Drug therapy shows significant benefit in treating a leading cause of childhood blindness

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A readily available, inexpensive drug therapy showed a significant benefit in treating premature infants with the worst and historically most difficult-to-treat cases of retinopathy of prematurity.

The results of a multicenter clinical trial led by researchers at The University of Texas Health Science Center at Houston (UTHealth) are published in the Feb. 17 issue of The *New England Journal of Medicine*.

Retinopathy of prematurity is a leading cause of childhood blindness worldwide. In the immature retina of babies born before 30 weeks' gestational age, the disease results in disorganized growth of retinal blood vessels, which can lead to scarring and retinal detachment.

In this study, Helen A. Mintz-Hittner, M.D., the Alfred W. Lasher, III, Professor in the Department of Ophthalmology and Visual Science at the UTHealth Medical School, and colleagues compared the use of intravitreal bevacizumab, an anti-vascular endothelial growth factor, to conventional laser treatment.

The study investigators treated infants with acute retinopathy of prematurity affecting zone I and posterior zone II – the retinal zones with the highest rate of treatment failure.

Data on the outcomes of 143 infants enrolled in the study showed that,

among infants with zone I disease, the recurrence rate was 6 percent with intravitreal bevacizumab and 42 percent with conventional laser therapy. The drug therapy resulted in mild anatomical retinal abnormality in just one eye of 31 infants, whereas conventional laser treatment resulted in a mild structural abnormality in 16 eyes and severe abnormality in two eyes of 33 infants.

"When I started working with babies almost 40 years ago, there was nothing we could do for those with retinopathy of prematurity," said Mintz-Hittner, the study's principal investigator. "We've gone from nothing to a real solution. It you are careful and administer this therapy appropriately in stage 3+, you can get wonderful outcomes."

Mintz-Hittner, an attending physician at Children's Memorial Hermann Hospital and the Robert Cizik Eye Clinic, stressed that timing is critical with this drug therapy. If administered too early, in stages 1 and 2 of the disease, it can cause retinal dystrophy. Given too late, in stages 4-5 of the disease, the drug can accelerate retina detachment.

"In that window, as the abnormal vessels begin to proliferate but before the retinal begins to detach, that's when you want to treat," Mintz-Hittner said.

In addition to the significantly reduced recurrence rate for patients with retinopathy of prematurity in zone I, Mintz-Hittner said, compared with conventional laser therapy, the drug therapy appears to do the best job preserving vision. Plus, when administered, there is no need to intubate the baby and there is a faster recovery.

"Our first available treatment for babies with retinopathy of prematurity was cryotherapy," Mintz-Hittner said. "It was very painful and it wiped out all posterior ocular layers. The visual field was decreased and myopia or nearsightedness occurred. It was a long procedure – 2 to 3 hours –

requiring intubation. With laser treatment, you still had to intubate, which could cause major setbacks for the baby, and field loss and myopia still occurred, but it was less painful and only destroyed the inner retinal layers."

"With this drug therapy, we use a few drops of anesthetic to numb the eye. We take a syringe with a tiny needle and administer a small amount of the drug directly into the eye. The whole process takes two to three minutes, and you begin to see results within 24 hours," she said. "The abnormal vessels virtually disappear and then normal vessels begin to grow out again. The field of vision is preserved and myopia is less."

The results of the study were so promising that Children's Memorial Hermann Hospital has discontinued the use of conventional laser therapy and now offers only the drug therapy to premature infants with this type of retinal disease.

"As compared with conventional laser therapy in treating patients with zone I retinopathy of prematurity, intravitreal bevacizumab represents a true breakthrough in disease management," James D. Reynolds, M.D., wrote in an accompanying editorial in The New England Journal of Medicine. "…Intravitreal bevacizumab should become the treatment of choice for zone I retinopathy of prematurity." Reynolds is with the Department of Ophthalmology at the University of Buffalo in Buffalo, N.Y.

Compared with laser therapy, Mintz-Hittner cautioned, the drug therapy does require longer follow-up, "You must follow the child for at least 16 weeks following the injection to make sure there isn't a recurrence. Approximately 4 percent of patients (one in every 25 patients) may require a second injection. I explain to parents that it's like a cancer. It can come back and if it isn't treated in time, it can lead to blindness – so follow-up is very important."

The next steps in research, Mintz-Hittner said, will be to further evaluate the drug therapy's safety, refine the dosage and timing of follow-up and also study long-term visual function.

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