European Journal of Ophthalmology / Vol. 15 no. 1, 2005 / pp. 158-161

SHORT COMMUNICATION

Cystoid macular edema associated with latanoprost after uncomplicated cataract surgery

Ö. ALTINTAŞ , N. YÜKSEL, V.L. KARABAŞ , G. DEMİRCİ

Department of Ophthalmology, Medical Faculty, Kocaeli University, Kocaeli - Turkey

PURPOSE. *To report clinically symptomatic and angiographically documented cystoid macular edema (CME) associated with the use of latanoprost in two pseudophakic eyes after uncomplicated cataract surgery.*
METHODS. *Retrospective review of two patients who had history of latanoprost use and uncomplicated cataract surgery and described blurred vision in the first postoperative month.*
RESULTS. *Ocular examination revealed CME, which was confirmed by fluorescein angiography. The visual acuities of patients improved and the CME was angiographically resolved after discontinuation of latanoprost and the initiation of nonsteroidal anti-inflammatory eyedrops and oral acetazolamide.*
CONCLUSIONS. *Until a causal relationship between CME and latanoprost is proved or disproved, caution in its use in pseudophakic patients would be prudent. (Eur J Ophthalmol 2005; 15: 158-61)*

KEY WORDS. *Latanoprost, Cystoid macular edema, Uncomplicated, Pseudophakia*

Accepted: July 12, 2004

INTRODUCTION

Latanoprost, a prostaglandin analogue that lowers intraocular pressure (IOP), is one of the most commonly prescribed branded glaucoma medications. Although the major mechanism of latanoprost in lowering IOP is thought to be an increase in uveascleral outflow, the drug's physiologic mechanism and adverse effects are not fully understood (1-5). Recently, in several reports, cystoid macular edema (CME) has been reported in association with the use of latanoprost, especially in high-risk eyes, but the causative relationship is debated (6-13). Here we report CME associated with the use of latanoprost in two pseudophakic eyes after uncomplicated extracapsular cataract extraction with phacoemulsification and posterior chamber intraocular lens implantation (PHACO-PC IOL).

Case 1

An otherwise healthy 58-year-old man with pseudoexfoliative glaucoma in the left eye (OS) had been treated with latanoprost once a day and combination dorzolamide 2 %–timolol 0.5% twice a day with good control of IOP for 3 years. He underwent uncomplicated planned PHACO-PC IOL in his right eye in November 2001 and OS in March 2002. The clear corneal incision was 2.8 mm in size on the upper quadrant of cornea. Capsulorrhexis was intact. A silicone foldable IOL was implanted in the bag. A postoperative anti-inflammatory drug regimen was prescribed that included prednisolone acetate 1% 6 times a day and ciprofloxacin 4 times a day in the first week. The ciprofloxacin was discontinued at 1 week and prednisolone acetate 1% 4 times a day was discontinued at 5 weeks. Ten days postoperatively, using la-

1120-6721/158-04$15.00/0

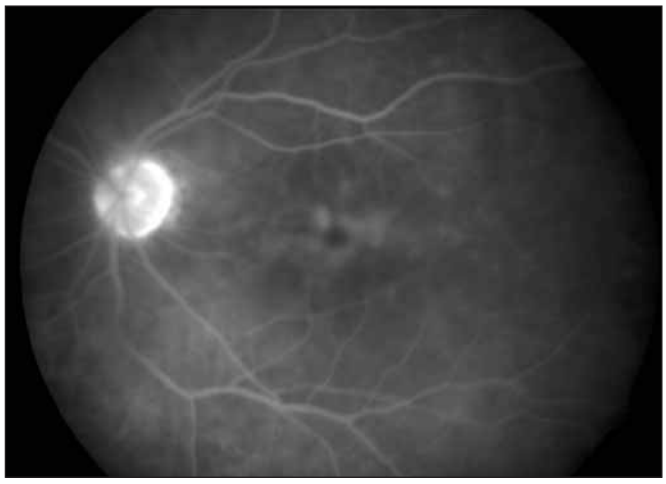

Fig. 1 - *Fluorescein angiogram shows cystoid macular edema in Case 1 on latanoprost therapy.*

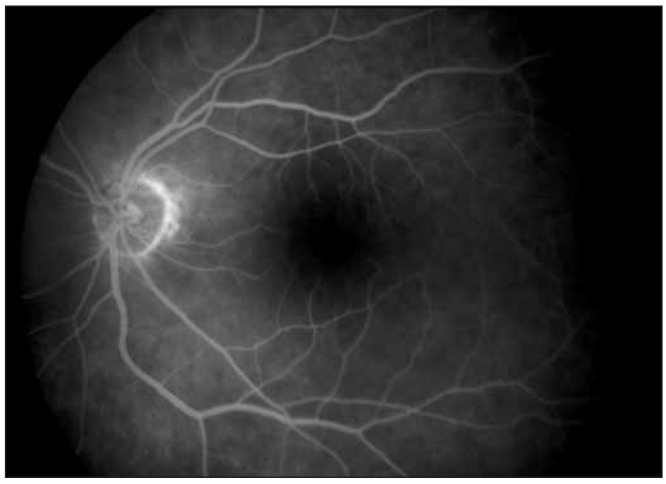

Fig. 2 - *Fluorescein angiogram of Case 1 after treatment of cystoid macular edema and discontinuation of latanoprost.*

tanoprost once a day and combination dorzolamide 2 %–timolol 0.5% twice a day OS, he spontaneously noted a reduction in vision OS. He was found to have best-corrected visual acuity of 0.4 in April 2002. Yellowish pigmentary macular changes in a patelloid distribution were noted, and fundus fluorescein angiogram (FFA) confirmed vascular macular leakage (Fig. 1). Latanoprost was discontinued, and he was put on ketorolac 0.5% OS four times daily and oral acetazolamide 125 mg four times daily besides the antiglaucomatous medication with combination dorzolamide 2%–timolol 0.5% twice a day OS only. One month later, the best-corrected visual acuity had improved to 1.0. Although the macular patelloid pattern was still present, FFA showed the CME to be markedly improved. Three months later, in his last control, he had a visual acuity of 1.0 and IOP of 16 mm Hg with combination dorzolamide 2%–timolol 0.5% twice a day OS only. The CME showed improvement on FFA and patelloid macular pattern was undetectable (Fig. 2).

Case 2

An otherwise healthy 73-year-old woman who was referred for treatment of cataract OS had a history of latanoprost treatment for 1 month. Latanoprost was discontinued 1 day prior to cataract surgery. The corneal incision size was 2.8 mm. Capsulorrhexis was intact. We could not complete the phacoemulsification due to vacuum problem in the machine. Then corneal incision was widened to 7 mm and remaining nucleus particles were extracted with extracapsular extraction. The capsulorrhexis and posterior capsule remained intact after these procedures. The previously prepared foldable silicone IOL was implanted in the bag. A postoperative anti-inflammatory drug regimen was prescribed that included prednisolone acetate 1% 6 times a day and ciprofloxacin 4 times a day in the first week. The ciprofloxacin was discontinued at 1 week and prednisolone acetate 1% 4 times a day was discontinued at 5 weeks. At the first postoperative month, the patient reported decreased visual acuity OS. An examination showed that the best-corrected acuity was 0.1 and IOP was 10 mm Hg OS. Fundus examination revealed distinct yellowish patelloid macular changes. FFA was obtained the same day and demonstrated vascular leakage in that eye (Fig. 3). The patient was told to begin ketorolac 0.5% four times daily and oral acetazolamide 125 mg four times daily. One month later, the best-corrected acuity was 0.4 and IOP was 16 mmHg . The patelloid macular pattern was still present. At the last visit at the postoperative fifth month, her corrected acuity was 0.7 and IOP was 10 mm Hg. CME showed improvement on FFA (Fig. 4) and patelloid macular pattern was undetectable.

DISCUSSION

CME has been reported in eyes described in prior publications in association with the use of latanoprost and widely accepted risk factors for the oc-

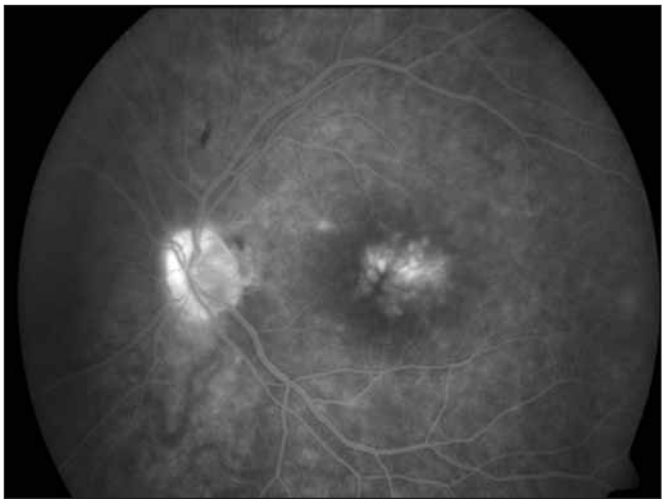

Fig. 3 - *Fluorescein angiogram shows cystoid macular edema in Case 2.*

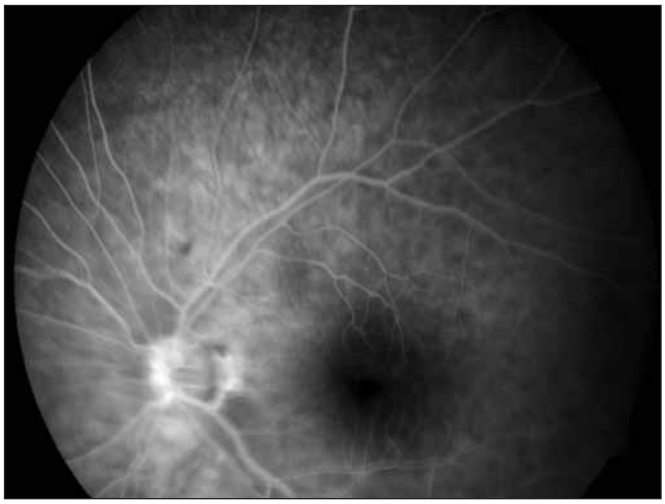

Fig. 4 - *Fluorescein angiogram of Case 2 after treatment of cystoid macular edema.*

currence of CME (13-17). Recently, CME was identified in 4 (3%) cases using latanoprost in a retrospective review of a cohort of 145 patients after uneventful PHACO IOL. The authors recommended discontinuing latanoprost before surgery since none of the patients who were prophylactically taken off the latanoprost before surgery developed postoperative CME in this cohort (18). Miyake et al encountered an increased incidence of angiographic CME in eyes receiving latanoprost shortly after cataract and IOL surgery. They concluded that latanoprost itself is probably not the major factor related to angiographic CME formation, but its instillation affects the wound healing process of lens epithelial cells, resulting in biosynthesis of prostaglandins and other mediators that eventually lead to angiographic CME. They also suggested that the diminished active transport of prostaglandins in pseudophakics receiving latanoprost plays a small role in inducing blood–aqueous barrier disruption especially when there is a vitreous prolapse and the active transport mechanism is completely lost (5). Also, Rowe et al reported a pseudophakic eye that disclosed angiographic CME at an early postoperative stage and recurrent angiographic CME a year after topical latanoprost application (6). Watanabe et al also reported a case in which latanoprost use induced CME in late postoperative pseudophakia and suggested that blood–ocular barrier remains fragile to latanoprost application even 5 years after surgery (16).

Clinically, the characteristic drugs that lead to CME are antiglaucoma eyedrops such as timolol (19), epinephrine (20, 21), and latanoprost (5, 9-11). A recent clinical study by Miyake et al suggested that the main cause of CME induced by these eyedrops was not the active agent of the eyedrops, but rather added preservative (19). The preservative stimulates lens epithelial and other cells during the postoperative wound healing process, and enhances the synthesis of prostaglandins and cytokines, causing increases in the disruption of the blood–aqueous and blood–retinal barriers, and the incidence of CME (22). The cases in the literature with surgical complications had consistently used several ophthalmic solutions containing benzalkonium chloride before the initiation of latanoprost ophthalmic solution (12, 14-16). Simultaneous occurrence of CME with latanoprost initiation and disappearance after discontinuation of this agent cannot be disregarded. Therefore, it is unlikely that it was the benzalkonium chloride that caused the CME. Our first case was still using the combination dorzolamide 2%–timolol 0.5% twice a day after CME treatment with good control of IOP and did not experience decrease in visual acuity again. It is probable that the latanoprost use might have caused CME, even though a causal relationship cannot be established in the absence of rechallenging with latanoprost. Only our first case had pseudoexfoliative glaucoma.

The blood–aqueous barrier is disturbed in pseudoexfoliation (23). However, there is no reported association between pseudoexfoliation and CME in the prior literature, and pseudoexfoliation may contribute to development of CME in pseudophakic patients us-

ing latanoprost. Until definitive, well-controlled studies are done proving or disproving the association between latanoprost or preservative agent and CME, it would be prudent to exercise caution in the use of latanoprost not only in high-risk pseudophakic eyes.

Reprint requests to:
Özgül Altintaş, MD
Yavuz Sultan mah., Rıhtım cad.
Sahil Konak., M blk
Kat:3, D:12, 60 evler
41900 Derince, Kocaeli, Turkey
ozgulaltintas@yahoo.com

REFERENCES

1. Lindsey JD, Kashiwagi K, Kashiwagi F, Weinreb RN. Prostaglandin action on ciliary smooth muscle extracellular matrix metabolism: implications for uveascleral outflow. Surv Ophthalmol 1997; 41(Suppl): S53-9.
2. Toris CB, Camras CB, Yablonski ME. Effects of PhXA41, a new prostaglandin F2a analog, on aqueous humor dynamics in human eyes. Ophthalmology 1993; 100: 1297-304.
3. Nilsson SFE, Samuelsson M, Bill A, Stjernschantz J. Increased uveascleral outflow as a possible mechanism of ocular hypertension caused by prostaglandin F2a-1-isopropylester in the cynomolgus monkey. Exp Eye Res 1989; 48: 707-16.
4. Gabelt BT, Kaufman PL. Prostaglandin F2a increase uveascleral outflow in the cynomolgus monkey. Exp Eye Res 1989; 49: 389-402.
5. Miyake K, Ota I, Maekubo K, Ichihashi S, Miyake S. Latanoprost accelerates disruption of the blood-aqueous barrier and the incidence of angiographic cystoid macular edema in early postoperative pseudophakias. Arch Ophthalmol 1999; 117: 34-40.
6. Rowe JA, Hattenhauer MG, Herman DC. Adverse side effects associated with latanoprost. Am J Ophthalmol 1997; 124: 683-5.
7. Warmar RE, Bullock JD, Ballal D. Cystoid macular edema and anterior uveitis associated with latanoprost use; experience and incidence in a retrospective review of 94 patients. Ophthalmology 1998; 105: 263-8.
8. Avakian A, Anderson Renier S, Butler PJ. Adverse effects of latanoprost on patients with medically resistant glaucoma. Arch Ophthalmol 1998; 116: 679-80.
9. Heier JS, Steinert RF, Frederick AR Jr. Cystoid macular edema associated with latanoprost use. Arch Ophthalmol 1998; 116: 680-2.
10. Callanan D, Fellman RL, Savage JA. Latanoprost associated cystoid macular edema. Am J Ophthalmol 1998; 126: 134-5.
11. Ayyala RS, Cruz DA, Margo CE, et al. Cystoid macular edema associated with latanoprost in aphakic and pseudophakic eyes. Am J Ophthalmol 1998; 126: 602-4.
12. Moroi SE, Gottfredsdottir MS, Schteingart MT, et al. Cystoid macular edema associated with latanoprost therapy in a case series of patients with glaucoma and ocular hypertension. Ophthalmology 1999; 106: 1024-9.
13. Schumer RA, Camras CB, Mandahl AK. Latanoprost and cystoid macular edema: is there a causal relation? Curr Opin Ophthalmol 2000; 11: 94-100.
14. Wand M, Gaudio A, Shields B. Latanoprost and cystoid macular edema in high-risk aphakic or pseudophakic eyes. J Cataract Refract Surg 2001; 27: 1397-401.
15. Tokunaga T, Kashiwagi K, Saito J, et al. A case of cystoid macular edema associated with latanoprost ophthalmic solution. Jpn J Ophthalmol 2002; 46: 656-9.
16. Watanabe K, Hayasaka S, Hayasaka Y, Nagaki Y, Watanabe K. Cystoid macular edema associated with latanoprost use in a pseudophakic eye with a history of surgical complications. Jpn J Ophthalmol 2003; 47: 110-2.
17. Jäger M, Jonas JB. Cystoid macular edema associated with latanoprost therapy in a pseudophakic vitrectomized patient after removal of silicone oil endotamponade. Eur J Ophthalmol 2003; 13: 221-3.
18. Yeh PC, Ramanathan S. Latanoprost and clinically significant cystoid macular edema after uneventful phacoemulsification with intraocular lens implantation. J Cataract Refract Surg 2002; 28: 1814-8.
19. Miyake K, Ota I, Ibaraki N, et al. Enhanced disruption of the blood-aqueous barrier and the incidence of angiographic cystoid macular edema by topical timolol and its preservative in early postoperative pseudophakia. Arch Ophthalmol 2001; 119: 387-94.
20. Kolker AE, Becker B. Epinephrine maculopathy. Arch Ophthalmol 1968; 79: 552-62.
21. Michels RG, Maumenee AE. Cystoid macular edema associated with topically applied epinephrine in aphakic eyes. Am J Ophthalmol 1975; 80: 379-88.
22. Miyake K, Nobuhiro I. Prostaglandins and cystoid macular edema. Surv Ophthalmol 2002; 47 (Suppl): S203-18.
23. Küchle M, Nguyen N, Hannappel E. The blood-aqueous barrier in eyes with pseudoexfoliation syndrome. Ophthalmic Res 1995; 27 (Suppl): S136-42.