Systemic Effects of Optos versus Indirect Ophthalmoscopy for Retinopathy of Prematurity Screening

Timothy H.M. Fung, MBChB, [1] Janine Abramson, [1,2] Shalini Ojha, PhD, [1,2] Roger Holden, MBBS,[1]

[1] Royal Derby Hospital, Uttoxeter Road, Derby, DE22 3NE, United Kingdom

[2] School of Medicine, University of Nottingham, Nottingham, NG7 2UH, United Kingdom

To be presented in part at: Association for Research in Vision and Ophthalmology Annual Meeting May 2018, Honolulu, Hawaii.

Financial support: We thank Optos PLC (Scotland, Dunfermline, United Kingdom) for providing us with £2000 to cover the costs of conducting the study. Optos PLC had no part in the design or conduct of this research. Optos PLC also had no part in the analysis of the data or the presentation of the findings.

No conflicting relationship exists for any author.

Correspondence to Dr Timothy HM Fung, Department of Ophthalmology, Royal Derby Hospital, Derby, DE22 3NE, United Kingdom. Email: timothyfung@doctors.org.uk

Unstructured abstract

A prospective randomised cross over study demonstrating for the first time that bedside retinopathy of prematurity screening is more stressful with the Optos California than with conventional binocular indirect ophthalmoscopy.

Many regions of the world have a relative shortage of ophthalmologists trained and willing to screen for retinopathy of prematurity (ROP).[1] As a result, many regions have turned to retinal imaging and telemedicine.[2] Optos ultra-widefield retinal imaging (Optos PLC, Dunfermline, UK) has recently been used as a screening tool for ROP.[3,4] However, there is no data available regarding the systemic effects or stress induced by an ROP screening examination with the Optos. In this prospective randomised cross over study we determined the effects of Optos ultra-widefield screening examination on cardiorespiratory indices, as a measure of stress, and compared the stress response to that of conventional binocular indirect ophthalmoscopy (BIO) examination. The East Midlands Leicester South Research Ethics Committee granted permission to undertake the study. Written informed consents were obtained from the mothers of all infants involved in the study. The study adhered to the tenets of the Declaration of Helsinki.

Any infants born at ≤32 week's gestation or weighing ≤1500 grams at birth were included. Each infant underwent bedside examination with the Optos California (Optos) and BIO for all of its scheduled screening sessions. The order of the examination methods performed was determined by randomisation via sealed envelopes prepared remotely by a member of the team not involved in the recruitment or screening of infants. Mydriasis was achieved with cyclopentolate 0.5% and phenylephrine 2.5% instilled in each eye at 30 minutes prior to examination commencing. Optos examination began with the instillation of proxymetacaine 0.5% into each eye followed by placement of a speculum in the right eye. The infant was gently lifted out of the incubator or cot and held upright to the Optos. Pseudocolour retinal images were acquired and the speculum was

then transferred to the fellow eye. Once images were captured from the fellow eye, the speculum was removed and the examination was deemed complete. BIO examination began with the instillation of proxymetacaine 0.5% into each eye followed by insertion of a speculum in the right eye. A 28-diopter lens was used together with an indirect ophthalmoscope to examine the retina of the infant in the supine position. The speculum was then transferred to the fellow eye and the retinal examination was repeated. Scleral indentation was not used. Once the examination was completed in the fellow eye, the speculum was removed and the examination was deemed complete. One neonatology nurse recorded observations of SaO_2, HR in beats per minute, and respiratory rate (RR) in breaths per minute on data collection forms for each examination method. SaO_2 and HR were measured using pulse oximetry, whereas the RR was recorded manually. All of the above cardiorespiratory indices were recorded immediately before instillation of topical anesthesia into both eyes (baseline values), immediately after insertion of the speculum into the first eye to be examined, immediately after the start and completion of the examination, and 10 minutes after the completion of the examination. The examination time, measured from the time of instillation of anesthetic drops to the removal of the speculum from the second eye examined, was recorded for each examination method.

The results of 50 screening examinations with the Optos and BIO on 26 infants (16 males and 10 females) were analysed. Of the 26 infants screened, two infants had stage 3 ROP and one infant had stage 1 ROP. The rest of the infants had no ROP. The mean gestational age was 27.9 weeks (standard deviation [SD], 2.2; range, 24-34) and the mean birth weight was 1135 g (SD, 375.8; range, 684-2110). The mean postnatal age at the time of examination was 34.5 weeks (SD,

2.2; range, 28-39). There was a median of two screening examinations per infant (range, 1-4). Of the 50 screening examinations, 50% were randomised to have the ROP screening examination starting with the Optos followed by BIO.

The cardiorespiratory indices over time for the two examination methods are shown in Figure 1. Using the paired T-test, none of the three cardiorespiratory indices varied significantly at baseline between the Optos and BIO. Some infants in the study underwent more than one screening examination with the Optos and BIO. Additionally, some infants underwent repeated measurements from each screening examination, due to both multiple timepoints and measurements by two examination methods. To account for this, a three level model linear regression analysis was used with individual measurements nested within individual screening examinations, which in turn was contained within infants. By using multilevel linear regression analysis, we found no significant difference in HR or RR between the two examination methods (P = 0.49 and P = 0.56, respectively). However, a significant difference in SaO_2 (P = 0.04) between the examination methods was found. The Optos examination method gave lower SaO_2 values, with values being, on average, 0.8% lower for the Optos group than for the BIO group. Handling of the infants required to position for image capture with the Optos may explain this finding. Mean examination times were 3.0 minutes (SD, 0.7) in the Optos group and 1.8 minutes (SD, 0.5) in the BIO group ($P < 0.001$). The longer duration of screening examination with the Optos might be a contributing factor to the lower SaO_2 levels found when compared to BIO examinations. No episodes of clinically significant bradycardia (HR < 100 beats per minute) or respiratory distress (RR < 30 breaths per minute) occurred during or after any screening examinations with the Optos or BIO. Of the 50

screening examinations, 5 (10%) in the Optos group and only 1 (2%) in the BIO group developed clinically significant oxygen desaturation (SaO_2 < 85%) during examination, precluding statistical analysis. No additional supplemental oxygen administration to the infants during these screening examinations was required as SaO_2 levels increased spontaneously or with stimulation. All episodes of clinically significant oxygen desaturation occurred for screening examinations performed in infants in the intensive care unit of the neonatology department.

Limitations of our study include firstly the small number of infants in a single center. Further studies with larger number of infants are required to verify our findings. Secondly, our institution provides only level 2 neonatal care and our study population may not be generalisable to sicker infants with more co-morbidities. Thirdly, the majority of the infants screened in this study had no ROP. Examination with BIO in this study may therefore have been less extensive or caused less distress to the infants than would normally be experienced in neonatology units that have infants with more severe forms of ROP. Finally, further studies that measure both the physiological and behavioural responses of stress are required to determine the complete stress response of infants to screening with the Optos.

In summary, the statistical difference in SaO_2 and the difference in the number of clinically significant oxygen desaturations found may indicate that ROP screening is more stressful with the Optos than with BIO. Careful handling and close monitoring of SaO_2 should be performed when the Optos is used for bedside screening. Greater attention should be paid to the sicker infants in the intensive care unit who seem to be the most vulnerable to clinically significant oxygen desaturations with the Optos examination.

References

1. Gilbert C, Rahi J, Eckstein M, et al. Retinopathy of prematurity in middle-income countries. Lancet 1997;350:12-4.
2. Chiang MF, Wang L, Busuioc M, et al. Telemedical retinopathy of prematurity diagnosis: accuracy, reliability, and image quality. Arch Ophthalmol 2007;125:1531-8.
3. Patel CK, Fung THM, Muqit MM, et al. Non-contact ultra-widefield imaging of retinopathy of prematurity using the Optos dual wave-length scanning laser ophthalmoscope. Eye (Lond) 2013;27:589-96.
4. Arnold RW, Grendahl RL, Winkle K, et al. Outpatient, wide-field, digital imaging of infants with retinopathy of prematurity. Ophthalmic Surg Lasers Imaging 2017;48:494-7.
5. Laws De, Morton C, Weindling M, et al. Systemic effects of screening for retinopathy of prematurity. Br J Ophthalmol 1996;80:425-8.

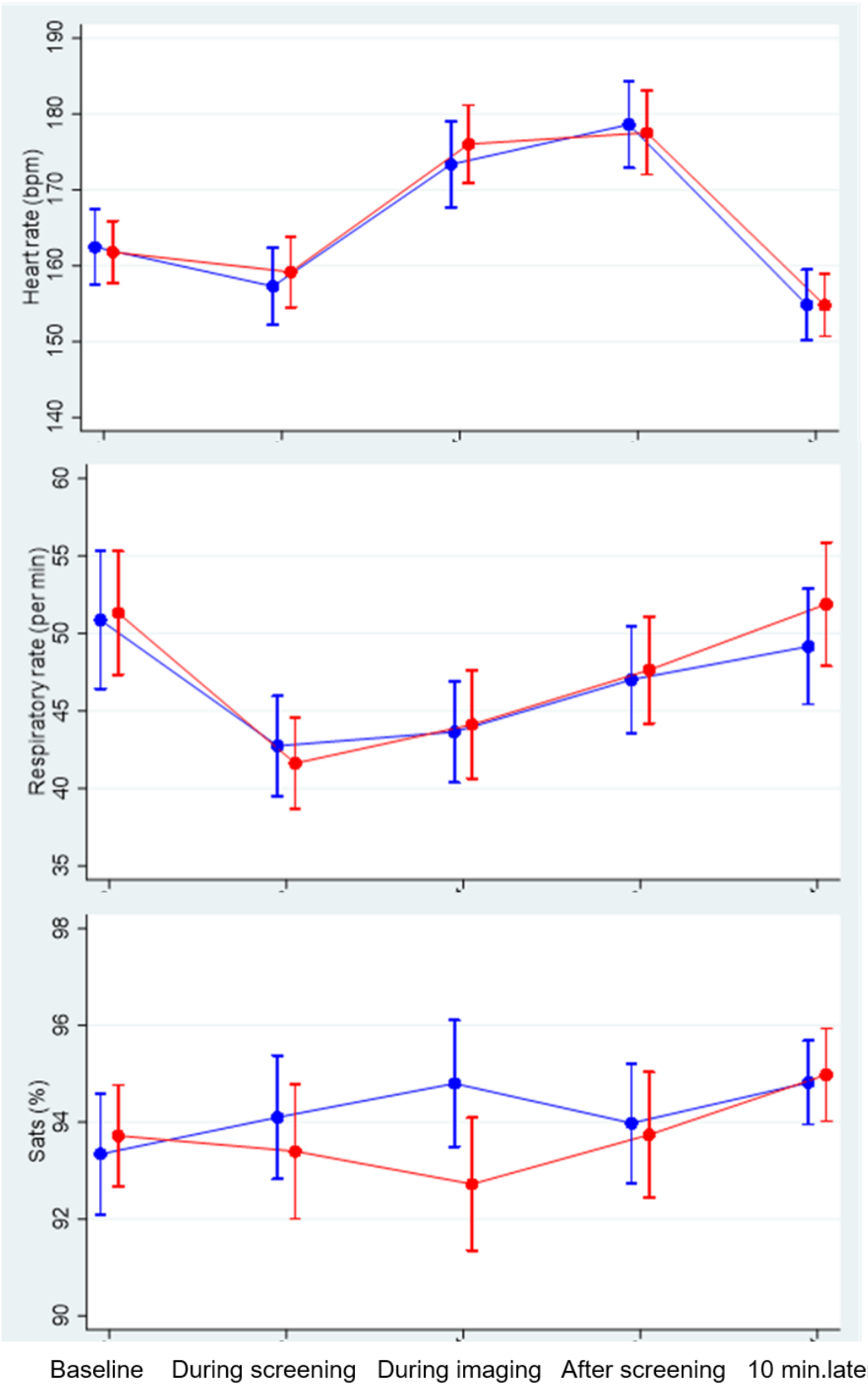

Figure 1. Cardiorespiratory indices during OPTOS and BIO examinations
Recordings during BIO are represented in blue and during OPTOS in red.
bpm, beats per minute; Sats, oxygen saturation level