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Non-contact retinal imaging compared to indirect ophthalmoscopy for retinopathy of prematurity screening: Infant safety profile

S. Grace Prakalapakorn, MD, MPH¹, Sandra S. Stinnett, DrPH¹, Sharon F. Freedman, MD¹, David K. Wallace, MD, MPH¹, J. Wayne Riggins, MD^{2,3}, and Keith J. Gallaher, MD³

¹Duke University, Department of Ophthalmology, Durham, NC, USA

²Cape Fear Eye Associates, Fayetteville, NC

³Cape Fear Valley Medical Center, Fayetteville, NC

Abstract

Objective: Most retinopathy of prematurity screening involves an ophthalmologist performing indirect ophthalmoscopy, which can be stressful to infants. The purpose of this study is to evaluate the safety profile (using cardiopulmonary events as an indicator) of imaging infants with a non-contact retinal camera compared to examining them using indirect ophthalmoscopy.

Study Design: Prospective cohort study of 99 infants at a community hospital who were examined using indirect ophthalmoscopy and imaged using a non-contact retinal camera for retinopathy of prematurity. We evaluated the difference in the occurrence of safety events (i.e. clinically significant bradycardia, tachycardia, oxygen desaturation, or apnea) following the clinical examination versus retinal imaging.

Result: Safety events occurred after 0.8% (n=1) of imaging sessions and 5.8% (n=18) of clinical examinations (mean difference = -0.055 (p=0.015), favoring imaging).

Conclusion: Retinal imaging with a non-contact camera was well tolerated and less stressful to infants compared to indirect ophthalmoscopy by an ophthalmologist.

INTRODUCTION

While current United States retinopathy of prematurity (ROP) screening guidelines recommend that a skilled ophthalmologist use indirect ophthalmoscopy to examine at-risk infants,¹ less than 10% of infants with a birthweight <1251 grams develop treatment-requiring ROP,² and the indirect ophthalmoscopy exam can cause physiologic stress to infants.^{3–8} Thus, many infants who never develop treatment-requiring ROP are subjected to unnecessary and stressful examinations. Less stressful screening strategies are needed. In recent studies, we found that images acquired using a non-contact retinal camera could be graded with high sensitivity to detect infants who developed treatment-indicated (type 1) ROP.^{9,10}

The purpose of this study is to evaluate the safety profile (using cardiopulmonary events as an indicator) of imaging infants with a non-contact retinal camera by trained non-physician healthcare workers compared to examining them using indirect ophthalmoscopy by an ophthalmologist.

MATERIALS AND METHODS

This study was conducted as part of a prospective study approved by the Institutional Review Boards at Cape Fear Valley and Duke University Health Systems and conformed to the requirements of the United States Health Insurance Portability and Privacy Act. Written informed consent was obtained from a parent or guardian of each study participant. The study was conducted in accordance with the Health Insurance Portability and Accountability Act and adhered to the tenets of the Declaration of Helsinki.

As part of a prospective study, infants undergoing routine ROP screening were imaged by trained healthcare workers using a non-contact retinal camera, Pictor™ (Volk Optical Inc., Mentor, OH), on the same day they were examined by an ophthalmologist using indirect ophthalmoscopy.¹⁰ Infants were eligible for inclusion in the study if they fulfilled current ROP screening guidelines criteria (i.e. birth weight $\geq$ 1500 grams; gestational age $\geq$ 30 weeks; and/or a birth weight of 1500–2000 grams or gestational age $>$ 30 weeks and an unstable clinical course)¹ and had not already been treated for ROP (i.e. laser or anti-vascular endothelial growth factor injection). After dilation with 3 sets of 1% tropicamide and 2.5% phenylephrine, infants were given a topical anesthetic (proparacaine 0.5%) and evaluated by one ophthalmologist with over 15 years of ROP screening experience (JWR) using indirect ophthalmoscopy, a lid speculum, and scleral depressor. Prior to examination/imaging, infants were swaddled and offered a pacifier. Within four hours of the clinical examination (either before or after the clinical exam), a healthcare worker imaged each eye without using a topical anesthetic or lid speculum (Figure 1).

During the examination and imaging sessions, a healthcare provider monitored the infant's health status. If there was a change in the infant's health status (defined as clinically significant bradycardia, tachycardia, oxygen desaturation, or apnea), examination/imaging was stopped. When the infant's health status stabilized, examination/imaging was resumed. Clinically significant "bradycardia" was defined as a heart rate $<$ 80 beats per minute and not rising for $>$ 5 seconds, "tachycardia" as a heart rate $>$ 230 beats per minute, "desaturation" as an oxygen saturation $<$ 80% or central cyanosis $>$ 5 seconds after the monitor alarm sounded, and "apnea" as no respiratory effort $>$ 20 seconds. We monitored infant health status over the following predefined time periods: between midnight and the time when dilating eye drops were instilled (usually 6–11am), for 10 minutes following the clinical examination, and for 10 minutes following imaging.

Statistical analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC). A change in health status (i.e. clinically significant bradycardia, tachycardia, oxygen desaturation, or apnea) was considered a safety event. Data was analyzed separately for those imaged first and for those examined first. Within each group, we evaluated the overall occurrence of safety events by weighting infants equally (i.e. if an infant was imaged/examined more than

once, we took an average of the infant's score). Among infants with paired data (i.e. had occurrences of both imaging first and examination first during the study), significance of the difference in per-infant average of how often they became unstable after each modality was assessed using the non-parametric Wilcoxon signed-rank test for paired data at a significance level of $p=0.05$. We also explored these findings by post menstrual age at time of examination/imaging.

RESULTS:

Ninety-nine infants were included. Infants were examined first in 293 sessions and imaged first in 119 sessions. Seven sessions were excluded because one eye was imaged before and the other after the clinical examination ($n=4$) or it was not noted which occurred first ($n=3$).

Safety events (i.e. clinically significant bradycardia, tachycardia, oxygen desaturation, or apnea) occurred after 5.8% ($n=18$) of clinical examinations and 0.8% ($n=1$) of imaging sessions. At baseline, 32.1% of those examined first and 40.0% of those imaged first had a safety event prior to being examined/imaged that day. Among the 60 infants with paired data (i.e. had occurrences of both imaging first and examination first during the study), the mean differences at baseline was 0.029 ($p=0.73$) favoring examination and mean difference after imaging versus examination was -0.055 ($p=0.015$) favoring imaging. We also looked at the occurrence of safety events by post menstrual age (Table 1).

DISCUSSION

Infants could be safely imaged by trained non-physician healthcare workers using a non-contact camera. Infants became unstable less often following non-contact imaging compared to indirect ophthalmoscopy ($p=0.015$). Only one safety event occurred within 10 minutes of imaging, even though a higher percentage of infants imaged first were unstable before imaging compared to those examined first (although there was no statistically significant difference between groups at baseline). Thus, the increased occurrence of safety events among those examined first was unlikely related to their baseline stability.

The use of a non-contact retinal camera was well tolerated by infants and has advantages in the setting of ROP screening compared to a contact retinal camera. In contrast to contact imaging, non-contact imaging avoids the risk of corneal abrasion or corneal toxicity from a topical anesthetic and reduces the risk of infection spread between infants being imaged. In addition, one study found that contact retinal imaging (i.e. RetCam™) caused greater oxygen desaturations in infants imaged for ROP compared to indirect ophthalmoscopy performed by ophthalmologists.³ During indirect ophthalmoscopy, the use of a lid speculum can cause bradycardia⁵ and more physiologic stress to the infant compared to no lid speculum.³ We did not use a lid speculum when performing non-contact retinal imaging.

A study limitation is that all infants were recruited from one study site with one ophthalmologist performing all clinical examinations. Thus, our results may not be generalizable to other sites and examiners. Also, we did not monitor infant stability beyond 10 minutes after examination/imaging.

In conclusion, compared to indirect ophthalmoscopy, non-contact retinal imaging may be a less stressful ROP screening alternative for infants assuming screening guidelines with this modality are validated.

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Potential Conflict of Interest/Sources of Funding:

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Figure 1:

A trained non-physician healthcare worker uses a non-contact retinal camera to image an infant at-risk for retinopathy of prematurity without the use of a topical anesthetic or lid speculum. The infant's eyelids are being held open gently with the aid of another healthcare worker. Extra care was taken to ensure that the front surface of the eye was not touched or dried out.

Table 1.

Occurrence of safety events^a by post menstrual age (PMA) at time of clinical examination or imaging and at baseline for those infants

PMA ^b (weeks)	Infants examined first			Infants imaged first		
		Unstable at baseline ^c	Became unstable after clinical exam		Unstable at baseline ^c	Became unstable after imaging
	#	# (%)	# (%)	#	# (%)	# (%)
26	1	1 (100)	0	-	-	-
27	-	-	-	1	1 (100)	0
30	1	1 (100)	0	1	1 (100)	0
31	27	7 (25.9)	0	15	6 (40.0)	0
32	21	9 (42.9)	2 (9.5)	6	2 (33.3)	0
33	36	15 (41.7)	3 (8.3)	13	5 (38.5)	0
34	31	11 (35.9)	2 (6.5)	9	5 (55.6)	0
35	37	13 (35.5)	4 (10.8)	22	8 (36.4)	0
36	26	7 (26.9)	1 (3.8)	9	6 (66.7)	0
37	27	6 (22.2)	3 (11.1)	14	4 (28.6)	0
38	20	8 (40.0)	0	8	2 (25.0)	0
39	12	7 (58.3)	0	7	3 (42.9)	0
40	12	3 (25.0)	0	6	3 (50.0)	1 (16.7)
41	8	2 (25.0)	0	1	1 (100)	0
42	9	3 (33.3)	2 (22.2)	1	0	0
43	5	0	0	2	0	0
44	6	0	1 (16.7)	1	1 (100)	0
45	2	1 (50.0)	0	-	-	-
46	4	0	0	-	-	-
47	-	-	-	-	-	-
48	1	0	0	-	-	-
50	1	0	0	-	-	-
51	-	-	-	1	0	0
Total	287 ^d	94 (32.8)	18 (6.3)	117 ^d	48 (41.0)	1 (0.85)

^aThe occurrence of a safety event was counted as present if the infant had any of the following occur: clinically significant bradycardia, tachycardia, desaturation, or apnea. Clinically significant “bradycardia” was defined as a heart rate <80 beats per minute and not rising for >5 seconds, “tachycardia” as a heart rate >230 beats per minute, “desaturation” as an oxygen saturation <80% or central cyanosis >5 seconds after the monitor alarm sounded, and “apnea” as no respiratory effort >20 seconds.

^bIf infants were examined/imaged on multiple days at a given PMA, we used the average occurrence of safety events at that PMA.

^cBaseline is considered the time between midnight and the time when dilating eye drops were instilled (usually 6–11 am)

^dFive infants were examined or imaged more than once at a given PMA and on 3 occasions infants imaging was not attempted due to patient instability after clinical examination.