

# Reducing angiographic cystoid macular edema and blood–aqueous barrier disruption after small-incision phacoemulsification and foldable intraocular lens implantation

## Multicenter prospective randomized comparison of topical diclofenac 0.1% and betamethasone 0.1%

Sayaka Asano, MD, Kensaku Miyake, MD, Ichiro Ota, MD, Gentaro Sugita, MD, Wataru Kimura, MD, Yuji Sakka, MD, Nobuyuki Yabe, MD

**PURPOSE:** To compare the effectiveness of a topical nonsteroidal drug (diclofenac 0.1%) and a topical steroidal drug (betamethasone 0.1%) in preventing cystoid macular edema (CME) and blood–aqueous barrier (BAB) disruption after small-incision cataract surgery and foldable intraocular lens (IOL) implantation.

**SETTINGS:** Shohzankai Medical Foundation Miyake Eye Hospital, Tokyo, Japan.

**METHODS:** This multicenter interventional double-masked randomized study comprised 142 patients having phacoemulsification and foldable IOL implantation. Seventy-one patients were randomized to receive diclofenac eyedrops and 71, betamethasone eyedrops for 8 weeks postoperatively. The incidence and severity of CME were evaluated by fluorescein angiography. Blood–aqueous barrier disruption was determined by laser flare–cell photometry.

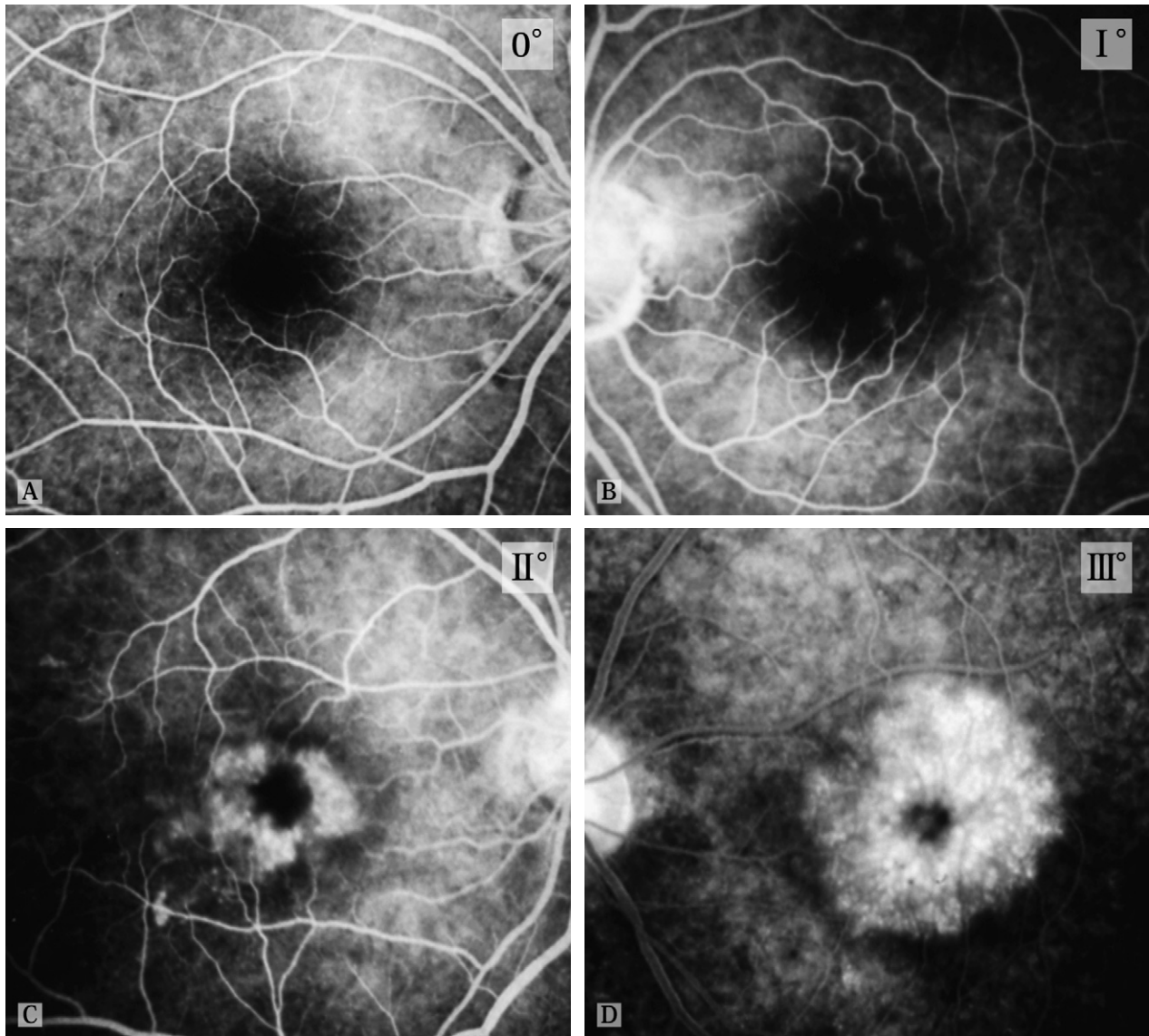
**RESULTS:** Of the patients, 63 were men and 79 were women. Five weeks after surgery, the incidence of fluorescein angiographic CME was lower in the diclofenac group (18.8%) than in the betamethasone group (58.0%) ( $P < .001$ ). At 1 and 2 weeks, the amount of anterior chamber flare was statistically significantly less in the diclofenac group than in the betamethasone group ( $P < .05$ ). At 8 weeks, intraocular pressure was statistically significantly higher in the betamethasone group ( $P = .0003$ ).

**CONCLUSIONS:** Diclofenac was more effective than betamethasone in preventing angiographic CME and BAB disruption after small-incision cataract surgery. Thus, nonsteroidal antiinflammatory agents should be considered for routine treatment of eyes having cataract surgery.

*J Cataract Refract Surg 2008; 34:57–63 © 2008 ASCRS and ESCRS*

The exact mechanism of aphakic or pseudophakic cystoid macular edema (CME) has not been determined. Proposed factors include hypotony,<sup>1</sup> inflammation,<sup>2,3</sup> photo damage,<sup>4</sup> and vitreous traction.<sup>2,5</sup> Much attention has been focused on prostaglandins (PGs), one of the inflammatory mediators synthesized by the uvea and lens epithelial cells (LECs) after cataract surgery.<sup>6–8</sup> One approach to preventing the negative effects of these mediators is to treat eyes with CME using nonsteroidal antiinflammatory drugs (NSAIDs) that inhibit PG synthesis.<sup>9–22</sup> Although

systematic reviews acknowledge there is convincing clinical evidence that NSAIDs are effective in preventing and treating CME, they also indicate that further studies are warranted as previous studies had shortcomings involving the design and the length of the observation period.<sup>23,24</sup> The rate of CME differs depending on the surgical technique used. There are few reports describing CME after small-incision phacoemulsification and foldable intraocular lens (IOL) implantation using current techniques and fewer studies comparing the therapeutic effects of steroids



**Figure 1.** Representative example of each grade of CME using the Miyake classification at the late phase of fluorescein angiography (ie, 15 minutes after intravenous injection of sodium fluorescein 10%). *A:* In grade 0, there is no sign of fluorescein leakage. *B:* In grade I, there is slight fluorescein leakage into the cystic space, but not enough to enclose the entire fovea centralis. *C:* In grade II, there is complete circular accumulation of the fluorescein in the cystic space, but the diameter of the accumulation is smaller than 2.0 mm. *D:* In grade III, the fluorescein leakage surrounds the fovea and is larger than 2.0 mm in diameter.

Accepted for publication August 25, 2007.

From the Shohzankai Medical Foundation Miyake Eye Hospital (Asano, Miyake, Ota) and Sugita Eye Hospital (Sugita), Nagoya; Kimura Eye and Internal Medicine (Kimura), Hiroshima; Sakka Eye Clinic (Sakka), Kitakyushu; and Oshima Eye Hospital (Yabe), Fukuoka, Japan.

No author has a financial or proprietary interest in any material or method mentioned.

Corresponding author: Kensaku Miyake, MD, Shohzankai Medical Foundation, Miyake Eye Hospital, 3-15-68, Ozone, Kita-ku, Nagoya, 462-0825, Japan. E-mail: [miyake@spice.or.jp](mailto:miyake@spice.or.jp).

with those of NSAIDs in preventing and treating CME.<sup>25</sup> Finally, studies reporting simultaneous evaluation of the incidence and severity of CME and its relationship to blood-aqueous barrier (BAB) disruption are scarce.<sup>7,26</sup>

We report the results in a prospective randomized double-masked multicenter trial comparing diclofenac, the most potent NSAID, and betamethasone in the prevention of BAB disruption and fluorescein angiographic CME resulting from small-incision phacoemulsification and foldable IOL implantation.

## PATIENTS AND METHODS

This study comprised 150 cataract patients who had phacoemulsification and posterior chamber IOL implantation between April 2004 and September 2005. Inclusion criteria were age 55 to 75 years of age, nuclear hardness of Emery-Little grade IV or less,<sup>27</sup> and surgery in 1 eye only. Exclusion criteria were acute infection or inflammation within 1 month after initiation of the study; allergy to NSAIDs, steroids, or fluorescein; history of eye trauma or intraocular disease other than cataract; pseudoexfoliation syndrome; uveitis; glaucoma; diabetes and related complications; kidney disease; asthma or chronic airway disease; uncontrolled hypertension; severe heart failure; myocardial infarction or cerebrovascular disorders; and intraoperative complications such as posterior capsule rupture, vitreous loss, retained lens nucleus, or lens fragments in the vitreous.

### Informed Consent

The study was conducted in accordance with the Declaration of Helsinki and received approval from the institutional review board at each site. All patients received a detailed explanation that included the study's purpose and methods, expected outcomes and risks, and availability of other therapies. Patients were also told that their refusal to take part in the study would not compromise their treatment and that if they decided to participate, they were free to withdraw from the study at any time. All patients choosing to participate in the study provided informed consent.

### Study Design

The study was a multicenter randomized double-masked trial of diclofenac sodium 0.1% versus betamethasone sodium 0.1%. The test drugs were assigned to patients at random after the controller validated that the assigned therapy was indistinguishable from the alternative therapy. The controller kept the assignment code until completion of the study. The controller created an emergency code, which was given to the principal investigator in an envelope. The investigator could open the envelope if severe adverse effects developed. The test drugs were administered to each patient 3 hours, 2 hours, 1 hour, and 30 minutes before surgery and 3 times a day for 8 weeks after surgery. Concomitant mydriatic and antibiotic agents were permitted.

### Surgical Technique

One surgeon from each institute (I.O., G.S., W.K., Y.S., N.Y.) performed phacoemulsification with implantation of an acrylic foldable IOL (AcrySof MA60BM, Alcon) in the capsular bag.

### Clinical Observation and Assessment

At the initial assessment, the patient's background, surgical history, visual acuity, intraocular pressure (IOP), and amount of anterior chamber flare and cells measured by laser-cell flare photometry (FC-1000, Kowa Co., Ltd.) were recorded. Approximately 30 minutes after phenylephrine 0.5% was administered, the presence of CME, determined by fluorescein fundus angiography, was recorded. Fluorescein angiographic CME was evaluated 5 weeks after surgery using the Miyake classification.<sup>6</sup> This classification has 4 grades based on the results of the angiogram. Figure 1

**Table 1.** Patient demographics.

Characteristic	Diclofenac Group	Betamethasone Group	P Value
Mean age (y) ± SD	66.07 ± 5.51	66.23 ± 5.55	.868*
Eyes (n)			.866 <sup>†</sup>
Male	31	32	
Female	40	39	

\*Student *t* test  
<sup>†</sup>Chi-square test

shows a representative example of the 4 grades and describes each grade. After surgery, visual acuity, IOP, and flare were evaluated at 1 and 3 days as well as 1, 2, 5, and 8 weeks.

### Statistical Analysis

The patients' characteristics were analyzed using the chi-square and Student *t* tests. Surgical procedure, visual acuity, IOP, and flare were analyzed using the Welch *t* test. The incidence of CME was analyzed using the Mann-Whitney *U* test. A *P* value less than 0.05 was considered statistically significant.

## RESULTS

Of the 150 eyes initially included in this study, 75 were assigned to the diclofenac group and 75 to the betamethasone group. Four patients in each group dropped out of the study: 1 in each group due to complications; 3 in the diclofenac group and 2 in the betamethasone group due to a discontinuation proposal (there were patients who withdrew their consent during the course of this study); 1 in the betamethasone group for not returning to the hospital 2 weeks after surgery. Seventy-one eyes in each group completed the study.

**Table 2.** Surgical parameters.

Parameter	Mean ± SD		P Value*
	Diclofenac Group	Betamethasone Group	
Duration of surgery (min)	10.81 ± 3.60	10.30 ± 3.57	.394
Ultrasound time (s)	38.0 ± 23.67	42.52 ± 21.49	.236
Irrigating solution (mL)	82.54 ± 50.21	80.92 ± 45.78	.841
Hardness of crystalline lens <sup>†</sup>	2.27 ± 0.76	2.34 ± 0.70	.511

\*Welch *t* test  
<sup>†</sup>Emery-Little grade<sup>27</sup>

**Table 3.** Postoperative visual acuity (logMAR) over time.

Group	Preoperative	Postoperative					
		1 Day	3 Days	1 Week	2 Weeks	5 Weeks	8 Weeks
<b>Diclofenac</b>							
Mean acuity ± SD	0.384 ± 0.340	-0.004 ± 0.134	-0.046 ± 0.094	-0.068 ± 0.087	-0.064 ± 0.082	-0.068 ± 0.086	-0.071 ± 0.080
Eyes (n)	65	64	66	64	62	62	58
<b>Betamethasone</b>							
Mean acuity ± SD	0.457 ± 0.413	-0.006 ± 0.118	-0.026 ± 0.119	-0.051 ± 0.088	-0.083 ± 0.083	-0.050 ± 0.098	-0.066 ± 0.078
Eyes (n)	67	59	59	59	57	56	52
<i>P</i> value*	.263	.911	.304	.292	.318	.285	.753

\*Welch t test

Table 1 shows the patients' demographics; there was no statistically significant difference in age or sex between the 2 groups. Table 2 shows the surgical parameters; there was no statistically significant difference between the 2 groups in duration of surgery, phacoemulsification time, amount of irrigating solution used, and hardness of the crystalline lens. Table 3 shows the postoperative visual acuity; there was no statistically significant difference between groups at any time point.

Table 4 shows the course of IOP over time. In both groups, the IOP was relatively stable for up to 5 weeks. However, in the betamethasone group, the IOP gradually rose and became significantly higher than the IOP in the diclofenac group after 8 weeks ( $P = .0003$ ).

Table 5 shows the incidence and severity of CME 5 weeks after surgery. Cystoid macular edema was detected in 13 (18.8%) of 69 eyes in the diclofenac group and 40 (58.0%) of 69 eyes in the betamethasone group. The difference between groups was statistically significant ( $P = 1.638 \times 10^{-6}$ ).

Table 6 shows the amount of postoperative flare. At 1 and 2 weeks, the amount of flare was significantly

lower in the diclofenac group than in the betamethasone group ( $P = .048$  and  $P = .010$ , respectively).

## DISCUSSION

This double-masked trial was performed at 5 centers to compare the efficacy of diclofenac and betamethasone in reducing BAB disruption and the incidence of CME in eyes having small-incision phacoemulsification and foldable IOL implantation. The results show that diclofenac was more effective than betamethasone as the incidence of CME and the amount of anterior chamber flare were less in the diclofenac group.

Although the efficacy of NSAIDs in minimizing complications after ocular surgery has been described,<sup>6-22,26,28,29</sup> their effectiveness has not been adequately compared with that of betamethasone.<sup>23</sup> Topical indomethacin was the first NSAID confirmed to block miosis during aspiration of soft cataracts<sup>29</sup> and to prevent CME after intracapsular cataract extraction.<sup>6</sup> We report that diclofenac is more effective than betamethasone.

**Table 4.** Intraocular pressure over time.

Group	Preoperative	Postoperative					
		1 Day	3 Days	1 Week	2 Weeks	5 Weeks	8 Weeks
<b>Diclofenac</b>							
Mean IOP ± SD (mm Hg)	13.89 ± 3.13	14.34 ± 4.17	11.97 ± 3.51	12.59 ± 4.25	11.93 ± 3.49	11.79 ± 3.06	11.39 ± 2.47
Eyes (n)	71	71	71	71	71	71	65
<b>Betamethasone</b>							
Mean IOP ± SD (mm Hg)	13.85 ± 2.91	14.23 ± 4.10	11.20 ± 2.84	12.41 ± 3.09	12.11 ± 3.18	12.55 ± 2.99	13.27 ± 3.18
Eyes (n)	71	71	71	71	71	71	63
<i>P</i> value*	.934	.871	.151	.471	.744	.136	.0003

IOP = intraocular pressure

\*Welch t test

**Table 5.** Frequency and severity of CME according to Miyake classification using fluorescein fundus angiography.

Group	CME Grade				Incidence (%)	P Value*
	0	I	II	III		
Diclofenac	56	9	3	1	18.8	$1.638 \times 10^{-6}$
Betamethasone	29	20	17	3	58.0	

\*Mann-Whitney U test

In this article, we describe our working hypothesis of the pathogenesis of CME.<sup>6,26</sup> Prostaglandins and other inflammatory mediators are mainly synthesized by the iris and LECs. Prostaglandins or a disrupted BAB can lead to accumulation of other mediators in the aqueous humor.<sup>30-33</sup> It is believed these accumulations diminish the active transport mechanism of PGs from the ciliary body.<sup>34</sup> Other factors in BAB disruption include systemic vasculopathy resulting from aging or diabetes and predisposition to pathological conditions such as glaucoma or uveitis. The aqueous humor containing these mediators also diffuses into the vitreous body, increasing BAB permeability. Cystoid macular edema is thought to develop in association with these changes. Furthermore, weakened retinal vessels and loss of an intact retina due to conditions such as aging, hypertension, and sustained diabetes predispose the eye to CME.

According to this hypothesis, BAB disruption is the dominating factor in the development of CME. In 1978, Miyake<sup>7</sup> showed that BAB disruption is involved in the development of CME after cataract surgery. However, the supporting evidence for this hypothesis was limited at that time.<sup>26,28</sup>

The current study provides additional support as laser flare-cell photometry was used in all patients to simultaneously assess the BAB function and the

incidence of CME. Disruption of the BAB was more severe in patients with CME than in those without it, and the severity was associated with a prolonged duration of CME after cataract surgery. The data confirm that BAB disruption plays a major role in concomitant CME, a finding that has clinical relevance. In other words, it is now apparent that in patients with conditions that may lead to BAB disruption (eg, uveitis and diabetes), it is important to use therapeutic agents that might lower the incidence and lessen the severity of CME. That diclofenac was more effective than betamethasone in reducing the incidence of CME suggests that suppressing the synthesis of causative agents is of greater value than reducing swelling and inflammation resulting from exposure to PG and its mediators. This agrees with the concept that minimizing loss of the BAB and blood-retinal barrier functions is important in reducing the incidence of surgically induced CME.

The iris and the uvea are thought to be the main sites of synthesis of inflammatory mediators such as PG.<sup>30,31</sup> In addition, recent reports<sup>32,33</sup> state such synthesis also occurs after LEC injury and during the wound-healing process. Miyake et al.<sup>32</sup> implanted IOLs in baboon eyes and found that the amount of prostaglandin E<sup>2</sup> (PGE<sup>2</sup>) in the aqueous humor 1 day and 8 days after surgery increased more in eyes with IOLs implanted in the capsular bag than in unoperated eyes. Furthermore, Nishi et al.<sup>33</sup> cultured LECS and found that the amount of PGE<sup>2</sup> and interleukin 1 increased in the culture medium and that the cells underwent metaplasia. These data suggest that the amount of inflammatory mediators in the aqueous humor increases a few days after cataract surgery, which may explain the so-called flare spikes 1 week postoperatively in cases in which fluorometholone, a weak corticosteroid, is the only agent used.<sup>26</sup> In that same study, however, another strong steroid, betamethasone, was also unable to block the mediators. In

**Table 6.** Amount of flare over time.

Group	Preoperative	Postoperative					
		1 Day	3 Days	1 Week	2 Weeks	5 Weeks	8 Weeks
Diclofenac							
Mean flare ± SD (photons/millisecond)	7.37 ± 4.67	14.71 ± 10.35	13.19 ± 9.18	12.10 ± 7.42	11.67 ± 6.99	9.45 ± 6.75	8.45 ± 5.99
Eyes (n)	71	70	71	71	71	70	65
Betamethasone							
Mean flare ± SD (photons/millisecond)	7.38 ± 5.19	12.92 ± 6.84	15.27 ± 13.13	15.65 ± 12.99	16.02 ± 12.14	9.45 ± 5.73	7.98 ± 3.78
Eyes (n)	70	70	71	71	71	70	62
P value*	.984	.230	.275	.048	.010	.989	.589

\*Welch t test

contrast, NSAIDs prevented flare spikes after cataract surgery,<sup>26</sup> confirming that an ophthalmic steroid application is of less value in preventing inflammation after cataract surgery.

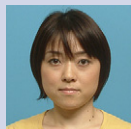
Cystoid macular edema after cataract surgery with IOL implantation has been categorized using several terms including *acute*, *angiographic*, and *clinical*.<sup>23,28</sup> In the present study, we used the most sensitive classification to detect and diagnose CME during its most intense occurrence.<sup>6</sup> Thus, we specifically discussed acute or angiographic CME in this study, which is why the incidence of CME was higher than that in previous studies.<sup>19-21,23,35</sup> Acute or angiographic CME resolves spontaneously approximately 13 weeks after surgery.<sup>36</sup>

In conclusion, diclofenac was more effective than betamethasone in preventing CME and BAB disruption in pseudophakic eyes that had modern small-incision cataract and IOL surgery. We recommend that NSAIDs be considered for routine treatment in eyes having cataract surgery.

## REFERENCES

- Dellaporta A. Fundus changes in postoperative hypotony. *Am J Ophthalmol* 1955; 40:781-785
- Irvine SR. A newly defined vitreous syndrome following cataract surgery; interpreted according to recent concepts of the structure of the vitreous; the Seventh Francis I. Proctor Lecture. *Am J Ophthalmol* 1953; 36:599-619
- Henry MM, Henry LM, Henry LM. A possible cause of chronic cystic maculopathy. *Ann Ophthalmol* 1977; 9:455-457
- Gass JDM, Norton EWD. Cystoid macular edema and papilledema following cataract extraction: a fluorescein fundoscopic and angiographic study. *Arch Ophthalmol* 1966; 76:646-661
- Tolentino FI, Schepens CL. Edema of posterior pole after cataract extraction; a biomicroscopic study. *Arch Ophthalmol* 1965; 74:781-786
- Miyake K. Prevention of cystoid macular edema after lens extraction by topical indomethacin (I). A preliminary report. *Albrecht von Graefes Arch Klin Exp Ophthalmol* 1977; 203:81-88
- Miyake K. Prevention of cystoid macular edema after lens extraction by topical indomethacin. II. A control study in bilateral extractions. *Jpn J Ophthalmol* 1978; 22:80-94
- Miyake K, Sugiyama S, Norimatsu I, Ozawa T. Prevention of cystoid macular edema after lens extraction by topical indomethacin (III). Radioimmunoassay measurement of prostaglandins in the aqueous during and after lens extraction procedures. *Albrecht von Graefes Arch Klin Exp Ophthalmol* 1978; 209:83-88
- Miyake K, Sakamura S, Miura H. Long-term follow-up study on prevention of aphakic cystoid macular oedema by topical indomethacin. *Br J Ophthalmol* 1980; 64:324-328
- Fechner PU. Die prophylaxe des zystoiden Makulaödems mit Indometacin-Augentropfen. [Prevention of cystoid macula edema using indomethacin eyedrops.] *Klin Monatsbl Augenheilkd* 1982; 180:169-172
- Yannuzzi LA, Landau AN, Turtz AI. Incidence of aphakic cystoid macular edema with the use of topical indomethacin. *Ophthalmology* 1981; 88:947-954; discussion by ML Klein, 953-954
- Kraff MC, Sanders DR, Jampol LM, et al. Prophylaxis of pseudophakic cystoid macular edema with topical indomethacin. *Ophthalmology* 1982; 89:885-890
- Tanabe N, Sagae Y, Hara K. [Effect of topical indomethacin treatment for cystoid macular edema after lens extraction]. [Japanese]. *Folia Ophthalmol Jpn* 1983; 34:178-182
- Hollwich F, Jacobi K, Kuchle H-J, et al. Zur prophylaxe des zystoiden makulaödems mit Indometacin-Augentropfen. [Prevention of cystoid macular edema with indomethacin eye drops.] *Klin Monatsbl Augenheilkd* 1983; 183:477-478
- Urner-Bloch U. Prävention des zystoiden makulaödems nach Kataraktextraktion durch locale Indomethacin Applikation. [Prevention of aphakic cystoid macular edema by topical indomethacin.] *Klin Monatsbl Augenheilkd* 1983; 183:479-484
- Miyake K, Miyake Y, Maekubo K, et al. Incidence of cystoid macular edema after retinal detachment surgery and the use of topical indomethacin. *Am J Ophthalmol* 1983; 95:451-456
- U.S. Food and Drug Administration. Summary basis of approval for Profenal (Alcon's Suprofen) subsequent to new drug application 19-3387. Washington, DC, Department of Health and Human Services, 1989
- Quentin C-D, Behrens-Baumann W, Gaus W. Prophylaxe des zystoiden makulaödems mit Diclofenac-Augentropfen bei i.c. Kataraktextraktion mit Choyce-Mark-IX-Vorderkammerlinse. [Prophylactic treatment of cystoid macular oedema with diclofenac eyedrops in intracapsular cataract extraction with the Choyce Mark IX anterior chamber lens.] *Fortschr Ophthalmol* 1989; 86:546-549
- Flach AJ, Stegman RC, Graham J, Kruger LP. Prophylaxis of aphakic cystoid macular edema without corticosteroids; a paired-comparison, placebo-controlled double-masked study. *Ophthalmology* 1990; 97:1253-1258
- Solomon LD. Efficacy of topical flurbiprofen and indomethacin in preventing pseudophakic cystoid macular edema; the Flurbiprofen-CME Study Group I. *J Cataract Refract Surg* 1995; 21:73-81
- Ginsburg AP, Cheetham JK, DeGryse RE, Abelson M. Effects of flurbiprofen and indomethacin on acute cystoid macular edema after cataract surgery: functional vision and contrast sensitivity. *J Cataract Refract Surg* 1995; 21:82-92
- Otuka M, Yamane I, Sakka Y. [Comparison of postoperative inflammation produced by anti-PGs(KTL), steroids, and antibiotics after cataract surgery]. [Japanese] *IOL & RS* 1994; 8:71-75
- Rossetti L, Chaudhuri J, Dickersin K. Medical prophylaxis and treatment of cystoid macular edema after cataract surgery; the results of a meta-analysis. *Ophthalmology* 1998; 105:397-405
- Sivaprasad S, Bunce C, Wormald R. Non-steroidal anti-inflammatory agents for cystoid macular oedema following cataract surgery: a systematic review. *Br J Ophthalmol* 2005; 89:1420-1422
- O'Brien TP. Emerging guidelines for use of NSAID therapy to optimize cataract surgery patient care. *Curr Res Med Opin* 2005; 21:1131-1137; erratum, 1431-1432
- Miyake K, Masuda K, Shirato S, et al. Comparison of diclofenac and fluorometholone in preventing cystoid macular edema after small incision cataract surgery: a multicentered prospective trial. *Jpn J Ophthalmol* 2000; 44:58-67
- Emery JM, McIntyre DJ. Patient selection in extracapsular cataract surgery. In: Emery JM, McIntyre DJ, eds, *Extracapsular Cataract Surgery*. St Louis, MO, Mosby, 1983; 95-100
- Miyake K. Indomethacin in the treatment of postoperative cystoid macular edema. *Surv Ophthalmol* 1984; 28:554-568

29. Sawa M, Masuda K. Topical indomethacin in soft cataract aspiration. *Jpn J Ophthalmol* 1976; 20:514–519
30. Ambache N, Kavanagh L, Whiting J. Effect of mechanical stimulation on rabbit eyes: release of active substance in anterior chamber perfusates. *J Physiol (Lond)* 1965; 176:378–408
31. Eakins KN. Prostaglandins and prostaglandin synthetase inhibitors. Actions in ocular disease. In: Robinson HJ, Vane Jr., eds, *Prostaglandin Synthetase Inhibitors: their Effects on Physiological Functions and Pathological States*; sponsored jointly by the Royal Society of Medicine Foundation, Inc. of New York and the Royal Society of Medicine of London, held November 28-30, 1973 at the Rockefeller University, New York City New York. New York, NY, Raven Press, 1974; 343–352
32. Miyake K, Mibu H, Horiguchi M, Shirasawa E. Inflammatory mediators in postoperative aphakic and pseudophakic baboon eyes. *Arch Ophthalmol* 1990; 108:1764–1767
33. Nishi O, Nishi K, Imanishi M. Synthesis of interleukin-1 and prostaglandin E<sup>2</sup> by lens epithelial cells of human cataracts. *Br J Ophthalmol* 1992; 76:338–341
34. Bito LZ, Salvador EV. Intraocular fluid dynamics. III. The site and mechanism of prostaglandin transfer across the blood intraocular fluid barriers. *Exp Eye Res* 1972; 14:233–241
35. Ursell PG, Spalton DJ, Whitcup SM, Nussenblatt RB. Cystoid macular edema after phacoemulsification: relationship to blood-aqueous barrier damage and visual acuity. *J Cataract Refract Surg* 1999; 25:1492–1497
36. Rho DS. Treatment of acute pseudophakic cystoid macular edema: diclofenac versus ketorolac. *J Cataract Refract Surg* 2003; 29:2378–2384



First author:

Sayaka Asano, MD

*Shohzankai Medical Foundation, Miyake  
Eye Hospital, Nagoya, Japan*