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Can topical ketorolac 0.5% improve the function of Ahmed glaucoma drainage devices?

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Abstract

Background and Objective—To determine whether postoperative use of topical ketorolac tromethamine 0.5% affects intraocular pressure (IOP) following Ahmed glaucoma drainage device implantation.

Study Design—Patients undergoing Ahmed implantation at the University of Michigan from January 2002-June 2008 were reviewed. Fourteen eyes received ketorolac after surgery; 50 eyes did not. Preoperative and postoperative IOP and glaucoma medications were recorded for both groups; the two-sided Student t-test was used to compare these parameters.

Results—Mean preoperative IOP was similar in the two groups (35.1 ± 11.9 mmHg versus 37.0 ± 12.2 mmHg; p=0.60). At postoperative month 6, the ketorolac eyes following Ahmed implantation had significantly lower IOP compared with the no ketorolac group (13.1 ± 3.7 mmHg versus 19.5 ± 9.3 mmHg respectively; p= 0.0003). There was no difference in the number of glaucoma medications postoperatively between the two groups.

Conclusion—Ketorolac may lead to lower postoperative IOP following Ahmed implantation.

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Introduction

The use of glaucoma drainage implants for the management of glaucoma has been rising substantially over the past decade. Between 1995 and 2004, the number of glaucoma drainage device surgeries performed in the United States increased almost fourfold.[1] The Ahmed glaucoma drainage implant (AGI; New World Medical, Inc, Rancho Cucamonga, California, USA) is a device that allows controlled aqueous flow in patients with glaucoma who are at high risk for trabeculectomy failure.[2] The AGI has been used effectively to lower intraocular pressure (IOP) in patients with neovascular, uveitic, and other refractory types of glaucoma, and ongoing studies suggest that aqueous drainage implants may be a safe and effective alternative to trabeculectomy for patients with primary open-angle glaucoma and other forms of glaucoma.[3]

Many patients who undergo AGI surgery experience a hypertensive phase that occurs within the first few months following device implantation. The hypertensive phase is characterized by elevation in IOP that can reach as high as the preoperative IOP levels and often requires hypotensive medications or occasionally additional surgery to lower the IOP to an acceptable level. Mitomycin-C and other antimetabolites have been used adjunctively during AGI implantation to try to limit or prevent the hypertensive phase, but these agents can have detrimental side effects such as overfiltration, hypotony and questionable long term efficacy in preventing subconjunctival fibrosis.[4] With increasing numbers of patients undergoing AGI implantation and the indications for use of these devices expanding, it is becoming increasingly important to identify ways of optimizing postoperative IOP control. The aim of this study is to investigate whether the use of the topical non-steroidal anti-inflammatory eye drop ketorolac tromethamine ophthalmic solution 0.5% (Acular®, Allergan, Irvine, California, USA) improves postoperative IOP following AGI surgery and reduces the occurrence of a postoperative hypertensive phase.

Patients/Materials and Methods

The study was approved by the University of Michigan Institutional Review Board. A retrospective chart review of all consecutive patients who underwent at least one AGI surgery (models S2 or FP7) between Jan 1, 2002 and June 30, 2008 at the W.K. Kellogg Eye Center, University of Michigan, was performed. Individuals were excluded if they were under 18 years of age, had less than 6 months of follow-up from the date of AGI surgery, or underwent any type of combined surgery (i.e. AGI implantation plus a concomitant ocular surgical procedure).

The AGIs were inserted by five different glaucoma specialists using a standard technique. Briefly, the AGI was primed with balanced salt solution to ensure patency. A conjunctival incision was made either at the limbus or approximately 5 mm posterior to the limbus. The AGI plate was sutured to the sclera between two recti muscles in either the superonasal or superotemporal quadrant at least 8 mm posterior to the limbus. A 23-gauge needle was used to create a sclerostomy into either the anterior chamber or pars plana through which the AGI was inserted. The exposed tube was covered with a human donor scleral patch graft and the conjunctival wound was closed. None of the patient received intraoperative or postoperative antimetabolites. In the patients who were prescribed ketorolac following the AGI surgery, this medication was prescribed 4 times per day in the operative eye starting at the postoperative week one visit and given for a total of 3 months postoperatively. Two of the five glaucoma specialists routinely used ketorolac after AGI surgery, according to surgeon preference. All patients were started on a topical antibiotic eye drop of the surgeon's choosing as well as topical prednisolone acetate 1% on postoperative day 1; the antibiotic

drop was discontinued at the postoperative 1 week visit while the prednisolone acetate 1% was tapered throughout the postoperative course according to the surgeon's judgment.

For each patient, the following data were collected from the medical records: age, sex, race, eye which underwent the surgery (right or left), glaucoma diagnosis, smoking status, preoperative and postoperative best corrected Snellen visual acuity, preoperative and postoperative IOP by Goldmann applanation tonometry, AGI type (S2 or FP7), location of AGI tube insertion (anterior chamber vs. pars plana), intraoperative and postoperative surgical complications, postoperative medications, and additional glaucoma surgeries. The preoperative best corrected visual acuity was recorded from the visit immediately prior to surgery. The IOP was recorded at the 3 visits immediately preceding surgery, and these 3 results were averaged to compute the preoperative IOP. The postoperative best corrected visual acuity and IOP measurements were recorded at postoperative day 1, 1 week, 2–4 weeks, 6–8 weeks, 3 months, 6 months, 12 months and 24 months. The frequencies of ketorolac, topical corticosteroids, and the number and types of glaucoma medications prescribed were recorded at each of the above postoperative visits.

The two-sided Student t-test was used to compare mean IOP and mean number of glaucoma medications between the ketorolac and no ketorolac groups at each postoperative time point. The Wilcoxon test was used to compare the frequency of postoperative topical corticosteroid usage in the ketorolac and no ketorolac groups. A p-value of < 0.05 was considered statistically significant. In addition, the presence or absence of a hypertensive phase was noted at each postoperative visit from week 1 to month 6. We defined a hypertensive phase as an IOP>21 mm Hg within the first 6 months after surgery with no evidence of AGI obstruction and no contribution from suprachoroidal hemorrhage or aqueous misdirection.

Results

A total of 64 eyes of 62 patients were included in the study. Patient follow-up averaged 16.0 (SD 7.4) months with a range from 6 to 24 months. Fourteen eyes (22%) were treated with ketorolac postoperatively and 50 eyes (78%) did not receive ketorolac. There were no significant differences in the preoperative descriptive and demographic characteristics of the ketorolac and no ketorolac groups except that there were more Native Americans in the ketorolac group and more blacks in the no ketorolac group. (see table 1)

The mean preoperative IOP (±SD) was similar in both groups: 35.1±11.9 mm Hg in the ketorolac group and 37.0 ±12.2 mm Hg in the no ketorolac group (p=0.60). The mean postoperative IOP was lower in the ketorolac group compared to the no ketorolac group at the 6–8 week postoperative visit: 15.7 mm Hg vs. 19.7 mm Hg (p=0.12); 3 months: 15.5 mm Hg vs. 18.7 mm Hg (p=0.09); 6 months: 13.1 mm Hg vs. 19.5 mm Hg (p=0.0003); and 12 months (n=11 in the ketorolac group at this time point): 13.2 mm Hg vs. 17.5 mm Hg (p=0.21). Therefore, only the 6 month postoperative visit showed a statistically significant IOP difference between the two groups (Figure 1), although the mean postoperative IOP was lower in the ketorolac group at all 4 of those postoperative time points. Only 1 ketorolac patient had data at the 24 month visit, so an IOP difference between the two groups at this time point was not calculated.

The mean frequency of prescribed prednisolone acetate 1% usage was significantly different between the ketorolac and no ketorolac groups only at the postoperative 1 week and 2–4 week visits. At 1 week, the mean frequency of prednisolone acetate 1% usage was 4.4 ± 1.2 times per day in the ketorolac group compared to 6.4 ± 2.7 times per day in the no ketorolac group (p=0.005), while at the 2–4 week visit, the mean frequency was 3.5 ± 0.9 times per day in the ketorolac group compared to 5.0 ± 3.1 times per day in the no ketorolac group

(p=0.04). At all subsequent postoperative visits through the 12 month visit (the last visit analyzed for this comparison), the frequency of this topical corticosteroid usage was not significantly different between the two groups. The mean number of glaucoma medications was not significantly different at baseline or at any postoperative time point between the two groups (Figure 2).

Seven of the 14 (50%) patients who received ketorolac and 36 of 50 (72%) patients who did not receive ketorolac exhibited a hypertensive phase (p=0.12) in the first 6 months following the surgery. Two patients (14%) in the ketorolac group required additional glaucoma surgery for elevated IOP compared to 8 (16%) patients in the no ketorolac group (p>0.2).

Preoperative best corrected visual acuity ranged from 20/25 to hand motion in the ketorolac group and 20/25 to light perception in the no ketorolac group. In the ketorolac group, final postoperative visual acuity improved on average by −0.27 logMAR, or about 3 lines of Snellen visual acuity. In the no ketorolac group, final postoperative visual acuity was essentially unchanged from preoperative visual acuity, with an average change of logMAR 0.02. This difference in change in visual acuity between the two groups was not statistically significant (p=0.15).

No patients had serious intraoperative complications. There were 2 significant postoperative complications in each group. In the ketorolac group, one patient developed aqueous misdirection and one experienced a vitreous hemorrhage. Both of these patients required pars plana vitrectomy. In the no ketorolac group, one patient experienced a suprachoroidal hemorrhage and one developed large serous choroidal effusions secondary to hypotony. These two patients were treated conservatively and their complications resolved spontaneously.

Discussion

In this retrospective study, the postoperative use of ketorolac following AGI implantation resulted in consistently lower postoperative IOP values, with a significantly lower IOP at 6 months, as compared with patients who did not receive this medication (13.1 mm Hg vs. 19.5 mm Hg [p=0.0003]). The difference in IOP between the two groups persisted at 12 months follow-up (13.2 mm Hg vs. 17.5 mm Hg [p=0.21]) although this difference was not statistically significant. Comparing our findings to other studies in the literature which report IOP measurements at the 6 month postoperative visit shows that a mean IOP of 13.1 mm Hg at postoperative month 6 in our ketorolac group was lower than the 6-month IOP reported in prior studies, which ranged from 16.5–17.5 mm Hg.[6–9]

Previous studies have found that the hypertensive phase occurs in 58–82%[6–10] of patients up to 6 months after AGI implantation. In a study by Ayyala et al[7], over one-third of patients who experienced a hypertensive phase required a secondary surgery to control IOP. In our study, the proportion of patients in the no ketorolac group who experienced a hypertensive phase (72%) was similar to existing reports in the literature. By comparison, only 50% of individuals in the ketorolac group developed a hypertensive phase following AGI implantation. Although this was not a statistically significant difference (p=0.12), an absolute IOP reduction of 22% in the ketorolac group compared with the group not receiving this medication may be of clinical significance. We hypothesize that the anti-inflammatory properties of ketorolac may reduce fibrosis around the plate, which has been reported histopathologically during the hypertensive phase.[11]

Since early exposure of subconjunctival tissue to aqueous flow through the AGI is thought to lead to fibrosis which may increase likelihood of a hypertensive phase, we also investigated whether the number of glaucoma medications used postoperatively differed

between the ketorolac and no ketorolac groups as the use of these medications may affect the development of a hypertensive phase, irrespective of ketorolac usage. Considering that there was no statistically significant difference in the number of glaucoma medications prescribed at any time point postoperatively, this suggests the differences in the proportion of patients who experienced a hypertensive phase was more likely due to ketorolac usage rather than aqueous suppression in our sample of patients. We hypothesize that the anti-inflammatory effects of ketorolac may reduce the subconjunctival fibrosis around the Ahmed plate, thus reducing the likelihood of a hypertensive phase.

The frequency of topical corticosteroid use was significantly different between the ketorolac and no ketorolac groups at the postoperative 1 week and 2–4 week visits, although not at subsequent postoperative visits. It is possible that this difference in frequency of initial topical corticosteroid use could contribute to differences in subconjunctival fibrosis around the Ahmed plate. However, if that were the case in this study, one would expect that the no ketorolac group with its more frequent initial topical corticosteroid usage would potentially have less subconjunctival fibrosis around the plate and therefore lower postoperative IOP, which was not consistent with our findings.

There are several study limitations that need to be acknowledged. This study was conducted retrospectively, there were limited numbers of patients in the ketorolac group, and the follow-up was relatively short. However, our findings that patients receiving ketorolac had on average lower postoperative IOPs than no ketorolac patients at several time points may be clinically significant, although the study numbers may not be large enough to reach statistical significance except at the 6 month postoperative time point. Also, the ketorolac group included two Native American patients, while the no ketorolac group included five black patients. While there is no published study to our knowledge describing the outcomes of glaucoma drainage device implantation in Native American populations per se, Ishida et al did find that African-American race is a risk factor for Ahmed glaucoma drainage implant failure.[12] While their findings could possibly be explained by other confounding factors,[13] it is possible that the racial difference in our ketorolac versus no ketorolac groups could have influenced our results. If larger prospective studies are able to substantiate the findings from our study, postoperative use of ketorolac or other topical nonsteroidal anti-inflammatory medications may play a role in improving long-term postoperative IOP outcomes following AGI surgery.

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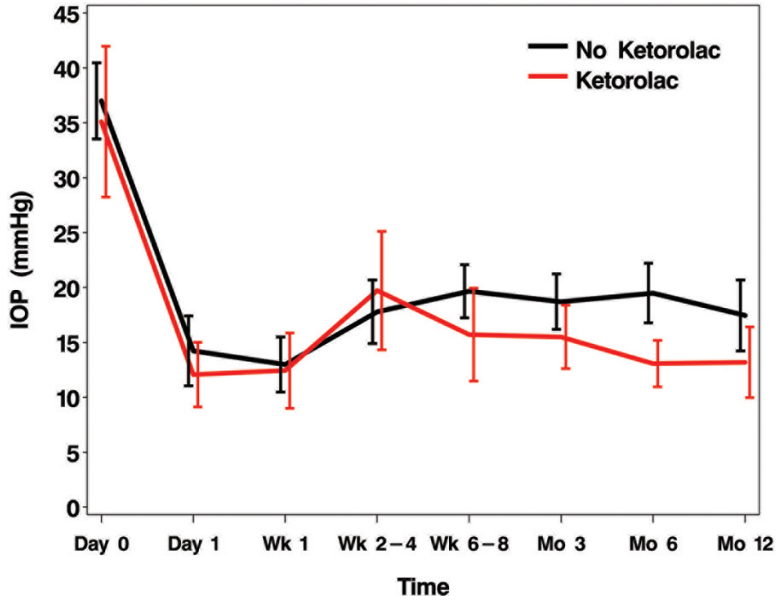

Figure 1.
Intraocular pressure over time by ketorolac use.

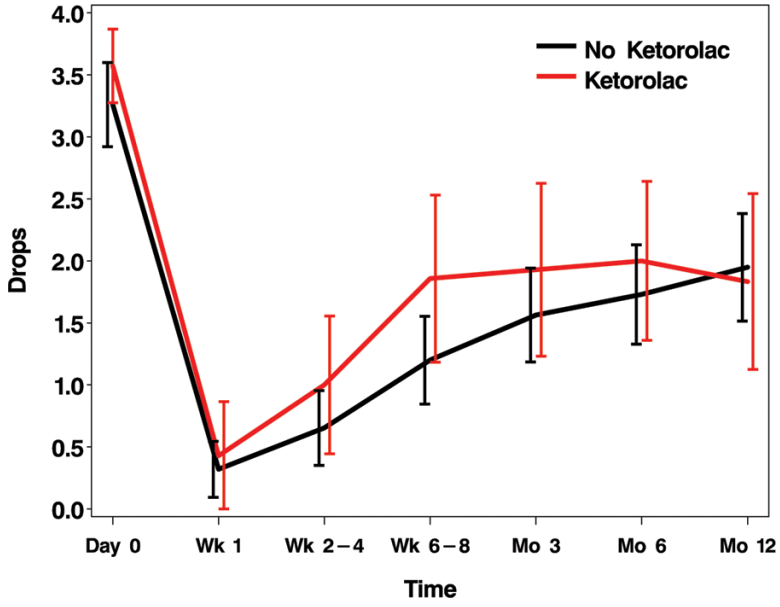

Figure 2.
Number of glaucoma medications over time by ketorolac use.

Table 1

Demographics of Study Population (N=64)

Demographic	Ketorolac group	No ketorolac group	p-value
N	14	50	
Mean Age	63	65	0.74
Gender			0.28
Female	5(36%)	26(52%)	
Male	9(64%)	24(48%)	
Eye			0.63
Right	9(64%)	27(54%)	
Left	5(36%)	23(46%)	
Race			0.05
White	12(86%)	44(88%)	
Black	0	5(10%)	
Native American	2(14%)	1(2%)	
Glaucoma Diagnosis			0.36
Neovascular	3(21%)	17(34%)	
Uveitic	5(36%)	9(18%)	
Primary open-angle	0	7(14%)	
Secondary open-angle *	3(21%)	11(22%)	
Combined mechanism	1(7%)	3(6%)	
Chronic angle closure	2(14%)	3(6%)	
Ahmed type			0.43
FP7	14 (100%)	41(82%)	
S2	0	9(18%)	
Ahmed insertion location			0.44
Anterior chamber	13 (93%)	41 (82%)	
Pars plana	1 (7%)	9 (18%)	
History of prior cyclodestruction	0	2 (4%)	1.00

* pseudoexfoliative or pigmentary