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Saving preemies' vision

Drug may offer new option to reverse aberrant blood vessel growth in the eyes of babies born preterm

By Nathan Seppa
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Some premature infants with a potentially blinding eye condition called retinopathy may now have an alternative to the laser surgery currently used to treat it. A drug outperforms the surgery in newborns who have abnormal blood vessel growth in the back of the retina near the optic nerve, researchers report in the Feb. 17 New England Journal of Medicine.

The drug, bevacizumab, is used against some cancers because it inhibits manufacture of a protein called vascular endothelial growth factor, or VEGF, that drives vessel growth. Although VEGF is necessary for normal organ development, some premature newborns make too much in the eyes, fostering aberrant vessel networks that can lead to a detached retina and blindness if untreated.

Babies born 10 weeks or more prematurely and weighing less than 3 pounds at birth are at highest risk for this condition, called retinopathy of prematurity. It usually resolves on its own. If not, laser surgery can burn off abnormal vessels, curbing VEGF and stopping vessel growth, reducing the blindness risk to 1 percent from 50 percent in untreated eyes, says Kimberly Drenser, a retinal surgeon at Oakland University in Rochester, Mich., who wasn't involved in this study. "Laser surgery, when it's done well, is extremely effective," she says.

But laser treatment and cryotherapy, a freezing technique, damage peripheral areas of the retina, limiting side vision while saving more essential straight-on vision.

The new study is the first to pit laser surgery, currently the preferred treatment, against bevacizumab, also called Avastin, in children randomly chosen to get one treatment or the other, says study coauthor Helen Mintz-Hittner, a pediatric ophthalmologist at the University of Texas Health Science Center at Houston. In the past three years, she and her colleagues assigned 143 infants with retinopathy to get either laser surgery or an injection of bevacizumab in each eye.

Of these children, 64 had retinopathy centered around the area of the retina connected with the optic nerve, what doctors call zone 1. This group showed a benefit from the drug — only two of 31 had a recurrence of disease in the form of vessel growth in subsequent several months, compared with 14 of 33 babies getting laser surgery.

The other 79 infants had abnormal vessel growth in a ring outside the zone 1 area. They didn't show substantially greater benefit from one therapy over the other.

"Bevacizumab should become the treatment of choice for zone 1 retinopathy of prematurity," says pediatric ophthalmologist James Reynolds of the Ross Eye Institute and the University at Buffalo, writing in the same New England Journal of Medicine issue. "I speculate that intravitreal [within the eye] bevacizumab treatment will prove to be at least equal to laser therapy in clinical effectiveness for most forms of retinopathy of prematurity."

Mintz-Hittner says bevacizumab injection wouldn't require an eye surgeon to perform. That could be an advantage in developing countries lacking laser surgery facilities, she says.

"Given that a significant effect of Avastin was only seen in zone 1 disease, there might be a case for using this therapy in that condition," says Brian Darlow, a neonatal pediatrician at the University of Otago in Christchurch, New Zealand. "But parents would need to be carefully counseled that the long-term harm or benefit is not known — so essentially the treatment is still experimental."

Drenser notes that comparing the drug against laser surgery is tricky because some surgeons are much better at the surgery than others.

Meanwhile, some researchers remain uneasy about introducing a VEGF inhibitor in a preemie because VEGF is important for development of the brain and other organs. Bevacizumab could pose a risk if it escaped the eye, Drenser says. An earlier study in adults with retinopathy had noted that treating one eye with bevacizumab seemed to have an effect on the other eye. And Darlow notes that data from studies in animals show bevacizumab found its way into circulation after it was injected into an eye.

Mintz-Hittner counters that infants' eyes contain very thick vitreous fluid, which limits flow. This becomes thinner and more watery only later in life.

Drenser acknowledges one potential advantage for bevacizumab: It might buy the eye time to regrow more functional retina later in life

than does laser surgery. But a treated eye would require close follow-up, she says.

SUGGESTED READING :

National Eye Institute site on retinopathy of prematurity.

H. Quiroz-Mercado et al. Anti-angiogenic therapy with intravitreal bevacizumab for retinopathyof prematurity. Retina, Vol. 28, 2008, Supplement S19-S25.

G.A. Lalwani et al. Off-label use of intravitreal bevacizumab (Avastin) for salvage treatmentin progressive threshold retinopathy of prematurity. Retina, Vol. 28, 2008, Supplement S13. [Erratum, Retina, Vol. 29, 2009, p. 127.]

Early Treatment for Retinopathy of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the Early Treatment for Retinopathy of Prematurity randomized trial. Archives of Ophthalmology, Vol. 121, 2003, p. 1684.

CITATIONS & REFERENCES :

H.A. Mintz-Hittner et al. Efficacy of Intravitreal Bevacizumab for Stage 3+Retinopathy of Prematurity. New England Journal of Medicine, Vol. 364, Feb. 16, 2011, p. 603.

J.D. Reynolds. Bevacizumab for Retinopathy of Prematurity. New England Journal of Medicine, Vol. 364, Feb. 16, 2011, p. 677.