Comparison of analgesic effect of preoperative topical diclofenac and ketorolac on postoperative pain after photorefractive keratectomy

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PURPOSE: To investigate changes in the pain-suppressing potency of 2 preoperatively applied topical nonsteroidal antiinflammatory drugs (NSAIDs) after photorefractive keratectomy (PRK) using a time-serial pain-scoring system.

SETTING: Saeyan Eye Center, Seoul, South Korea.

DESIGN: Comparative case series.

METHODS: Ninety-four patients were randomly assigned to 2 groups: ketorolac group (ketorolac 0.5% in 1 eye and ofloxacin 0.3% in the other eye) and diclofenac group (diclofenac 0.1% in 1 eye and ofloxacin 0.3% in the other eye). One drop of each ophthalmic drug was applied 3 times to each eye 30 minutes before PRK. No other NSAID or steroid was prescribed until 4 days after PRK. The patients were asked to score the postoperative pain in each eye with a visual analog scale at 6, 18, 24, 36, 48, 72, and 96 hours.

RESULTS: The natural peak of pain was located between 24 and 36 hours. Initially, the degree of pain reduction was constant for both NSAIDs; it dropped after 24 hours and 36 hours in the ketorolac group and the diclofenac group, respectively. The postoperative time-serial pattern of the pain score changed in the diclofenac group but not in the ketorolac group compared with the pattern in the ofloxacin-treated eye. The visual outcome was not affected by either NSAID, and significant complications were not noticed for a mean of 7 months.

CONCLUSIONS: The duration and pattern of the action may vary according to types of NSAIDs. Preemptive topical diclofenac 0.1% was a safe and effective method for post-PRK pain control.

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Photorefractive keratectomy (PRK) or surface ablation is one of the most widely used surgical procedures to correct myopia, along with laser in situ keratomileusis (LASIK).[1,2] In PRK, the corneal epithelium is removed by various techniques such as diluted alcohol, manual debridement, or brush before laser ablation of the corneal stroma.[3,4] After PRK, ocular discomfort such as foreign-body sensation or pain can be present for 2 to 3 days.[5–7] The postoperative discomfort arises primarily from the exposed corneal nerve endings after removal of the corneal epithelium.[8] Various chemical mediators such as prostaglandin, histamine, and substance P are secreted from the corneal tissue damaged by the excimer laser. These mediators stimulate the exposed corneal nerve endings.[9]

To eliminate ocular pain after PRK, the bandage contact lens, dilute topical anesthetics, oral analgesics, topical morphine, and topical nonsteroidal antiinflammatory drugs (NSAIDs) have been introduced.[7,10–14] Topical NSAIDs are commonly prescribed to mitigate inflammation and pain related to ocular surgery.[15] Administration of a single drop of topical diclofenac 0.1% 2 hours before PRK has been reported to be helpful in managing postoperative pain.[16] Preoperative

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application also decreases pain for 1 day after PRK when topical diclofenac is applied for 2 days postoperatively.[16]

Recently, diclofenac 0.1% and ketorolac 0.5% instilled in a dose of 1 drop administered 30 minutes before surgery were equally beneficial in preventing post-PRK pain and discomfort for 2 days.[17] In that study, a single dose of topically applied NSAID prevented pain without postoperative administration.[17] However, topical betamethasone 0.1% was administered postoperatively and may have influenced the postoperative inflammation and pain.[17]

Postoperative pain control with preoperative topical NSAIDs is clinically important because previous studies suggest that topical NSAIDs decrease corneal epithelium migration and delay wound healing.[18] Severe corneal toxicity has been reported with various NSAIDs such as diclofenac 0.1%, ketorolac 0.5%, nepafenac 0.1%, and bromfenac 0.09%.[19–24] With a corneal surface disturbed by PRK, the capacity of the corneal epithelium to self-repair may be diminished by topical NSAIDs and cause serious complications, including corneal melting. Ameliorating post-PRK pain with the preoperative application of topical NSAIDs only would be a safe and useful way to treat PRK patients.

In our study, no postoperative NSAID or steroid was used so the effect of preoperative topical NSAID treatment could be assessed. In addition, the post-PRK pain was scored at 7 different times for 4 days to provide a detailed report of the duration and intensity of the drug's effect over time. Similar to previous studies, a paired-eye comparison design was used to observe the changes in pain. The action patterns of topical ketorolac and diclofenac were also compared.

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PATIENTS AND METHODS

This randomized double-masked paired-eye comparison single-center trial (No. 4-2012-0440) was approved by the institutional review board of our institution. Informed consent was obtained from all participants, and the study adhered to the tenets of the Declaration of Helsinki.

One hundred thirteen patients who had PRK from January 2011 to March 2011 at Saeyan Eye Center were recruited. Preoperative examinations included history, corrected distance visual acuity (CDVA), manifest refraction, intraocular pressure, keratometry, central corneal thickness, pupil size, slitlamp examination, topography (Orbscan II, Bausch & Lomb), and higher-order aberration (HOA) analysis (WASCA Analyzer, Carl Zeiss Meditec AG).

The inclusion criteria were age of at least 19 years, simultaneous bilateral PRK, a greater than 400 μm (including epithelium) postoperative corneal thickness, and a thinner than 150 μm ablation depth. The exclusion criteria were a history of ocular surgery or trauma, 2.0 diopters (D) greater difference in spherical equivalent (SE) between the eyes, keratoconus or other corneal pathology, use of systemic or topical NSAIDs within 1 month of the surgery, history of allergic reaction to aspirin or other NSAIDs, glaucoma or ocular hypertension (>20 mm Hg), collagen vascular disease, diabetic retinopathy, pregnancy or lactation, and intraoperative complications. Recruited patients were excluded if they replaced their contact lenses, took analgesics arbitrarily, used a topical steroid irregularly, stopped arbitrarily, or were followed for fewer than 3 months.

Randomization and Preoperative Treatment

On the day of surgery, the patients were randomly assigned to one of 2 groups by a lottery drawn by a nurse who was unrelated to this research. The ketorolac group applied topical ketorolac 0.5% (Acular) in 1 eye and topical ofloxacin 0.3% (Ocuflox) in the other eye preoperatively. The diclofenac group applied topical diclofenac 0.1% (Voltaren) in 1 eye and ofloxacin 0.3% in the other eye preoperatively. Neither the surgeon nor the patients knew which ophthalmic drug went into which eye. A randomly assigned ophthalmic drug was first instilled into the right eye 3 times at 1-minute intervals 30 minutes before surgery, and the other ophthalmic drug was instilled into the left eye in the same manner 10 minutes later.

Surgical Method

All eyes (the right eye first, then the left eye) were operated on by a single surgeon (J.P.H). Before surgery, topical proparacaine hydrochloride 0.5% (Alcaine) was applied 3 times to both eyes. Then 20% alcohol was applied to an 8.0 mm diameter well for 30 seconds and rinsed from the eye using a cold balanced salt solution (BSS, Alcon Laboratories, Inc.). The corneal epithelial layer was then removed with a micro hoe. The exposed corneal stroma was ablated with a Mel-80 excimer laser (Carl Zeiss Meditec AG) and irrigated again with cold balanced salt solution for 30 seconds. A cellulose sponge soaked with mitomycin 0.02% was applied to the ablated stroma for 20 to 30 seconds before irrigation in cases