Combination therapy for retinopathy of prematurity

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Comment on: Toy BC, Schachar IH, Tan GS, *et al*. Chronic Vascular Arrest as a Predictor of Bevacizumab Treatment Failure in Retinopathy of Prematurity. Ophthalmology 2016;123:2166-75.

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Toy *et al*. described 17 infants (33 eyes) who were treated with intravitreal bevacizumab (0.625 mg) injection for type 1 retinopathy of prematurity (ROP) followed by subsequent exam under anesthesia and fluorescein angiography (FA) taken after 50 weeks of gestational age (1). All eyes had a "scalloped regression" pattern of the peripheral retina on FA. Recurrence or chronic vascular arrest based on FA findings were noted in 30 eyes (91%) for which secondary laser was added to areas of persistent non-perfusion.

This paper is not the first or the largest to report on FA findings after anti-vascular endothelial growth factor (anti-VEGF) for ROP. The paper's novelty is that it makes a strong argument for the practice of combination therapy for type 1 ROP: initial intravitreal anti-VEGF, close follow-up, and subsequent exam under anesthesia and laser. There are three main reasons for this approach:

(I) First and foremost, to prevent late ROP reactivation and subsequent retinal detachment. Delayed retinal detachment after anti-VEGF treatment has been reported from as early as 35 weeks gestational age to as late as 2.5 years of age. These rare but noteworthy cases are presumably from reactivation of untreated non-perfusion and adding laser to non-perfused peripheral retina diminishes if not eliminates the prospect of reactivated ROP;

(II) Secondly, to reduce the burden of follow-up in ROP care. The window of acute ROP has become prolonged, as infants need to be monitored weekly for extended periods of time after primary anti-VEGF. This makes for a difficult task as infants become too large to swaddle, parents become weary of complying with weekly eye exams, and eye clinics reach capacity. After a definitive exam under anesthesia, FA, and follow-up laser, clinic visits can be markedly reduced;

(III) Third, the approach described delays the risk of general anesthesia. In the paper, average age of primary laser was 37.7 weeks compared to 49.3 weeks for EUA with secondary laser. Studies have shown that delaying general anesthesia in premature infants reduces apnea episodes, which would allow for outpatient anesthesia, and may reduce neurotoxicity as well (2,3).

Another noteworthy observation is the gestational age and birthweights of this US cohort compared with published Chinese cohorts who developed type 1 ROP. In this paper which enrolled patients between 2013 and 2015, the median birthweight was 24.7/24.9 weeks and median birth weight was 645/700 grams (bevacizumab/primary laser). In a paper which published on infants treated for ROP in Beijing, China between 2009 and 2011 the mean BW and GA were 29.4 weeks and 1,241 grams, respectively (4). As China rapidly develops and advances its neonatal care and NICU protocols, the risk factor profile for ROP in China will continue to evolve.

The paper also leads to the question, is FA required for ROP care in the age of anti-VEGF? Although there are typically more ROP findings on FA than noticeable on clinical exam, and it is best to perform FA if available, I would argue that it may not be absolutely necessary to have

FA for ROP care. Laser can still be performed to avascular peripheral retina based on clinical exam alone.

What is on the horizon for ROP treatment? Right now, an important question is which anti-VEGF to use for ROP. Although bevacizumab is the most commonly used agent in the United States, it is not available in China and ranibizumab seems to have a safer systemic profile. Studies such as the RAINBOW Study which compares laser to ranibizumab for ROP (5) should help to get US Food and Drug Administration approval for the use of ranibizumab in ROP.

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None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

References

1. Toy BC, Schachar IH, Tan GS, et al. Chronic Vascular Arrest as a Predictor of Bevacizumab Treatment Failure in Retinopathy of Prematurity. Ophthalmology 2016;123:2166-75.
2. Coté CJ, Zaslavsky A, Downes JJ, et al. Postoperative apnea in former preterm infants after inguinal herniorrhaphy. A combined analysis. Anesthesiology 1995;82:809-22.
3. Jones LJ, Craven PD, Lakkundi A, et al. Regional (spinal, epidural, caudal) versus general anaesthesia in preterm infants undergoing inguinal herniorrhaphy in early infancy. Cochrane Database Syst Rev 2015;(6):CD003669.
4. Li Q, Wang Z, Wang R, et al. A Prospective Study of the Incidence of Retinopathy of Prematurity in China: Evaluation of Different Screening Criteria. J Ophthalmol 2016;2016:5918736.
5. RAINBOW Study: RAnibizumab Compared With Laser Therapy for the Treatment of INfants BOrn ClinicalTrials.gov. Prematurely With Retinopathy of Prematurity (RAINBOW). Available online: https://clinicaltrials.gov/ct2/show/NCT02375971

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