate uveitis, posterior uveitis, and panuveitis.⁶ However, one systematic review found that 66% of patients experienced ocular hypertension after the implant.³

In studies on postoperative CME, the intravitreal implant of 0.7 mg dexamethasone (Ozurdex™, Allergan Inc., Irvine, CA, USA) was effective in reducing macular edema and improving visual acuity, regardless of the duration of macular edema over a 1-year period. However, edema may recur within a mean period of 3 months after the implant and an additional application may be required.³⁰ Therefore, the use of Ozurdex™ may be a good alternative to the conventional topical treatment in patients with refractory CME.³¹ The incidence of ocular hypertension after the use of Ozurdex™ has been found to be 15%.³

Transzonular Steroids and Other Approaches









































In the United States, a triamcinolone–moxifloxacin solution for transzonular use (TriMoxi™, Imprimis Pharmaceuticals, CA, USA) based on the concept of dropless surgery is available.²

However, the risk of increased IOP induced by corticosteroids is a reason why many ophthalmologists refrain from using them. The drops can be easily discontinued, whereas administration using the transzonular route cannot. Studies have shown that the increased risk of IOP with the use of triamcinolone is dose-dependent, and studies showing this characteristic with the transzonular dose are still rare.² Furthermore, randomized studies have shown that NSAIDs are superior to corticosteroids in terms of reducing CME.^{1,7} Therefore, patients will still need to use eyedrops in the postoperative period.

A Brazilian study used the Ozurdex™ intracapsular implant (0.7 mg dexamethasone) after an IOL implant and compared the outcomes to those of the contralateral eye, in which topical dexamethasone was used as per the protocol. The implants were cut in the middle to obtain a size of 3 mm. Some were sutured to the edge of IOL using 10-0 nylon. Some of the non-sutured implants shifted to the anterior chamber, and reintervention was required. The implant was effective in controlling inflammation and did not cause unexpected side effects; however, this is not a viable option because of the need for suturing.²⁵

There have also been reports on the use of Ozurdex™ in the lacrimal canaliculus during surgery in an attempt to decrease postoperative inflammation and pain³².

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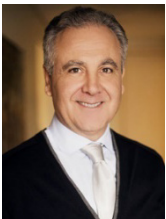
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