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CORRESPONDENCE

Sir,
Difluprednate versus prednisolone acetate for inflammation following cataract surgery in pediatric patients: a randomized safety and efficacy study

We read with great interest the article by Wilson *et al.*[1] The authors must be congratulated for this randomized control study on pediatric cataract. Potential concern with the use of a highly potent steroid like difluprednate 0.05% is the possibility of intraocular pressure (IOP) elevation. In children, the ocular hypertensive response occurs more frequently and more severely than that reported in adults, and monitoring the IOP is essential in children receiving steroids in any form.[2] Clinically significant rise in IOP after difluprednate is seen in 50 to even 80% cases in pediatric studies.[3]

The current treatment regimen used by the authors is same for a neonate and a toddler, that is, four times daily. It is difficult to understand why the same frequency was used in a 10-day-old baby and a 3-year child as the inflammatory response would be much more in younger child necessitating aggressive steroid instillation. This could then have an adverse effect on the IOP even though it may control the inflammation. In such a scenario there could be a question on the safety profile of difluprednate. Our own surgical experience is that, younger the child the more frequent dosing he needs.[4] Some of these authors who were also part of the Infant Aphakia Treatment Study (IATS) believe that the infants received more corticosteroids than the minimal protocol in their study because the surgeons felt the requirement.[5]

The technique of IOP estimation is not mentioned in the study. There are numerous factors affecting the measurement of IOP in children. Anesthetic gases lower IOP and on the other hand in an office-setting tight squeezing of the lids may increase IOP. What were the preoperative baseline IOP measurements in these children to actually comment on the raised IOP postoperatively? The cut off value of 21 mm Hg in an adult has been extrapolated to children. Since the IOP measured in children is usually lower; this cut off value may be higher for children especially neonates and infants less than 6 months. Authors have also mentioned that the IOP rise in one patient is unrelated to the treatment. We would be interested to know on how this conclusion was reached.

The global inflammation score used by the authors is a very subjective scale. Future advances in the form of a hand-held flare photometer may be a more objective and quantifiable method to monitor the inflammatory response in children.

The IATS group has recommended contact lens use as early as 1 week after surgery for aphakia correction. In the present study the authors used topical medicine over the contact lens. Although 0.05% difluprednate (Durezol ophthalmic emulsion, Alcon laboratories, Inc, Irvine, CA, USA) has sorbic acid as preservative instead of benzalkonium chloride, the statutory warning with the drug prohibits its use over the contact lens. What is the opinion of the authors in this regard?

Although difluprednate 0.05% is a welcome addition to the steroid family to curb inflammatory response after cataract surgery, it would not be wise to authenticate its safety from this study considering the more frequent and longer dosing schedule required in infants as compared with older children.

Conflict of interest

The authors declare no conflict of interest.

References

1 Wilson ME, O'Halloran H, VanderVeen D, Roarty J, Plager DA, Markwardt K *et al.* Difluprednate versus prednisolone acetate for inflammation following cataract surgery in pediatric patients: a randomized safety and efficacy study. *Eye (Lond)* 2016; **30**: 1187–1194.
2 Kaur S, Dhiman I, Kaushik S, Raj S, Pandav SS. Outcome of Ocular Steroid Hypertensive Response in Children. *J Glaucoma* 2016; **25**(4): 343–347.
3 Slabaugh MA, Herlihy E, Ongchin S, van Gelder RN. Efficacy and potential complications of difluprednate use for pediatric uveitis. *Am J Ophthalmol* 2012; **153**(5): 932–938.
4 Sukhija J, Kaur S, Ram J. Outcome of primary intraocular lens implantation in infants: Complications and rates of additional surgery. *J Cataract Refract Surg* 2016; **42**(7): 1060–1065.
5 Lambert SR, Plager DA, Buckley EG, Wilson ME, DuBois L, Drews-Botsch CD *et al.* Infant Aphakia Treatment Study Group. The Infant Aphakia Treatment Study: further on intra- and postoperative complications in the intraocular lens group. *J AAPOS* 2015; **19**(2): 101–103.

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Sir,
Difluprednate versus prednisolone acetate for inflammation following cataract surgery in pediatric patients: a randomized safety and efficacy study

We thank Drs. Kaur and Sukhija for their interest in our article. They make several interesting and important points in their letter. They mention that difluprednate is a highly potent steroid that may cause intraocular pressure elevation. They also mention that they dose steroids more frequently than four times per day in infants and young children.

Our study was a multicenter randomized controlled trial comparing difluprednate 0.05% to prednisolone acetate 1% in children aged 0–3 years after cataract surgery.[1] The U.S. FDA requested that the study be performed on children of this age.

We personally use four times per day dosing of topical prednisolone acetate in our practices after cataract surgery in infants and children. Over the last several years, we have each adopted a four times per day dosing regardless of age and increase the frequency only in

unusual circumstances such as uveitic cataracts or some patients with trauma. This study provides support for that dosing choice since postoperative inflammation was adequately controlled in even our youngest enrollees. Infants less than 7 months of age were routinely left aphakic. Although it is true that some surgeons in the Infant Aphakia Treatment Study (IATS) used steroid drops more frequently than four times per day, the rate of inflammatory complications was not lower in those dosed more than four times per day.[2] We can make no statement about the use of difluprednate more frequently than four times per day, but our study demonstrated good control of postoperative inflammation at that dosage and no increase in adverse events when compared with prednisolone acetate, the current standard.

The centers in our study were chosen, in part, because they were experienced and routinely successful at checking intraocular pressure in infants and small children. The Icare (Finland) rebound tonometer has become a popular device among pediatric cataract surgeons in the USA for measuring IOP in this age group without sedation pediatric cataract surgeons in the USA and it was used in this study.[3] Both pre-surgery IOP and post-operative IOP readings were taken in a clinical area outside of the operating room. Our study IOP readings were not done under general anesthesia.

Since the IATS recommended that most infants under 7 months of age be left aphakic and treated with a contact lens, infants treated in this manner were enrolled and randomized in our study.[4] Extended-wear silicone contact lenses or daily-wear rigid gas permeable contact lenses were used. With these materials (0% water content), we found no adverse events related to placing the drops on the eye while the contact lens was being worn. It is likely that the package insert advising against the instillation of topical difluprednate while wearing contact lens is for high water content contact lenses that are not available in the powers needed to correct aphakic infants.

Drug choice and dosing in infants and young children after cataract surgery will remain a personal choice of the surgeon. Our study provides evidence that difluprednate can be safely used at QID dosing in children aged 0–3 years.

Conflict of interest

The authors declare no conflict of interest.

References

1 Wilson ME, O'Halloran H, VanderVeen D, Roarty J, Plager DA, Markwardt K *et al.* Difluprednate versus prednisolone acetate for inflammation following cataract surgery in pediatric patients: a randomized safety and efficacy study. *Eye (Lond)* 2016; **30**(9): 1187–1194.

2 Lambert SR, Plager DA, Buckley EG, Wilson ME, DuBois L *et al.* Infant Aphakia Treatment Study Group. The Infant Aphakia Treatment Study: further on intra- and postoperative complications in the intraocular lens group. *J AAPOS.* 2015; **19** (2): 101–103.

3 Lambert SR, Buffenn AN, Chiang MF, Coats DK, Melia M, Simpson JL *et al.* Rebound tonometry in children. *Ophthalmology* 2013; **120**: e21–e27.

4 Lambert SR, Lynn MJ, Hartmann EE, DuBois L, Drews-Botsch CD *et al.* (Writing Committee) The Infant Aphakia Treatment Study Group. Comparison of contact lens and intraocular lens correction of monocular aphakia during infancy: a randomized clinical trial of HOTV optotype acuity at age 4.5 years and clinical findings at age 5 years. *JAMA Ophthalmol* 2014; **132**(6); 676–684.

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Sir,

Two-year outcomes of intravitreal bevacizumab for choroidal neovascularization associated with a dome-shaped macula in pathologic myopia

A dome-shaped macula (DSM) is an inward protrusion of the macula seen on optical coherence tomography (OCT) in highly myopic eyes, which was first described in 2008 by Gaucher *et al.*[1] Since DSM appears to be a distinct feature of highly myopic eyes,[2,3] it could be suspected that choroidal neovascularization (CNV) that develops in myopic eyes with DSM may have different clinical features and may follow a course different from that of CNV found in myopic eyes without DSM. However, studies on the therapeutic outcome of CNV associated with DSM are limited. When searching PubMed using the keyword 'dome-shaped macula', only one brief report that showed the visual outcome of myopic CNV with DSM after 1-year intravitreal ranibizumab treatment was identified.[3] The purpose of this study was to determine the 2-year visual and anatomical outcomes of intravitreal bevacizumab (IVB) treatment for myopic CNV with DSM features. The secondary objective was to compare patients with and without DSM, to investigate whether there was any difference in the clinical features and therapeutic outcome in these two groups after IVB treatment.

We retrospectively reviewed the medical records of 50 patients with myopic CNV who received IVB injections between 1 January 2009 and 30 April 2014. Inclusion criteria were as follows: (1) a refractive error ≤ -6.0 D or an axial length ≥ 26.5 mm, (2) the presence of subfoveal, juxtafoveal, or extrafoveal CNV, (3) treatment-naive patients who were treated with at least one IVB, and (4) follow-up of 2 years or more after intravitreal injection. The study was approved by the institutional review board of Yonsei University College of Medicine. After the initial IVB at baseline, retreatments were applied pro re