Non-ophthalmologist screening for retinopathy of prematurity

Richard A Saunders, Margaret L Donahue, Jerry E Berland, Eric L Roberts, Billy Von Powers, Philip F Rust

Abstract

Aim—To determine if a non-ophthalmologist can accurately screen for retinopathy of prematurity (ROP) by evaluating the posterior pole blood vessels of the retina. ROP is a common ocular disorder of premature infants and may require multiple screening examinations by an ophthalmologist to allow for timely intervention. Since there is a strong correlation between posterior pole vascular abnormalities and vision threatening ROP, screening examinations performed by non-ophthalmologist may yield useful clinical information in high risk infants.

Methods—Infants born at the Medical University of South Carolina who met screening criteria (n = 142) were examined by a single non-ophthalmologist using a direct ophthalmoscope to evaluate the posterior pole blood vessels for abnormalities of the venules and/or arterioles. To determine the accuracy of the non-ophthalmologist’s clinical observations, infants were also examined by an ophthalmologist, using an indirect ophthalmoscope, who graded the posterior pole vessels as normal, dilated venules, or dilated and tortuous venules and arterioles (including “plus disease”).

Results—There was significant correlation (p <0.001) between the non-ophthalmologist’s and ophthalmologist’s diagnoses of posterior pole vascular abnormalities. 47 infants had normal posterior pole blood vessels by the non-ophthalmologist examination. Of these, 31 (66%) were considered to have normal vessels and 16 (34%) to have dilated venules by the ophthalmologist. The non-ophthalmologist correctly identified abnormal posterior pole vessels in all 21 infants diagnosed with abnormal arterioles and venules by the ophthalmologist. No infants with clinically important ROP (“prethreshold” or worse) would have failed detection by this screening method.

Conclusion—Using a direct ophthalmoscope, a non-ophthalmologist can screen premature infants at risk for ROP by evaluating the posterior pole blood vessels of the retina. While not necessarily recommended for routine clinical practice, this technique may nevertheless be of value to those situations where ophthalmological consultation is unavailable or difficult to obtain.

Retinopathy of prematurity (ROP) is a proliferative vascular disease characterised by abnormal blood vessel development and subsequent fibrosis in the peripheral retinas of prematurely born infants. ROP is a common disorder, occurring in up to 80% of infants born at 28 weeks’ gestation or less, and can lead to serious long term vision loss and even blindness. Clinical studies have documented improved visual outcomes in infants with “threshold” ROP after treatment with either trans-scleral cryotherapy or transpupillary laser therapy. The American Academy of Pediatrics, the American Association for Pediatric Ophthalmology and Strabismus, and the American Academy of Ophthalmology recently released a joint statement recommending that initial screening examinations be performed in “at risk” infants between 4 and 6 weeks of chronological age or 31 weeks and 33 weeks of post-conceptional age. Other detection strategies have also been proposed.

These examinations are usually performed by a paediatric ophthalmologist, retinal specialist, or general ophthalmologist experienced in the diagnosis of infants with ROP. Infants in many countries outside the United States, Western Europe, and Canada often fail to receive appropriate screening examination because of the unavailability of routine ophthalmological consultation. In a recent survey of schools for the blind in 23 “middle income” countries the proportion of severe visual impairment of blindness due to ROP ranged from 0% (most African countries) to 39% (Cuba). The authors recommend development of alternative screening programmes with guidelines appropriate to settings where routine ophthalmological consultation may assume a low priority because of the limited number of available ophthalmologists. Out of necessity, it follows that some of these examinations would have to be performed by non-ophthalmologist examiners. However,
little is known about the potential effectiveness of alternative screening programmes.

A recent study in premature infants has shown a significant correlation between the appearance of the posterior pole blood vessels and the severity of peripheral retinal disease in ROP. Infants with normal appearing posterior pole vessels had mild or no ROP, lessening the need for concurrent indirect ophthalmoscopic examination of the peripheral retina. Examination of the posterior pole vessels can be accomplished using a standard hand held (direct) ophthalmoscope and, more importantly, potentially be performed by non-ophthalmologists with reasonable accuracy after only minimal training. Our current study was undertaken as part of the training of a staff neonatologist (MLD) to evaluate the status of the posterior pole blood vessels in premature infant eyes. If deemed sufficiently reliable, preliminary screening by non-ophthalmologists could be used to detect infants with evidence of progressive ROP who might then receive expedited referral to a specialist for evaluation and appropriate intervention.

Subjects and methods

Premature infants admitted to the intensive care nursery at the Medical University of South Carolina Children’s Hospital between October 1993 and December 1994 (excluding 15 October to 7 December 1993) with birth weights less than 1600 g, were enrolled in the study. Approval of the protocol was obtained by the university’s institutional review board for human research. Routine screening examinations for ROP were performed before discharge or by 33 weeks post-conceptional age. Follow up examinations were performed as necessary, depending on clinical findings. Before each examination, the pupils were dilated with either Cyclomydrl or sequential instillation of cyclopentolate 0.5% and phenylephrine HCl 2.5%. Using a Cook-style paediatric eyelid speculum, funduscopic examination was performed 30–60 minutes later at the bedside.

A non-ophthalmologist (MLD) examined both retinas of each infant using a halogen bulb direct ophthalmoscope and recorded whether the blood vessels were normal or abnormal, based on reference photographs (Figs 1–4). Other than explanation of the fundus photographs and viewing several examples of vascular abnormalities through the teaching mirror of the indirect ophthalmoscope, the non-ophthalmologist examiner received no in-depth training in ophthalmoscopy or the evalu-
ation of posterior pole blood vessels before beginning this study. A vessel pair was considered abnormal if there was venous dilatation with or without accompanying dilatation or tortuosity of the retinal arteries. Venules were considered dilated if they were greater than twice the calibre of normal appearing arteries in the same eye, whereas the normal diameter ratio of venules to arteries is approximately 3:2. Twelve eyes could not be evaluated using direct ophthalmoscopy because of vitreous haze, poorly dilated pupils, or inability to obtain adequate focus on the posterior pole structures.

After the non-ophthalmologist’s findings had been recorded, a paediatric ophthalmologist (RAS) or paediatric ophthalmology fellow (JEB or ELR) examined both eyes using the indirect ophthalmoscope and graded the posterior pole blood vessels as 1, normal, 2, dilated venules, or 3, dilated and tortuous arteries and venules using the same photographic guidelines. Dilated and tortuous vessels did not necessarily imply that “plus disease” was present; but plus disease is included as a subset in this third group. Finally, an examination of the peripheral retina was performed using scleral depression and the findings recorded using the International Classification of ROP. The ophthalmologist examiner was not aware of the findings of the non-ophthalmologist examiner until each posterior pole examination was complete and the data recorded for both eyes. Infants with previously identified retinovascular abnormalities who were familiar to the non-ophthalmologist were excluded from the data analysis.

Results

Our results are summarised in Tables 1–4. A total of 142 infants were evaluated by both an ophthalmologist and non-ophthalmologist examiner. Twelve infants had incomplete examinations by the non-ophthalmologist because of inability to assess the posterior pole with the direct ophthalmoscope. These 12 infants are included in the “abnormal blood vessel” category in Tables 1 and 2. On peripheral retinal examination, eight had immature vessels without ROP, three had zone II, stage 2 ROP, and one had zone II, stage 3 ROP.

Table 1 shows the correlation between the non-ophthalmologist’s interpretation of the posterior pole vessels and the ophthalmologist’s findings for the same infants. Of the 142 infants examined by the non-ophthalmologist, 95 (67%) were felt to have retinovascular abnormalities.

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**Table 1** Posterior pole vascular findings, ophthalmologist’s versus non-ophthalmologist’s examination

<table>
<thead>
<tr>
<th>Ophthalmologist’s examination</th>
<th>Normal blood vessels</th>
<th>Abnormal blood vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal posterior pole</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td>Dilated venules</td>
<td>16</td>
<td>58</td>
</tr>
<tr>
<td>Abnormal arterioles and venules</td>
<td>0</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>95</td>
</tr>
</tbody>
</table>

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**Table 2** Non-ophthalmologist’s posterior pole vascular findings compared with severity of retinopathy of prematurity on peripheral retinal examination

<table>
<thead>
<tr>
<th>Normal blood vessels</th>
<th>Abnormal blood vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ROP, mature</td>
<td>12</td>
</tr>
<tr>
<td>No ROP, immature</td>
<td>30</td>
</tr>
<tr>
<td>Zone III, stage 1</td>
<td>2</td>
</tr>
<tr>
<td>Zone III, stage 2</td>
<td>1</td>
</tr>
<tr>
<td>Zone III, stage 3</td>
<td>2</td>
</tr>
<tr>
<td>Zone II, stage 1</td>
<td>1</td>
</tr>
<tr>
<td>Zone II, stage 2</td>
<td>1</td>
</tr>
<tr>
<td>Zone I, stage 1</td>
<td>1</td>
</tr>
<tr>
<td>Zone I, stage 2</td>
<td>1</td>
</tr>
<tr>
<td>Zone I, stage 3</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
</tr>
</tbody>
</table>

*One infant with zone II, stage 2 had “plus disease”, consistent with prethreshold retinopathy of prematurity.
†All of these infants were considered to have either prethreshold or threshold retinopathy of prematurity.

Of these, 16 (17%) were judged by the ophthalmologist to have normal posterior pole blood vessels. By the non-ophthalmologist’s examination, 47 infants had normal posterior pole blood vessels. Thirty one of these were also considered normal by the ophthalmologist, while 16 were found to have dilated venules. Importantly, all 21 infants with both abnormal arterioles and venules according to the ophthalmologist’s examination were correctly identified as abnormal by the non-ophthalmologist.

Table 2 compares the non-ophthalmologist’s posterior pole vascular findings with the severity of ROP on peripheral retinal examination as determined by the ophthalmologist. None of the 17 children diagnosed with prethreshold or threshold ROP was thought to have normal posterior pole vessels by the non-ophthalmologist. With one exception, all infants with ROP of zone II, stage 2 severity or worse were identified as having abnormal posterior pole vessels by the non-ophthalmologist. Table 3 compares the ophthalmologist’s posterior pole vascular findings with the severity of ROP on peripheral retinal examination. Dilated venules seemed to be a non-specific finding; 16 of 74 infants (22%) with dilated venules had mature retinal vessels and 30 of 74 (41%) had immature retinal vessels, but no evidence of ROP. The majority of infants (77%) with prethreshold ROP had both...
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Table 4 Posterior pole vascular findings. Three dimensional frequency analysis of interreader interaction, non-ophthalmologist/retinopathy of prematurity interaction, and ophthalmologist/retinopathy of prematurity interaction

<table>
<thead>
<tr>
<th>Non-ophthalmologist’s examination</th>
<th>Peripheral retinal findings</th>
<th>Normal</th>
<th>Abnormal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal blood vessels</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mature</td>
<td>5</td>
<td>7</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Immature or less than prethreshold</td>
<td>26</td>
<td>9</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Prethreshold or threshold</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>16</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Abnormal blood vessels</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mature</td>
<td>0</td>
<td>11</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Immature or less than prethreshold</td>
<td>16</td>
<td>51</td>
<td>67</td>
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<tr>
<td>Prethreshold or threshold</td>
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<td>17</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>79</td>
<td>95</td>
<td></td>
</tr>
</tbody>
</table>

abnormal arterioles and venules, and the remaining (23%) dilated venules but normal arterioles. By definition, all four infants with threshold ROP had abnormal arterioles and venules.

Table 4 is a three dimensional frequency analysis that shows three interactions: 1, the non-ophthalmologist’s evaluation of the posterior pole blood vessels correlated with the ophthalmologist’s evaluation of the same vessels (interobserver interaction); 2, the relation of the non-ophthalmologist’s posterior pole findings with the peripheral retinal examination (non-ophthalmologist/ROP interaction); and 3, the relation of the ophthalmologist’s posterior pole diagnosis with the peripheral retinal findings using indirect ophthalmoscopy (ophthalmologist/ROP interaction). Using log linear analysis, each of these interactions is significant: interobserver interaction, \( \chi^2 = 31.05, df = 1 (p <0.001) \); non-ophthalmologist/ROP interaction, \( \chi^2 = 14.44, df = 2 (p <0.001) \); ophthalmologist/ROP interaction, \( \chi^2 = 17.18, df = 2 (p <0.001) \). In this table, dilated venules and abnormal arterioles and venules are combined into the “abnormal” category for the ophthalmologists’ findings since infants found to have any vascular abnormalities by the non-ophthalmologist were considered abnormal. In each of the 17 prethreshold and threshold cases, both the non-ophthalmologist and the ophthalmologist considered the posterior pole vessels to be abnormal.

Discussion

Our results suggest that a non-ophthalmologist can be trained to screen premature infants for retinovascular abnormalities associated with severe ROP. While the standard of practice in the United States currently calls for ophthalmological screening for high risk premature infants, staffing considerations may make this impractical in other parts of the world. A screening protocol relying on non-ophthalmologists could potentially be more comprehensive and cost effective by obviating the need for specialist consultation for every infant, yet allowing appropriate referral for the majority of high risk cases potentially requiring surgical intervention. In our experience, preventable blindness from ROP has almost always been associated with failure to perform appropriate screening or follow up examinations, not failure to diagnose correctly. Therefore, even in nursery environments where ophthalmic consultation is more readily available, examination of posterior pole retinal blood vessels by non-ophthalmologists may still have diagnostic value.

Although a non-ophthalmologist screening protocol may be a useful clinical tool, there are several points that must be addressed. Firstly, consistent agreement on the diagnosis of dilated venules, even among ophthalmologists, was difficult to achieve. The comparison of the diameter of venules to arterioles was often borderline at a 2:1 ratio and might vary among vessel pairs within the same eye. In an emmetropic eye, image magnification with the direct ophthalmoscope is approximately five times greater than the indirect ophthalmoscope using a 20 dioptre condensing lens, and seven times greater than a 30 dioptre condensing lens. A certain amount of disagreement among examiners using different ophthalmoscopes would therefore be expected. Furthermore, during examination with the direct ophthalmoscope, often only one vessel pair can be adequately visualised. It is possible that the specific pair examined may or may not be abnormal, although vessel pairs that were not examined may have dilated venules or even arteriolar tortuosity. This problem can be overcome by examining more than one vessel pair in each fundus. Examiner persistence and perhaps prolonged or sequential examinations may sometimes be required.

While our high sensitivity for detecting posterior pole vascular abnormalities indicates that a non-ophthalmologist would not be likely to miss clinically important ROP on routine screening, specificity was poor. In this study, “abnormal” posterior pole blood vessels were identified in two thirds of infants undergoing screening examination by the non-ophthalmologist examiner using a direct ophthalmoscope (Table 1). This would lead to many unnecessary referrals of low risk infants. Our arbitrary definition of dilated venules (greater than 2:1 ratio of the diameter of venules to arterioles) may therefore need to be revised to improve specificity in the correlating of posterior pole findings with important peripheral retinal disease. More precise grading of posterior pole vascular abnormalities, as we have proposed using the indirect ophthalmoscope, might also be possible.

Secondly, dilatation of the pupils and use of an eyelid speculum is generally required regardless of whether a non-ophthalmologist or ophthalmologist performs the screening examination. Dilating eye drops need to be available in appropriate concentrations for premature infant to minimise potential medication side effect. The non-ophthalmologist will require appropriate training to place an eyelid speculum in the eye without scratching the cornea or damaging adnexal structures.

Thirdly, training of our non-ophthalmologist examiner using reference photographs and funduscope examination through the teaching mirror of an indirect ophthalmoscope probably improved our results. Other non-ophthalmologists interested in using this screening protocol would presumably require
similar instruction to achieve an acceptable level of accuracy. Currently, there are no known programmes teaching these techniques to non-ophthalmologists. However, the experience needed to become competent in posterior pole vessel evaluation with the supervision of an ophthalmologist may be as few as 20–25 examinations, assuming that these would include infants with varying degrees of abnormal posterior pole vascular findings.

It must also be stressed that the finding of normal posterior pole vessels at one point in time does not rule out the potential for developing blinding ROP later on. This screening protocol requires sequential examinations, documenting repeatedly normal posterior pole vessels or, alternatively, referral to an ophthalmologist for further evaluation. Previous studies on the natural progression of ROP have documented that the majority of infants with varying degrees of abnormal posterior pole vascular findings.

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