A NEW FRONTIER IN PEDIATRIC RETINA

Universal eye screening is on course to play an increasingly important role in the evaluation of newborns.

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The use of trained experts to examine standardized wide-angle photographs of infants at risk of developing retinopathy of prematurity (ROP) is a successful screening strategy, and one that can be conducted remotely. However, I would hazard that no more than 10% of neonatal intensive care units in America utilize telemedicine. Telemedicine in pediatric retina using wide-angle imaging has been validated over a 17-year period for screening infants for ROP.

The photo-ROP trial demonstrated telemedicine’s equivalence to bedside binocular indirect ophthalmoscopy (BIO) in detecting signs of ROP.1 Since then, local community access programs such as the Stanford University Network for Diagnosis of ROP (SUNDROP),2 of which I am the director, have helped to confirm the efficacy of telemedicine screening for ROP, leading to acceptance of this screening modality by the American Academy of Pediatrics (AAP) and the American Academy of Ophthalmology (AAO).3 The eROP trial took the additional step of adding trained nonphysician graders and demonstrated sensitivity and specificity of 81.9% and 90.1%, respectively, for identification of referral-warranted ROP (RW-ROP) in a single session.4 Although this was an impressive finding, it remains to be determined whether there is a legal framework for using nonphysician graders in ROP screening.

It is not for lack of data, but rather because of intransigence, anticipated infrastructure costs, and a widely held, if possibly misplaced, belief that bedside BIO is a superior screening technique, that telemedicine screening is not more widely practiced. Those of us who have been championing the value of telemedicine have focused on the upsides: cost savings, the ability to conduct longitudinal comparisons and make objective evaluations, normalization of practice patterns, and the ability to seamlessly solicit second opinions.

It is increasingly clear that telemedicine screening for ROP is being rapidly adopted. It is also clear that this remote screening modality may bring us to a new frontier in pediatric retina, a dedication to universal eye screening in full-term newborns.

CURRENT PRACTICES IN NEWBORN EYE SCREENING

At its core, universal newborn eye screening is inherently appealing; we screen all newborn infants for ocular disease at birth. Currently, the only universal eye screening of children in America mandated by the AAP is the red reflex examination, to be performed at every well-baby and well-child examination until the age of maturity.5 The red reflex examination is useful in the setting of leukocoria but contains little screening benefit outside of this rare occurrence.

Most children do not receive formal screening examinations until before their entry into kindergarten, at which point most treatable ophthalmic diseases have progressed beyond clinicians’ ability to restore anatomy or return function to normal levels. In an attempt to address this deficiency, numerous national and local screening programs employing photographic and digital systems to assess ocular misalignment (a proxy for underlying pathology) have been deployed with varying levels of success.

The United States Preventive Services Task Force evaluated screening strategies to prevent or reverse visual impairment in children.6 The task force recommended that all children between the ages of 3 and 5 years be screened for amblyopia and concluded that there was no benefit to screening those under age 3 years.6 However, the caveat to the task force’s

AT A GLANCE

- Most children do not receive formal screening examinations until just before entering kindergarten.
- The use of trained experts to examine standardized wide-angle photographs of at-risk infants is a successful screening strategy for ROP.
- Benefits of telemedicine include cost savings, normalization of practice patterns, and the ability to make objective evaluations and longitudinal comparisons.
position on screening children younger than 3 years is that it evaluated only studies including children between the ages of 1 and 3 years, leaving open the possibility that earlier screening in younger patients may have benefits.

GLOBAL INFANT SCREENING EFFORTS

Teams led by Li Hong Li in China; Issa Romagossa in Spain; and Homero Augusto de Miranda II and Marcelo Costa in Brazil, have been screening the newborn populations in those countries for ocular disease from birth up to age 7 years (unpublished data). These initiatives have been offered on a cash-pay basis, are not structured as studies, and do not have formalized screening protocols. Yet they have demonstrated remarkable uniformity of results. Up to 25% of the screened populations have ocular fundus hemorrhages, 2% to 3% of the hemorrhages involve the fovea, and 1.5% to 2.5% have nonhemorrhagic pathology (unpublished data). These last two points are critical, as the foveal hemorrhages and nonhemorrhagic pathology have incidences approaching 3%.

Even if one were to discard the overall incidence of fundus hemorrhages (20% to 25%) on the basis that they spontaneously resolve and are thought not to be linked to any adverse ocular outcomes—which has not been definitively demonstrated—the foveal hemorrhages and nonocular pathology represent real threats to visual function. More specifically, the incidence of these findings meets the threshold for socioeconomic benefit of a screening program as put forth by the Bayes theorem. This theorem, as applied to health screenings, states that knowledge of the prevalence of a disease improves confidence in the results of screening for that disease. Thus, the higher the prevalence, the greater the likelihood that a positive test is actually positive. The tipping point is an incidence or prevalence of 2% in the screened population.

APPLES TO ORANGES

The AAP recommends that all newborn infants in America undergo hearing screening, although the incidence of hearing diseases in newborns is only between 0.1% and 0.6%. The incidence would be higher if patients were screened later because of the neuropressive nature of deafness. We tolerate this low screening yield because the adverse effects of deafness are profound. With incidences of foveal hemorrhages and nonhemorrhagic pathology occurring at approximately 3% in newborn infants, the potential for adverse visual acuity outcomes is also large, and one may reasonably argue that they have a more profound influence than deafness. Because much of the pathology that has been detected in these initiatives is amenable to conventional treatment, national health systems should seriously consider the merits of universal newborn eye screening.

To that end, Stanford University has initiated the Global Universal Eye Screen Testing (GUEST) study. We have to date amassed a database of more than 5,500 patients and nearly 90,000 images from the United States, China, and Brazil of infants who have undergone universal screening for eye disease at birth. The two main goals of the GUEST study are (1) to identify the least expensive population of screeners that can reliably differentiate normal from abnormal eye examinations based on standardized wide-angle photographs and (2) to identify the most efficient photographic screening protocol that reliably captures eye pathology in the newborn population. Data are still being collected.

MORE SCREENING, BETTER TECHNOLOGY, BRIGHTER FUTURE

Newborn eye screening will play an increasingly important role in the evaluation of the health and ocular status of the healthy, full-term newborn population (Figure). This will be facilitated by the introduction of new cameras and other imaging technologies (ie, optical coherence tomography) and by the use of artificial intelligence algorithms to enhance screening.