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 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 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 altered 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 post-conceptional 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,
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 Cyclomydrol 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 consid-
ered abnormal if there was venous dilatation with or without accompanying dilatation or
tortuosity of the retinal arterioles. Venules were consi-
cidered dilated if they were greater than

twice the calibre of normal appearing arterioles in the same eye, whereas the normal diameter
ratio of venules to arterioles 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 ophthalmo-
ologist (RAS) or paediatric ophthalmology fellow
(JEB or ELR) examined both eyes using the
indirect ophthalmoscope and graded the pos-
terior pole blood vessels as 1, normal, 2, dilated
venules, or 3, dilated and tortuous arterioles
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 sub-
set in this third group. Finally, an examination of
the peripheral retina was performed using
ciliary depression and the findings recorded
using the International Classification of ROP.17

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 retino-
vascular 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 exam-
iner. Twelve infants had incomplete exami-
nations 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 reti-
nal 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 ophthalmolo-
gist's findings for the same infants. Of the 142
infants examined by the non-ophthalmologist,
95 (67%) were felt to have retinovascular
abnormalities.

<table>
<thead>
<tr>
<th>Ophthalmologist’s examination</th>
<th>Non-ophthalmologist’s examination</th>
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</thead>
<tbody>
<tr>
<td>Normal posterior pole</td>
<td>Normal blood vessels</td>
</tr>
<tr>
<td></td>
<td>Abnormal blood vessels</td>
</tr>
<tr>
<td>31</td>
<td>16</td>
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<tr>
<td>Dilated venules</td>
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<td>Abnormal arterioles and</td>
<td>2</td>
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<td>venules</td>
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<td>Total</td>
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Table 2 compares the non-ophthalmologist’s
posterior pole vascular findings with the sever-
ity 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 in-

fants with ROP of zone II, stage 2 severity or
worse were identified as having abnormal pos-
terior pole vessels by the non-ophthalmo-
ologist.

Table 3 compares the ophthalmologists’ pos-
terior pole vascular findings with the severity
of ROP on peripheral retinal examination. Di-
lated 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

<table>
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<tr>
<th>Table 1 Posterior pole vascular findings, ophthalmologist’s versus non-ophthalmologist’s examination</th>
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<tr>
<td>Ophthalmologist’s examination</td>
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<td>95 (67%) were felt to have retinovascular</td>
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<td>abnormalities.</td>
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<table>
<thead>
<tr>
<th>Table 2 Non-ophthalmologist’s posterior pole vascular findings compared with severity of retinopathy of prematurity on peripheral retinal examination</th>
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<tbody>
<tr>
<td>Normal blood vessels</td>
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<tr>
<td>----------------------</td>
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<tr>
<td>No ROP, mature</td>
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<tr>
<td>No ROP, immature</td>
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<tr>
<td>Zone III, stage 1</td>
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<tr>
<td>Zone III, stage 3</td>
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<tr>
<td>Zone I, stage 3</td>
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<td>Total</td>
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</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.
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>Examination</th>
<th>Ophthalmologist’s examination</th>
<th>Normal</th>
<th>Abnormal</th>
<th>Total</th>
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</thead>
<tbody>
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<td>26</td>
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<td>Total</td>
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<td>Abnormal blood vessels</td>
<td>Mature</td>
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<td>11</td>
<td>11</td>
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<tr>
<td></td>
<td>Immature or less than prethreshold</td>
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<td></td>
<td>Total</td>
<td>16</td>
<td>79</td>
<td>95</td>
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</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 funduscopy 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-opthalmologists. 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 infant retinas show mature vasculature by 38 weeks’ post-conceptional age. It would therefore seem prudent that each high risk infant receive, where available, at least one peripheral retinal examination by an ophthalmologist at approximately 38 weeks’ post-conceptional age to document retinal vascularisation into zone III. However, in countries where ophthalmological consultation is not routinely available and the incidence of cicatricial ROP is high, examinations by non-opthalmologists might represent the only screening a high risk infant receives before hospital discharge.

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