CORNEAL MELTING AND TOPICAL NONSTEROIDAL ANTI-INFLAMMATORY DRUG (NSAID).
A CASE REPORT

ABSTRACT

Purpose: To study the relationship between the use of nonsteroidal anti-inflammatory drug (NSAID) and the corneal melting.

Case report: We report a case of keratolysis after vitreoretinal surgery and topical use of ketorolac tromethamine (Acular®).

Discussion: It is proposed the multifactorial etiology in the cases of corneal melting related to the use of NSAID and it is recommended an reasonable use of them in each situation and to check the possible comorbility of other agents (Arch Soc Esp Oftalmol 2009; 84: 311-314).

Key words: Ketorolac, corneal melting, NSAID, vitreoretinal surgery, ocular surface desease.

INTRODUCTION

At present, topical non-steroid anti-inflammatory drugs (NSAID) are frequently used after several eye surgical procedures to control pain and inflammation.

Few complications have been associated with its use, although some have been described, including: Keratitis Punctata, subepithelial infiltrates, stromal level infiltrates, immune corneal rings, persistent corneal defects and, in severe cases, corneal melting (1,2).
In 1999, the American Society of Cataract and Refractive Surgery (ASCRS) reviewed corneal complications associated with the use of NSAID. Even though the first case studies to be published were attributed to the generic Diclofenac sodium (Falcon, Alcon Laboratories, Ft Worth, TX), other cases related to registered Diclofenac sodium (Voltaren®, Ciba Vision, Atlanta, GA) and ketorolac tromethamine (Acular®, Allergan Inc, Irving, CA) have also been reported, both administered as eye drops and single dose (preservative free) (1). More recently, Japan approved the topical use of Bromfenac sodium, a new NSAID, which has also been associated with severe corneal complications (3).

The case study described below refers to corneal melting associated with the use of ketorolac tromethamine ophthalmic solution (Acular®, Allergan Inc, Madrid) after vitreoretinal surgery. The potential multifactorial etiology for this type of complication is discussed together with recommendations for the proper administration of NSAID.

**CASE STUDY**

A seventy-year-old patient without relevant systemic history undergoes cataract surgery with posterior luxation of the lens nucleus. The treatment prescribed included Tobradex® (Alcon Cusi Inc, Barcelona) (1 drop 4 times a day), 0.5% Timoftol® (Merk Sharp & Dome Inc, Madrid) (1 drop twice a day) and Acular (1 drop 4 times a day.) Fifteen days later, a vitrectomy with phacoemulsification of the nucleus and intraocular lens implant in the anterior chamber were performed, maintaining the treatment with Acular and Tobradex. Ten days later, patient reported intense pain, reddening, epiphora and blepharospasm. Exploration under biomicroscopy revealed intense ciliary injection, peripheral corneal thinning with 5x3 mm epithelial defect and perilimbal stromal infiltration (fig. 1.) A culture is performed and intensive therapy is prescribed with Ciprofloxacino® (Farma-Lepori Inc, Barcelona) while maintaining Acular. Culture was negative and, since no improvement was observed, treatment was suspended and Medrivas® (Alcon Cusi Inc, Barcelona), artificial tears, Aureomicina® eye drops (Alcon Cusi Inc, Barcelona) and Redoxón® (Bayer Inc.) were prescribed instead. One week later, the infiltration disappeared and normal corneal thickness restored; only a slight corneal opacity remained.

**DISCUSSION**

NSAID are anti-inflammatory drugs inhibiting the activity of cyclooxygenases (COXs), reducing the synthesis of prostaglandins and mitigating postsurgical pain and inflammation.

Much has been said about the relation existing between the use of NSAID and corneal melting. The mechanism by which NSAID cause corneal melting remains partially unknown. Potential factors include: the inhibition of keratocyte proliferation, alterations in the regulation and expression of metal proteinases in the extracellular matrix (MMP-1, MMP-2 and MMP-8) and reduced corneal sensitivity, with delayed corneal scarring (2.) Additionally, at high doses, NSAID can promote inflammation since, although they usually inhibit COXs, at high concentrations they induce mRNAs and COX1 and COX2 proteins. On the other hand, the inhibition of COXs may boost the lipooxygenase pathway and its products, such as leukotrienes, thus increasing cellular inflammatory response (2).

Does this mean that NSAID are dangerous and caution should be advised when prescribed? Evidence is still needed. In the cases reported so far, the observed multifactor mechanisms are responsible for corneal melting. Thus, compromised ocular surfaces, associations with other drugs, inadequate and prolonged posology, the use of contact lenses and wrong indications may act individually or in association to cause corneal melting (2-4).
In the present case, the predisposing ocular factors were the two surgical procedures performed over a short period of time, the association with Tobradex and Ciprofloxacin together with their preservatives.

Therefore, in patients suffering from ocular surface pathologies, keratoconjunctivitis sicca, limbal deficiency, neurotrophic keratitis, exposure keratitis, persistent epithelial defects or collagen diseases should be considered as relative contraindications to the use of NSAID. If used, very frequent follow-ups are recommended to avoid potential corneal complications.

As for the dosage and duration of treatment in surface refractive surgery, their use is recommended for a brief period of time (2 or 3 days) 4 times a day, although some authors prolong treatment 2-3 weeks to regulate surgical hyper-correction (5), and after cataract surgery the dose is two weeks 4 times a day for Diclofenac sodium and ketorolac and twice a day when using bromfenac sodium.

In conclusion, whenever NSAID are to be prescribed, potential factors contributing to corneal toxicity should be previously discarded.

REFERENCES