

The Resumption of Lactation Following Trabeculectomy

BY SHAKEEL SHAREEF, MD, AND ALLAN E. KOLKER, MD

CASE PRESENTATION

In 2002, we evaluated a 34-year-old white female who was 2 months postpartum for elevated IOP in her right eye on maximal medical therapy and possible surgery. During the patient's pregnancy, her vision had deteriorated from 20/30 BCVA preconception to count fingers at 1 foot at the time of the evaluation.

The patient's past medical history was significant for polyarticular juvenile rheumatoid arthritis diagnosed at age 5 and chronic uveitis in both eyes. The latter was treated with methotrexate. Her surgical history included bilateral trabeculectomy with 5-fluorouracil for IOPs > 40 mm Hg and phacoemulsification for a steroid-induced cataract in her left eye. Since undergoing bilateral filtration surgery in 1994, her IOPs had ranged from the single digits to the low teens in both eyes without glaucoma medicines. Her low-grade uveitis was controlled with prednisolone acetate 1% q.d. or b.i.d. Automated perimetry repeated over 3 years revealed nonprogressive scotomata in her right eye (Figure 1A).

Prior to her pregnancy, the patient was advised to discontinue methotrexate for 3 months due to its abortogenic and teratogenic effects. At 14 weeks' gestation, she presented with blurred

vision (20/60), an IOP of 29 mm Hg, and progressive visual field loss in her right eye (Figure 1B). Although the patient's IOP quickly returned to the midteens with medical intervention, by 34 weeks of gestation the visual acuity of her right eye had deteriorated to 1/200. Due to her history of polyarticular juvenile rheumatoid arthritis requiring methotrexate treatment and to ensure a healthy planned pregnancy, surgical intervention was deferred.

Upon her initial postpartum examination, the patient's visual acuity was count fingers at 1 foot OD and 20/20 OS.

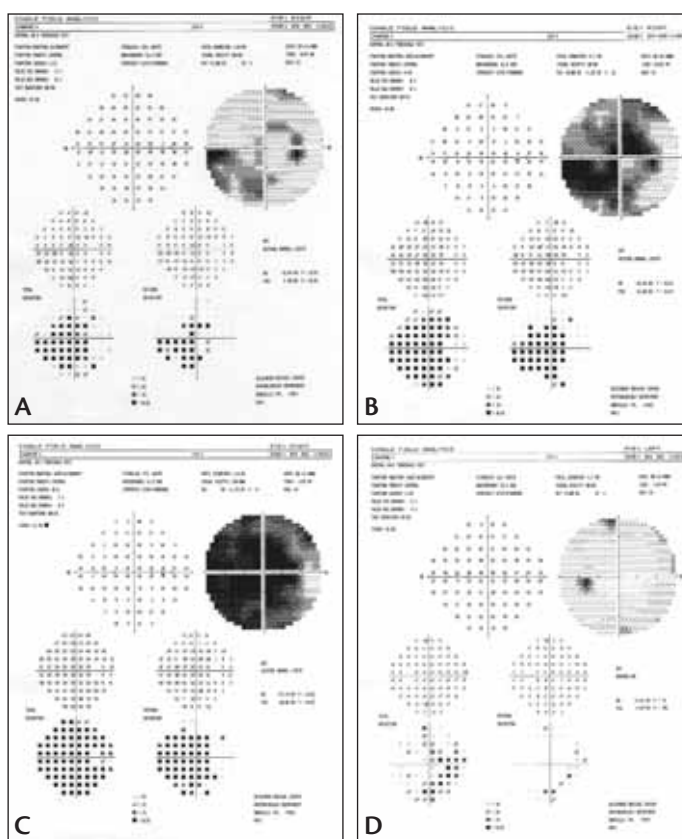


Figure 1. Repeat 30-2 Humphrey Visual Field testing showed that the patient's visual fields in her right eye were stable for a 3-year period before she became pregnant (A). At 14 weeks of gestation, the patient developed a noticeable scotoma in her right eye marked by visual field progression superiorly and inferiorly (B). Her visual field loss had worsened significantly by 2 months postpartum (C). Humphrey Visual Field testing of the patient's left eye was relatively normal with generalized depression secondary to a steroid-induced posterior subcapsular cataract (D).

We also noted an afferent pupillary defect, a superior flat bleb, and an intact PCIOI in her right eye. An examination of her left eye showed a diffuse, low-lying bleb and a posterior subcapsular cataract. Both eyes had undergone iridectomies, and the angles were open to the scleral spur. Pachymetry measured 491 μm OD and 459 μm OS. The patient's IOP was 20 mm Hg OD and 10 mm Hg OS.

A 30-2 Humphrey Visual Field test (Carl Zeiss Meditec, Inc., Dublin, CA) showed diffuse loss involving right-eye fixation with a foveal threshold of 21 dB (Figure 1C) and generalized depression in her left eye attributed to the posterior subcapsular cataract (Figure 1D).

An evaluation of the fundus with a 90.00 D lens revealed a total cup in the right eye (Figure 2A) and a cup-to-disc ratio of 0.7 vertically by contour in the left eye (Figure 2B).

The patient's current medications included one drop of latanoprost ophthalmic solution (Xalatan; Pfizer Inc., New York, NY) q.h.s., dorzolamide hydrochloride-timolol maleate ophthalmic solution (Cosopt; Merck & Co., Inc., West Point, PA) b.i.d., and brimonidine tartrate ophthalmic solution 0.2% (Alphagan; Allergan, Inc., Irvine, CA) b.i.d.

The patient was also taking loteprednol etabonate ophthalmic suspension (Lotemax; Bausch & Lomb, Rochester, NY) as needed to control her uveitis and minimize spikes in IOP. She expressed a desire for surgery to salvage the remaining vision in her right eye, but only if she could resume breastfeeding immediately after the procedure, because the baby was totally dependent upon her milk and intolerant of supplemental formula.

HOW WOULD YOU PROCEED?

1. Would you recommend a specific surgical procedure to accommodate the patient's desire to continue breastfeeding her child?

2. How soon would you recommend the patient resume breastfeeding after undergoing a surgical procedure with an antimetabolite?

3. What advice would you offer to the patient to preserve the vision in her left eye should she become pregnant again?

SURGICAL COURSE

After considering the patient's history of IOP control, completing a pharmacy consultation, and obtaining informed consent, we decided to perform a trabeculectomy supplemented with mitomycin C (MMC) (Mutamycin; Bristol-Myers Squibb Co., Princeton, NJ) on the patient's right eye. We instructed her to freeze any expressed milk 24 hours preoperatively and to breastfeed the infant immediately before surgery.

We prepared the patient for trabeculectomy by occluding all four of her puncta with plugs and administering a 2% lidocaine retrobulbar block for akinesia. We then performed a standard fornix-based trabeculectomy in the superotemporal quadrant of her right eye. Following intraoperative cautery and the creation of a scleral flap, we applied a cellulose sponge soaked in MMC (0.2 mg/mL) posterior to the flap in the sub-Tenon's space for 3 minutes and then irrigated the site profusely with saline solution.

OUTCOME

We advised the patient to discard any expressed milk for the first 24 hours after surgery and to feed the infant from the stored milk for that period. The patient resumed breastfeeding on the second postoperative day. A pediatrician monitored and assessed the infant periodically over the course of the next year, during which

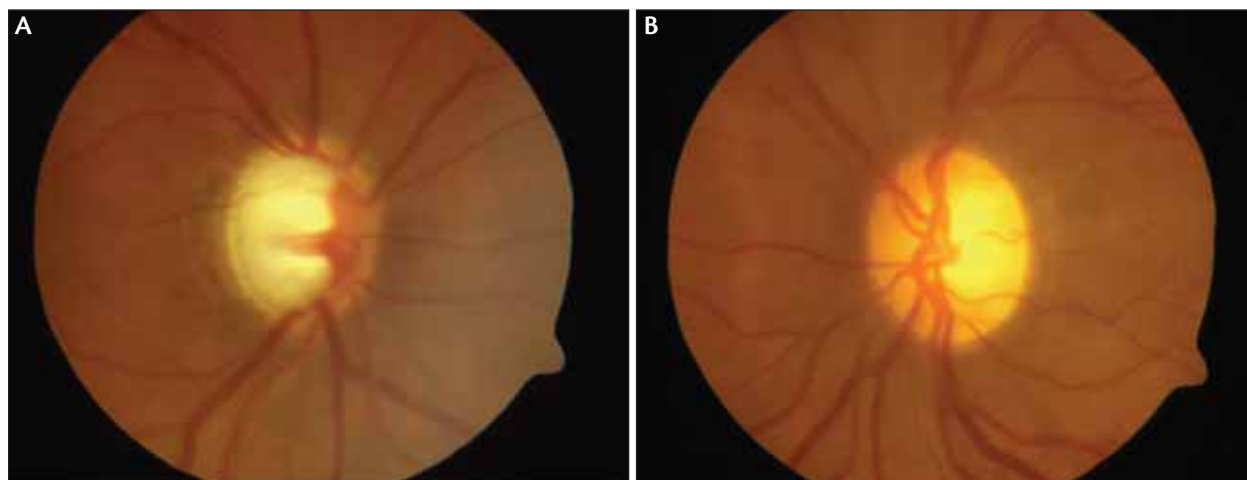


Figure 2. Fundus photographs taken 2 months postpartum showed advanced deep cupping of the optic nerve in the patient's right eye (A) and a cup-to-disc ratio of 0.7 vertically by contour in her left eye (B).

time the baby reached all developmental milestones and experienced no adverse effects warranting further work-up.

At 1 year postoperatively, the patient had an encapsulated bleb, and her IOP measured 13 mm Hg OD on b.i.d. dorzolamide hydrochloride-timolol maleate ophthalmic solution.

DISCUSSION

Assessing the Safety of Antimetabolites

MMC, an antineoplastic antibiotic isolated from *Streptomyces caespitosus*,¹ is an FDA pregnancy category D drug used to treat various carcinomas.² Side effects, including bone marrow suppression, arise primarily from the drug's intravenous administration.^{1,2} During our preoperative consultation with Bristol-Myers Squibb (via faxed letter), the company reported no systemic toxicity associated with MMC use during trabeculectomy. Neither was it clear if the drug was lipophilic. The drug's pharmacokinetics do indicate its wide distribution in a number of organs but not in the central nervous system, a finding further suggesting that MMC probably does not enter the mammary glands.²

In addition to being 2 months postpartum, the patient was subject to all of the risk factors that contribute to poor outcomes after glaucoma surgery, including uveitis, previous surgeries (trabeculectomy and cataract extraction), and young age. Our decision to use MMC during her trabeculectomy was based on advice from the hospital pharmacy, the nonintravenous application of the drug, and the potential for antimetabolite therapy to maintain a low postoperative IOP.³ We did consider implanting an aqueous shunt but decided to proceed with MMC-supplemented trabeculectomy based upon good IOP control spanning 8 years from a prior 5-fluorouracil-supplemented primary filtering surgery in her right eye. In light of her uveitis, diode cyclophotocoagulation was deferred due to concerns of exacerbating the uveitis and possible hypotony.

The potential benefits of treating a lactating mother with chemotherapy and the patient's desire to resume breastfeeding must be carefully weighed against potential harm to the fetus. Serious side effects of MMC for nursing infants can include immunosuppression from systemic absorption, interference with its cellular metabolism, growth lag, and long-term toxicity.⁴ Many reported adverse reactions to drugs in infants are dose related and occur when larger doses are delivered via breast milk.⁴

To minimize harm to the infant described herein, we used a low but effective dose of MMC to deter wound healing and implemented steps to minimize systemic

absorption. Before applying the MMC-soaked pledget to the patient's eye, we dabbed off any excess drug and cauterized the sclera to reduce vascular absorption. Punctal plugs inserted preoperatively blocked the nasolacrimal ducts and prevented the drug's absorption by the highly vascular nasopharyngeal mucosal membranes. According to one study,⁵ the amount of ophthalmic drugs absorbed systemically through these tissues can exceed that delivered by slow intravenous injections. Patients who performed digital ductal occlusion for 5 minutes after instilling one drop of a beta-blocker had absorbed 67% less of the drug into their systems (measured by radioimmunoassay in blood plasma) versus those who did not take this precaution.⁵

Following a 30-mg bolus injection of MMC, the half-life to reduce the drug's serum concentration by 50% is 17 minutes.¹ If a full bolus of 0.2 mg/mL MMC entered the vasculature, the amount would be immeasurable in 24 hours.

"Since it is not known if MMC enters breast milk, nursing infants need to be monitored for adverse effects when a lactating mother undergoes treatment with MMC."

A drug's ability to be excreted into breast milk depends in part on its molecular size, pharmacokinetics, lipid or water solubility, protein binding, pH, degree of ionization, active metabolite formation, and route of administration, all of which in turn determine its levels in the blood and breast milk. Drug safety during lactation can be assessed based on the ratio of milk to plasma.⁴

Since it is not known if MMC enters breast milk,¹ nursing infants need to be monitored for adverse effects subsequent to a lactating mother's undergoing treatment with the drug. Furthermore, the temporary cessation of breastfeeding is recommended while the patient is receiving a short course of drug therapy as in the case discussed herein.^{1,4}

Our decision to let the patient resume breastfeeding on the second day after surgery included consideration of MMC's half-life and an understanding that less than 1% of the dose given to the mother would be available for absorption by the infant.⁴

Glaucoma Drugs and Pregnancy

Although a thorough discussion of the use of topical glaucoma drugs during pregnancy and lactation is beyond the scope of the present article, some impor-

tant points should be addressed. Side effects associated with these drugs have been reported primarily with their systemic use or from case reports.⁶ This subject has been well covered elsewhere and in previous issues of this journal.⁷⁻⁹

Approximately 80% of ophthalmic medications are FDA pregnancy category C,¹⁰ meaning that no adequate or well-controlled studies have been conducted in humans but potential benefits may warrant the use of the drug in pregnant women despite potential risks. When prescribing category C glaucoma drugs, clinicians need to carefully balance the patient's risk of permanent visual loss with potential risk to the fetus or neonate.

"The use of ... nonintravenous MMC during trabeculectomy on a nursing mother poses minimal risk to an infant ... when steps are taken to reduce systemic absorption."

Patients should avoid using prostaglandins during pregnancy because these drugs can cause uterine contractions and thus are sometimes used to induce therapeutic abortions.¹¹ Patients may continue to use other topical glaucoma drugs such as timolol maleate ophthalmic solution 0.5%, but the fetus should be monitored for bradycardia.¹² In addition, beta-blockers are known to cause beta-blockade,⁶ and brimonidine tartrate ophthalmic solution 0.2% causes unresponsiveness, hypotonia, hypotension, and bradycardia when applied topically in infants.¹³ These medications should be discontinued in late pregnancy to prevent adverse effects in the newborn. In the case described herein, surgical intervention allowed the patient to discontinue brimonidine and eliminate any potential toxicity to the infant during lactation. The use of lidocaine, timolol, and dorzolamide (Trusopt; Merck & Co., Inc.), however, is considered compatible with breast feeding according to the American Academy of Pediatrics.¹⁴

Future Pregnancies

In this instance, we were able to reassure the patient that future pregnancies should pose no threat to the vision in her left eye, because the documented progressive visual field loss in her right eye was likely due to the failure of her primary trabeculectomy. IOPs normally decrease during pregnancy in women who do not have glaucoma, perhaps due to progesterone's tendency to enhance aqueous outflow.¹⁵

Furthermore, a study that followed 76 pregnancies among 51 patients with juvenile rheumatoid arthritis showed that 91% of the women either had an improvement in or no change in disease activity during gestation.¹⁶ Our patient reported no exacerbation of her juvenile rheumatoid arthritis during her first pregnancy. If she decides to conceive again, therefore, pregnancy should result in lower IOPs and an overall improvement in the signs and symptoms of juvenile rheumatoid arthritis.

In summary, the use of low-dose, nonintravenous MMC during trabeculectomy on a nursing mother poses minimal risk to an infant who resumes breastfeeding when steps are taken to reduce systemic absorption of the drug and the baby is monitored by a pediatrician. Under these conditions, a mother may seek help for elevated IOP and glaucomatous progression without compromising the welfare of her child. □

Shakeel Shareef, MD, is an Associate Professor in the Department of Ophthalmology at the University of Rochester Eye Institute in Rochester, New York. He acknowledged no financial interest in the products or companies mentioned herein. Dr. Shareef may be reached at (585) 275-5332; shakeel_shareef@urmc.rochester.edu.



Allan E. Kolker, MD, is in private practice in St. Louis, Missouri. He acknowledged no financial interest in the products or companies mentioned herein. Dr. Kolker may be reached at (314) 878-7962; akolker@sbcglobal.net.



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