Determination of the effectiveness of Diclofenac Sodium in relieving the initial discomfort of adaptation to rigid gas permeable contact lenses.

Nathan R. Bjork, B.S. **Matt T. Smith, B.S.**

Michigan College of Optometry, Ferris State University, Big Rapids, MI

Purpose: To evaluate the effectiveness of Diclofenac Sodium .1% (Voltaren) in relieving the foreign body sensation, itching, tearing and overall discomfort during the first three days of Rigid gas permeable lens adaptation.

Setting: Michigan College of Optometry, Ferris State University, Big Rapids, MI, USA.

Methods: A double-blind, placebo controlled, prospective, pilot study, comprised of four patients (8 eyes) was conducted. The patients were to wear the RGP lenses six hours each day for 3 days. During this time, the patient was to instill drops from the appropriate bottle into each eye four times per day. One eye would receive drops from a bottle which contained Voltaren the other eye would receive drops from a bottle which contained the Voltaren vehicle. Three surveys were completed each day during the study to subjectively evaluate the patients level of itching, tearing, foreign body sensation and overall discomfort. The results were analyzed to determine any differences between the two eyes.

Results: There were no significant differences in discomfort between the eyes treated with Voltaren and the eyes treated with the Voltaren vehicle.

Conclusion: These findings suggest that Voltaren is ineffective at relieving the discomfort during rigid gas permeable lens adaptation.

Introduction

Rigid gas permeable (RGP) lenses are superior to hydrogel lenses in several ways. RGP contact lenses allow more oxygen transmission and tear exchange when compared to soft lenses. Also, RGP materials are less likely to deposit and are easier to clean. These benefits decrease the chances for corneal edema, hypoxia, giant papillary conjunctivitis and infections. In addition, patients often favor the quality of vision experienced through rigid gas permeable lenses.

Even with their numerous advantages, many clinicians are reluctant to fit first time contact lens wearers with RGP lenses. This is due, in large part, to the initial discomfort experienced by new RGP lens wearers when they are adapting to these lenses. Clinicians and patients would benefit if more new contact lens wearers were fit with rigid gas permeable lenses. If the symptomology associated with adaptation could be reduced, fewer patients would discontinue wearing RGP lenses and clinicians would be more likely to fit them. This study was conducted to see if topical diclofenac sodium 0.1% (Voltaren) would reduce patient discomfort when adapting to RGP lenses.

Diclofenac sodium is the active substance in Voltaren, a nonsteroidal anti-inflammatory drug. This drug is available in topical and oral preparations. The topical form is indicated for the treatment of postoperative inflammation in patients who have undergone cataract surgery, and for the treatment of photophobia in patients who have had incisional refractive surgery.[1] Diclofenac sodium works like other nonsteroidal anti-inflammatory drugs; it interacts with the arachidonic acid pathway at the point of cyclo-oxygenase. By inhibiting cyclo-oxygenase, the formation of thromboxane, prostaglandin and prostacyclin is prevented as illustrated in figure 1.

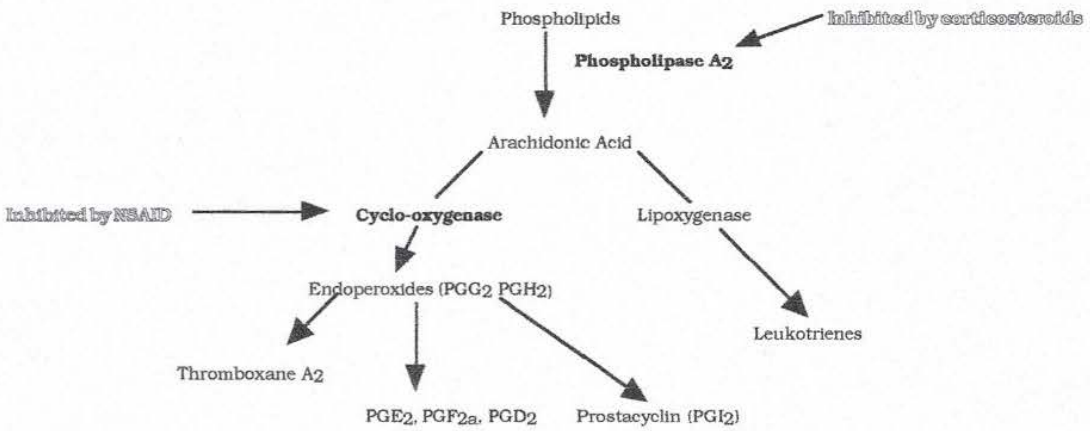

FIGURE 1. Pathway of synthesis of prostaglandins and leukotrienes. (Adapted from Bartlett JD. Clinical Ocular Pharmacology 1995; 318.)

Thromboxane A_2, PGE_2, PGF_{2a}, PGD_2, and prostacyclin are a group of lipids (unsaturated fatty acid derivatives) produced by nearly all cells in the body in response to some form of injury. These mediators of inflammation can cause smooth muscle relaxation, vasodilation, an increase in vascular permeability and the stimulation of pain receptors. Figure 1. suggests that NSAIDs do not block the formation of leukotrienes which can cause similar effects as the mediators mentioned above. However, one study indicated that diclofenac can inhibit arachidonic acid formation and stimulate its reuptake into triglycerides which would ultimately decrease the production of leukotrienes.[3] Diclofenac sodium's ability to decrease the inflammatory cascade (redness, swelling, and pain) could theoretically reduce the discomfort in a patient adapting to RGP contact lenses. Specifically, diclofenac could inhibit the release of the mediators of inflammation mentioned above, which are released from the mechanical trauma induced by the RGP lens edge as the superior palpebral conjunctiva passes over it with each blink. Decreasing the symptoms associated with this process would improve patient acceptance of the healthier RGP lens.

Materials and Methods

The study was conducted over a three day period with the RGP lenses to be worn six hours each day. Each patient was given two identical bottles of different ophthalmic solutions labeled with a designated number. The labeling of the bottles was randomized. The patients were instructed to instill two drops from the appropriate bottles into the corresponding eye thirty minutes prior to insertion of lenses (the two drops were to be spaced five minutes apart). The patients were also told to close their eyes for one minute after installation of all drops in the study. One of the bottles contained a placebo (the Voltaren vehicle supplied by Ciba) and the other contained Voltaren ophthalmic solution (diclofenac sodium 0.1%). Each participant was given a survey to complete one hour after the insertion of the lenses, followed by the installation of another drop. The survey indicated that the patient was to grade the amount of foreign body sensation, itching, tearing and overall discomfort experienced. The grading system was conducted on a scale of 0-4 (0=none, 1=trace,

2=mild, 3=moderate, 4=severe). The second survey was to be completed three hours after insertion of the lenses, followed by the final drop. The last survey was completed just prior to removal of the lenses and six hours after insertion. This procedure was to be repeated on two successive days for a total of three days. A double-blind format was followed throughout the study. The results of the surveys were analyzed for statistical significance.

Results

The surveys were analyzed with the Voltaren vehicle (placebo) being compared to the Voltaren. There was no statistically significant differences at any of the survey times during any of the days. The average of each category (foreign body sensation, itching, tearing and overall discomfort) for individual days were also compared and no statistically significant differences were found between the Voltaren and the placebo. These averages appear in the following table.

	Placebo			Voltaren		
Day	1	2	3	1	2	3
Foreign body sensation	2.75	2.17	1.92	3	2.5	2.08
Itching	1.25	1.08	0.67	1.25	1.08	0.75
Tearing	1.92	1	0.92	1.83	1.17	1.08
Overall discomfort	2.42	1.92	1.67	2.67	2	1.67

TABLE 1. Comparison of patient symptomology while adapting to RGP lenses while using Voltaren or a placebo.

The only area in which the Voltaren appeared to be effective was on the three-hour post insertion survey of day one in the tearing category. The vehicle was a 2.25 and the Voltaren was a 2.00. The tearing level on the other two surveys for day one was equal between the placebo and the Voltaren, giving the day one averages of 1.92

for the placebo and 1.83 for the Voltaren. On the remaining two days, the placebo appeared better than the Voltaren in the tearing category. In all other categories, if a difference was reported, it was the placebo that was slightly better.

Discussion

Voltaren has been proven to be effective in the reduction of post-cataract surgery discomfort[4] and inflammation.[5,6] A study has also demonstrated a small reduction in erythema and edema in Voltaren treated eyes compared to eyes treated with prednisolone following strabismus surgery.[7] In addition, Voltaren has performed significantly ($p < .001$) better than a placebo in reducing ocular pain, foreign-body sensation, and burning/stinging following radial keratotomy and has gained FDA approval for this use.[8,9]

Despite its effectiveness in these situations, Voltaren does not appear to be effective in reducing the symptoms associated with RGP lens adaptation. In a similar pilot study using Voltaren and a placebo for RGP adaptation, a slight, but not significant, increase in adaptation and comfort was found in the Voltaren treated eyes.[10] Another placebo controlled trial on 20 patients did not show a statistically significant effect on the signs or symptoms of RGP lens adaptation with Voltaren.[11]

In the studies of Voltaren's effectiveness in post-radial keratotomy and post-cataract surgery, the pain and inflammation was in the cornea or anterior segment of the eye. The symptoms of the RGP lens adaptation, on the other hand, are due to lens interaction with the eyelids. While at least one study has been done to measure the levels of diclofenac in the cornea, aqueous humor, and iris/ciliary body following topical administration,[12] studies have not been done to evaluate its penetrance in lid tissue. This leaves a possible explanation for the apparent ineffectiveness of Voltaren at relieving the symptoms of RGP lens adaptation -- the drug may have a limited amount of penetration into the lid tissue.

Voltaren's active ingredient, diclofenac sodium, and Acular's active ingredient, ketorolac tromethamine, both work by reducing the production of prostaglandins. Diclofenac, however, is a phenylacetic acid, while ketorolac is a pyrrolo-pyrolle acid.

There is some evidence that suggests that phenylacetic acids are more effective at reducing inflammation, photophobia, and pain that pyrrolo-pyrolle acids [9] Therefore, unless Acular was able to demonstrate a greater penetrance into the lid tissue, it is unlikely that it would perform any better than the Voltaren did.

The dosing schedule that was used provided an initial loading dose of two drops 30 minutes prior to insertion. The concentration of diclofenac in the cornea and the iris/ciliary body peaks at 30 minutes after instillation of topical drops.[12] Since similar studies have not been done for lid tissue, the pharmacokinetics of diclofenac in the cornea, iris/ciliary body was used as a guide. The recommended dosage of Voltaren is q.i.d.[1] and that is the same dosage schedule used in various studies on the effectiveness of Voltaren.[5-8] Since the lenses were only to be worn for six hours each day, the maximal effect of the four drops of Voltaren would occur if they were all instilled during this period. It is not likely that a different dosing schedule would produce more favorable results.

The generic diclofenac sodium has recently been recalled by Alcon Laboratories, Inc. and its affiliate Falcon Pharmaceuticals Ltd. Although the company's tests show that diclofenac is safe and effective when used as labeled, reports have surfaced about its aggressive use resulting in corneal complications.[13] One complication noted in some anectodal reports was corneal melting. It was unclear if the mechanism was due to the inhibition of collagen synthesis, as in topical steroid use, or due to some other etiology.

Conclusion

The use of diclofenac sodium for decreasing the symptoms in first time RGP lens wearers would seem to work theoretically. The small pilot study detailed here, along with the results from other research suggest that diclofenac is ineffective at relieving discomfort when used during RGP adaptation. This may be due to poor absorption into the upper lid or a failure through some other mechanism. These facts along with the reports of corneal complications would make it difficult to rationalize the use of diclofenac sodium for RGP lens adaptation.

References

1. Ciba Vision Ophthalmics, 1996. Voltaren Ophthalmic (diclofenac sodium) 1%, package insert.

2. Bartlett JD, Jannus SD. Clinical Ocular Pharmacology; 3rd ed. Boston, Butterworth-Heinemann, 1995: 318.

3. Scholer DW, Ku Edmond, et al. Pharmacology of diclofenac sodium. The American Journal of Medicine 1986; 80: 34-37.

4. Fry LL. Efficacy of diclofenac sodium solution in reducing discomfort after cataract surgery 1995; 21: 187-190.

5. Kraff MC, Martin RG, et al. Efficacy of diclofenac sodium ophthalmic solution versus placebo in reducing inflammation following cataract extraction and posterior chamber lens implantation. Journal of Cataract and Refractive Surgery 1994; 20: 138-144.

6. Vickers FF, Mcguigan LJB, et al. The effect of Diclofenac sodium ophthalmic on the treatment of postoperative inflammation. Investigative Ophthalmology & Visual Science 1991; 32: 79.

7. Apt L, Voo I, Isenberg SJ. A randomized clinical trial of the nonsteroidal eyedrop diclofenac after strabismus surgery. Ophthalmology 1998; 105: 1448-1451.

8. Hettinger ME, Gill GJ, Robin JB, et al. Evaluation of diclofenac sodium 1% ophthalmic solution in the treatment fo ocular symptoms after bilateral radial keratotomy. Cornea 1997; 16: 406-413.

9. Curtin KG, Solomon K. Which is the better post-refractive surgery NSAID: Voltaren or Acular. Review of Ophthalmology 1997; Feb: 88-92.

10. Miller WL, Cooper C. The effects of a topical nonsteroidal anti-inflammatory medication on rigid gas-permeable contact lens adaptation in neophyte wearers. FAAO poster #29; 1999.

11. Gordon A, Bartlett J, Lin M. The effect of diclofenac sodium on the initial comfort of RGP contact lenses: a pilot study. JAOA 1999; 70 (8): 509-513.

12. Palmero M, Bellot JL, et al. The ocular pharmacokinetics of topical diclofenac is affected by ocular inflammation. Ophthalmic Research 1999; 31: 309-316.

13. Barr JT. Industry briefs. Contact Lens Spectrum 1999; Feb: 1.