PHILIPPINE JOURNAL OF
Ophthalmology

VOL. 33 • NO. 1 JANUARY – JUNE 2008

ORIGINAL ARTICLE

Efficacy of oral diclofenac as preemptive analgesic for pterygium surgery

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ABSTRACT

Objective

To determine the efficacy of oral diclofenac as preemptive analgesic for pterygium excision.

Methods

A prospective, randomized, controlled, double-blind clinical trial was carried out involving 30 patients diagnosed with pterygium. They were randomly assigned to receive either placebo or oral diclofenac. A single surgeon performed the same technique of pterygium excision. Pain scores were determined using visual-analog-scale (VAS) questionnaires handed out to participants 30 minutes and 24 hours after surgery. Collected data were analyzed using two-tailed t-test, chi-square, and Fisher's exact test.

Results

There was no statistical difference between VAS pain scores in both groups in the intra- ($p = 0.33$) and postoperative periods ($p = 0.46$). No statistically significant difference was noted on the intake ($p = 0.68$) and dose (0.18) of supplemental analgesia. There appeared to be a trend for lower pain scores in the intraoperative (VAS = 2.00 ± 1.89 for diclofenac vs. 2.73 ± 2.22 for control) and postoperative (VAS = 3.86 ± 2.92 for diclofenac vs. 4.60 ± 2.44 for control) periods with intake of diclofenac. This group also took less supplemental analgesics.

Conclusion

The preemptive use of oral diclofenac showed a trend toward less intra- and postoperative pain, and less need for supplemental analgesics after pterygium surgery.

Keywords: *Oral diclofenac, Preemptive analgesia, Pterygium surgery, Surgical pain*

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No financial assistance was received for this study.

The authors have no proprietary or financial interest in any product used or cited in this study.

PHILIPP J OPHTHALMOL 2008; 33(1): 13-16

POSTOPERATIVE pain is a concern of both patients and surgeons. It is generally managed by pain relievers given intra- or postoperatively. Pain in ocular surgery is the result of nociceptive injury to peripheral neural structures. The use of local anesthesia during ocular surgery is primarily aimed at controlling intraoperative pain.

The concept of preemptive analgesia to reduce postoperative pain was founded on a series of successful animal experimental studies.[1] Preemptive analgesia stems from the importance of pain modulation through peripheral or central inhibition of nociception. It is the pharmacologic management producing effective analgesia prior to surgical trauma using central neural block, local anesthetic infiltration, opioids, nonsteroidal antiinflammatory drugs (NSAIDs), or ketamine.

The use of preemptive analgesics in ocular surgery is not well established. Weinberger used topical sodium diclofenac as a preemptive analgesic for retinal laser photocoagulation.[2] Kristin showed that preoperative peribulbar bupivacaine effectively reduced postoperative pain for vitrectomy surgery. [3] Fekrat demonstrated that intraoperative intravenous ketorolac tromethamine effectively controlled postoperative pain after vitreoretinal surgery.[4] A metaanalysis by Ong (2005) on preemptive analgesia, covering the period January 1987 to October 2003, however, showed equivocal effectiveness among various forms of preemptive analgesics for a variety of surgical procedures.[5]

Pain is still a concern in intra- and postoperative periods in minor ocular surgeries, such as pterygium excision where topical and local anesthetics are used. This is usually addressed by giving analgesics after surgery. However, patients' apprehension of pain and their actual pain perception may be markedly reduced if the pain reliever is given preoperatively. Diclofenac, a common pain reliever given postoperatively, is a nonselective cyclooxygenase inhibitor rapidly absorbed by the body following oral intake. It has a half-life of 1 to 2 hours, with an onset of action an hour after intake. Its duration of action lasts for approximately 12 hours and is, therefore, suitable for relieving postoperative pain.

This study determined the efficacy of oral diclofenac as a preemptive analgesic among patients undergoing pterygium excision. Intra- and postoperative-pain scores were determined including the need for supplemental analgesic within 24 hours after the procedure.

METHODOLOGY

We conducted a prospective, randomized, double-blind clinical trial involving patients from the outpatient clinics of the Department of Ophthalmology, East Avenue Medical Center. Patients were invited to participate in the study if they met the following inclusion criteria: at least 21 years old, diagnosed with pterygium at least >2 mm from the limbus, scheduled for pterygium excision under local anesthesia, and undergoing minor ocular surgery for the first time. Excluded were patients who have undergone previous ocular surgery, those taking other oral pain medication or other modes of analgesic therapy for other medical conditions, and those with diagnosed renal or liver failure. Informed consent was obtained from all participants.

Patients were asked to report 2 hours before their scheduled surgery and advised to have their lunch prior to oral intake of oral diclofenac to reduce the incidence of gastric irritation.

The participants were randomly assigned by toss coin to one of two groups: placebo or diclofenac. One hour prior to the scheduled surgery, the study participants were given one tablet of either 50-mg diclofenac or 100-mg ascorbic acid (control).

A single surgeon, blinded as to the status of preemptive analgesia, performed the pterygium excision under local anesthesia using the standard bare-sclera technique. 0.2% mitomycin C was applied over the bare sclera. The surgeon also gave the postoperative instructions, including the use of postoperative analgesic.

The primary outcome is the determination of the pain score within 30 minutes and 24 hours after surgery using the visual analog scale (VAS). The VAS pain-scoring system is a scale that ranks the level of pain from zero (no pain felt at all) to 10 (being the most painful or intolerable type of pain). The secondary outcome was the use of postoperative analgesic by the patient. The same investigator, blinded as to the medication received by the patient, conducted the pain survey within 30 minutes after the surgery and asked the participant to indicate the pain score felt during the procedure. She also retook the pain score at postoperative day 1 and noted whether additional analgesic was taken.

The sample size was computed based on the result of the study by Reuben[6] that showed a standard deviation of 0.7 for the control and a mean difference of 1.3 between the treatment and control groups. The sample size was calculated based on an α-error level of significance of 95% and a β-error level of significance of 90%. Each study group, therefore, had a minimum sample size of 15.

The data were entered in SPSS version11 and analyzed using the t-test comparing the mean between the control and treatment groups. Chi-square and the Fisher's exact tests were used to compare nominal data.

RESULTS

The study population consisted of 30 subjects, 15 in the placebo and 15 in the diclofenac groups. There was no significant difference in mean age and sex distribution (Table 1).

The mean VAS scores were not significantly different between the two groups for both the intra- ($p = 0.33$) and postoperative ($p = 0.46$) periods (Table 2). Relative risk was computed for VAS scores of zero as having no intraoperative pain and VAS scores above 1 as having significant postoperative pain. The relative risk for intraoperative pain was slightly less for the diclofenac group (RR = 0.73) but it was not significantly different ($p = 0.09$). It was also less in the postoperative period (RR = 0.73) but not significantly different from the control group ($p = 0.09$) (Table 3).

The need for postoperative supplemental analgesic was lesser for the diclofenac group (RR = 0.84) but the difference was not significant ($p = 0.68$) (Table 3). The most commonly used postoperative analgesic for both groups was mefenamic acid. The number of postoperative supplemental doses of analgesic was also lesser for the diclofenac group (RR = 1.20) but the difference was not significant ($p = 0.18$) (Table 2).

DISCUSSION

Pain intensity following induction of surgical trauma can be controlled not only by local wound infiltrate of anesthesia that blocks peripheral nerves, but also by anti-inflammatory medications. The amount of pain sensation is related to the amount of inflammation induced during surgery. Thus, blocking pain sensation by reducing postoperative inflammation is a logical option to reduce pain intra- and postoperatively.

Diclofenac is an NSAID that inhibits both peripheral and central pain. As a cyclooxygenase inhibitor, it reduces the release of inflammatory mediators in the cyclooxygenase pathway, resulting in reduction of inflammation and pain sensation.

Many surgeons still prescribe postoperative analgesics on "as needed" basis depending on the patient's level of pain tolerance. With better understanding of surgical trauma and resultant inflammation, there is growing interest in giving analgesics much earlier to minimize pain during and after surgery. The concept of preemptive analgesia is to minimize intra- and postoperative pain by giving analgesic before pain occurs and before local anesthesia wears off. Such intervention may lead to better management of postoperative pain.

Our study found diclofenac to be an insufficient preemptive analgesic following pterygium excision. Although there was a trend toward greater reduction in the VAS pain scores in the diclofenac group, meaning that a surgeon would only need to treat 1 out of 4 patients to get a reduction in the intra- and postoperative-pain scores—a 25% pain reduction—this was not statistically significant. The need for supplemental analgesic, mefenamic acid in this study, was also less in the diclofenac group, but the trend was not statistically significant. One explanation for diclofenac's insufficiency as a preemptive analgesic may be its half-life of 1 to 2 hours, which is rather

Table 1. **Demographic characteristics of the study population.**

Characteristics	Control (n = 15)	Diclofenac (n = 15)	*p*
Age (years)			
Mean	41.00 ± 9.64	42.93 ± 13.96	0.66[1]
20 – 30	3 (20.0%)	4 (26.7%)	
31 – 40	2 (13.3%)	2 (13.3%)	
41 – 50	8 (53.3%)	3 (20.0%)	
51 – 60	2 (13.3%)	5 (33.3%)	
61 – 70	0	1 (6.7%)	
Sex			
Male	9 (60.0%)	12 (80.0%)	0.42[2]
Female	6 (40.0%)	3 (20.0%)	

[1]Computed by t-test
[2]Computed by Fisher's exact test

Table 2. **Mean VAS scores and number of supplemental analgesic taken.**

Parameter	Control (n = 15)	Diclofenac (n = 15)	*p*[1]
VAS scores			
Intraoperative			
0	0	4 (26.7%)	
1	7 (46.7%)	4 (26.7%)	
2	2 (13.3%)	2 (13.3%)	
3	1 (6.7%)	0	
4	2 (13.3%)	3 (20.0%)	
5	1 (6.7%)	2 (13.3%)	
6	1 (6.7%)	0	
8	1 (6.7%)	0	
Mean	2.73 ± 2.22	2.00 ± 1.89	0.33
24 hours postoperative			
0	0	2 (13.3%)	
1	0	2 (13.3%)	
2	5 (33.3%)	3 (20.0%)	
3	1 (6.7%)	0	
4	2 (13.3%)	1 (6.7%)	
5	1 (6.7%)	1 (6.7%)	
6	2 (13.3%)	4 (26.7%)	
7	2 (13.3%)	0	
8	1 (6.7%)	1 (6.7%)	
9	1 (6.7%)	1 (6.7%)	
Mean	4.60 ± 2.44	3.86 ± 2.92	0.46
Supplemental analgesic			
0	3 (20.0%)	5 (33.3%)	
1	1 (6.7%)	3 (20.0%)	
2	6 (40.0%)	4 (26.7%)	
3	4 (26.7%)	3 (20.0%)	
4	1 (6.7%)	0	
Mean	1.93 ± 1.22	1.33 ± 1.18	0.18

[1]Computed by t-test

short compared with 50 hours for other oral pain medications. The more ideal analgesic is one that is potent enough that the patient will no longer have to take any form of supplemental therapy postoperatively. It is noteworthy that even though the mean pain scores were generally low in both the control and diclofenac groups during the intra- and postoperative periods, the participants still had to take some form of supplemental analgesic postoperatively.

Newer NSAIDs, such as rofecoxib and piroxicam, were used in arthroscopic knee surgery[6] and laparoscopic surgery[7] respectively and found to be significantly effective in reducing postoperative pain as measured by VAS scores (p = 0.005 and p < 0.05 respectively). Intake of supplemental analgesic was also found to be significantly less in these studies (p = 0.0001 and p < 0.04 respectively).

Rofecoxib, a cyclooxygenase-II inhibitor, has been withdrawn from the market due to its side effects while piroxicam is still available. It has a longer half-life of approximately 57 hours,[8] permitting once-daily dosing. It is rapidly absorbed in the body, with peak plasma concentration within an hour following intake. Piroxicam can, therefore, be a more suitable preemptive analgesic.

Although diclofenac failed to demonstrate conclusively its usefulness as a preemptive analgesic in pterygium excision, this study is limited by its small sample size. Larger sample using stronger NSAIDs may be more appropriate in demonstrating the utility of preemptive analgesia in ocular surgery.

In summary, the preemptive use of oral diclofenac showed a trend toward less intra- and postoperative pain and less need for supplemental analgesic after pterygium surgery.

Table 3. **Presence or absence of intra- and postoperative pain and intake of supplemental analgesic.**

Outcome	Control (n = 15)	Diclofenac (n = 15)	RR	95% CI[1]	NNT	p^2
Intraoperative						
No pain (VAS = 0)	0	4	0.73	0.54–1.00	3.7	0.09
With pain (VAS > 0)	15	11				
Postoperative						
No pain (VAS = 0)	0	4	0.73	0.54–1.00	3.7	0.09
With pain (VAS > 0)	15	11				
Supplemental analgesic						
No intake	3	5	0.84	0.34–1.18	7.8	0.68
With intake	12	10				

[1]Confidence interval
[2]Computed by Fisher's exact test

Acknowledgement
The authors acknowledge the assistance of Drs. Alejandro de Leon, Rudolfo Chuanico, Debbie Yap, Gerald Maceda, Grandyll Oca, and Ms. Grace Rosales.

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