Br Ir Orthopt J 2007; **4:** 54–57

Incidence and nature of orthoptic problems found in children previously screened for retinopathy of prematurity: an argument for orthoptic follow-up?

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Abstract

Aim: **To determine the incidence and type of visual and/or binocular defects in infants previously screened for and found to have insignificant or no retinopathy of prematurity (ROP).**
Methods: **The case notes of a consecutive cohort of children who had passed screening for ROP were reviewed retrospectively. Details of attendance, orthoptic assessments, related investigations and outcome were documented with particular attention to the incidence and type of ocular defect.**
Results: **One hundred and eight cases were reviewed; 78 cases met the inclusion criteria. Nineteen patients had an ocular defect that required treatment or ongoing orthoptic review. Eleven children had strabismus, of whom 8 had constant esotropia and 3 had intermittent exotropia. Other defects were refractive error (without strabismus), congenital idiopathic nystagmus and a case of an upper lid haemangioma.**
Conclusions: **The review confirmed a higher prevalence of strabismus and visual/binocular defects in patients who had previously passed screening for ROP compared with the normal population. Constant esotropia was the most common form of strabismus found.**

Key words: Amblyopia, National guidelines, Retinopathy of prematurity, Strabismus

Introduction

Retinopathy of prematurity (ROP) is a proliferative retinopathy which can affect preterm infants of low birth weight. It is still not fully understood what causes the condition. The most consistent risks remain low birth weight and a degree of prematurity, but other variable factors are also involved.

ROP is not entirely preventable but medical intervention is vital, as it has been conclusively demonstrated that severe ROP may be successfully treated, and this forms the basis for screening all children at risk of developing the condition.

The nationally accepted recommendation for screening of ROP, as set out by the Royal College of Ophthalmologists,[1] is to screen all infants born weighing less than 1500 g and those born before 32 weeks gestation at around 6 weeks postnatally. This is repeated at least every 2 weeks until 36 weeks gestational age or retinal vascularisation has progressed to retinal zone 3.

Whilst clear guidelines for ophthalmic screening of ROP exist there are no recommendations for the longer term follow-up of premature infants. In this review the infants previously screened for, and found to have no or mild ROP were followed up for 2 years by the orthoptic department. The purpose was to determine the incidence and type of visual and/or binocular defects in these preterm children.

Methods

A retrospective review of the case notes of pre-term infants who consecutively passed screening for ROP was performed. A pass was classed as no ROP, stage 1 or stage 2 ROP. All the children were screened by the same consultant in the neonatal unit of Countess of Chester Hospital between July 1998 and December 2002. All were given a 6 month review appointment with an orthoptist. If the child passed the orthoptic assessment at the 6 month review the parents were offered a review with the orthoptist and the ophthalmic consultant at 2 years of age. The parent could contact the orthoptic department for an earlier review if they had any concerns about their child's visual development.

At the review visits orthoptic assessment consisted of uniocular visual acuity, cover test, ocular motility and assessment of binocular single vision where possible. Cycloplegic refraction and fundus and media examination were conducted at the 2 year follow-up appointment by the consultant ophthalmologist if not necessitated before.

Although the ultimate decision to discharge at the 2 year follow-up was by the ophthalmologist, the criteria

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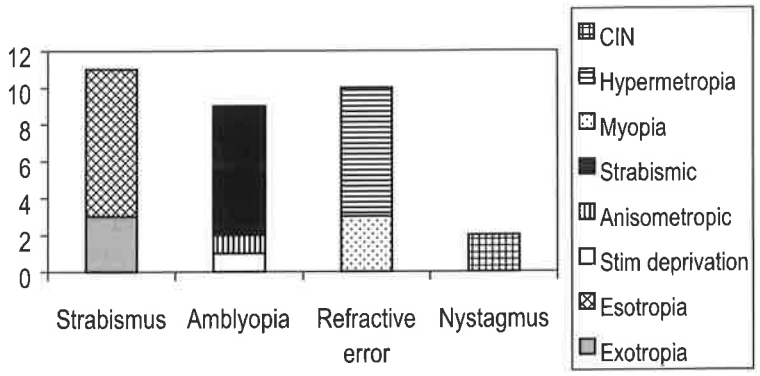

Fig. 1. The range of orthoptic-related defects found. CIN, congenital idiopathic nystagmus.

included satisfactory and equal monocular visual acuity, normal cover test and ocular motility, a normal response to a 20 dioptre prism, no defect of fundus and media, and no refractive error the consultant considered significant.

A patient who had failed to attend any review appointment was excluded from the case note analysis. Information recorded included gestational age, birth weight, mode of delivery, presence of documented intraventricular haemorrhage or periventricular leukomalacia, presence and degree of ROP, and the presence of strabismus, ocular motility or visual acuity defect.

For those patients diagnosed with an ocular defect the diagnosis, refractive error, presence of amblyopia, ophthalmic family history, general development, age of onset, and treatment were documented.

Results

One hundred and eight pre-term infants passed the ROP screening. Thirty infants subsequently failed to attend on, or prior to, the 2 year follow-up appointment and were therefore excluded. The data for 78 cases remained for analysis.

Fifty-nine patients (76%) were discharged at the 2 year follow-up appointment. Of the 29 who were not discharged, 19 were diagnosed with an ocular defect and for 10 the diagnosis was uncertain. The uncertainty was due to poor cooperation with uniocular vision testing or subnormal visual acuity in the absence of pathology or significant refractive error.

General findings

The mean gestational age for the 78 infants was 29.04 weeks (range 25–35 weeks) and the mean birth weight was 1.24 kg (range 0.55–1.97 kg). Forty-seven infants (60%) were born via emergency caesarean section, and 19 (24%) were born as part of a multiple birth.

Nineteen children (24%) were documented as having some degree of intraventricular haemorrhage (elicited by cranial ultrasound), and 4 (5%) were confirmed as having periventricular leukomalacia. Sixty-six (85%) children were felt to have 'age-appropriate' general development of the central nervous system at the 2 year follow-up, and 12 (15%) had some degree of developmental delay.

From the initial ophthalmic screening 61 infants (78%) had no ROP, 11 (14%) had stage 1 ROP, and 6 (8%) progressed to but not past stage 2 ROP. Fifty-nine infants passed the 6 month orthoptic assessment and the orthoptic and ophthalmic assessment at 2 years and were discharged. During the 2 year review period 19 patients were diagnosed with a defect of binocular vision, ocular motility or visual acuity which required intervention or monitoring. The type of defect is summarised in Fig. 1. The defects were strabismus ($n = 11$), refractive error without strabismus ($n = 5$), congenital idiopathic nystagmus (CIN) ($n = 2$) and upper lid haemangioma ($n = 1$). Regardless of aetiology 11 children developed amblyopia that required occlusion therapy and 8 had refractive error sufficient to require correction. The details of the 19 patients are summarised in Table 1.

Strabismus

Of the 11 patients with strabismus 3 had intermittent exotropia and were kept under orthoptic care. Eight children had constant esotropia, 4 of whom had esotropia with an accommodative element. All the cases of esotropia required active treatment of correction of hypermetropic refractive error ($n = 4$), occlusion therapy for amblyopia ($n = 7$) and squint surgery that was within the 2 year period ($n = 4$).

Refractive error (without strabismus)

Five patients had refractive error not associated with strabismus that required correction with glasses. The need for correction of the refractive error was based on the personal preference of the ophthalmologist. Three children were myopic (range –0.75 to –3.50 DS), 1 of whom required occlusion therapy for anisometropic amblyopia. Two children were hypermetropic (range +1.00 to +3.50 DS).

Nystagmus

Two patients were diagnosed in early infancy with manifest horizontal nystagmus. Following early ophthalmic review and electrodiagnostic testing both were confirmed as having congenital idiopathic nystagmus. One of these patients required glasses to correct hypermetropic astigmatism at 2 years of age.

Table 1. Characteristics of individual patients found to have an orthoptic problem

ID	Diagnosis	Treatment			Birth weight (kg)	Gestational age (weeks)	ROP stage	IVH/PVL	Family history	General health	Documented age at onset
		Occlusion	Glasses	Surgery							
01	Infantile esotropia	N	N	Y	1.13	30/40	1	IVH	Nil	Mild CP	9 months
02	Constant accommodative esotropia	Y	N	N	0.81	25/40	2	Nil	Nil	Age-appropriate	2 years
03	Intermittent distance exotropia	N	N	N	1.35	29/40	Nil	Nil	Nil	Pierre Robin syndrome	2 years
04	Anisomyopia	Y	Y	N	1.37	28/40	Nil	Nil	F myopic	Age-appropriate	2 years
05	Myopic astigmatism	N	Y	N	1.15	28/40	Nil	IVH	Nil	Age-appropriate	2 years
06	Congenital idiopathic nystagmus	N	N	N	1.18	30/40	Nil	Nil	M myopic	Age-appropriate	4 months
07	Hypermetropia	N	Y	N	1.13	28/40	Nil	Nil	Nil	Age-appropriate	2 years
08	Intermittent distance exotropia	N	N	N	1.35	31/40	Nil	Nil	Nil	Age-appropriate	2 years
09	Constant non-accommodative esotropia	Y	N	N	1.35	30/40	Nil	PVL	F myopic	Age-appropriate	1 year
10	Constant accommodative esotropia	Y	Y	N	1.2	29/40	Nil	Nil	Nil	Cerebral Palsy	2 years
11	Intermittent distance exotropia	N	N	N	1.16	32/40	Nil	Nil	Nil	Cerebral palsy	18 months
12	Infantile esotropia	Y	N	Y	0.82	25/40	2	IVH + PVL	Nil	Age-appropriate	6 months
13	Constant accommodative esotropia	Y	Y	N	1.13	30/40	1	PVL	Nil	developmental delay	2 years
14	Constant non-accommodative esotropia	Y	Y	Y	1.43	30/40	Nil	PVL	Nil	Mild CP	1 year
15	R upper lid haemangioma	Y	N	N	0.73	27/40	Nil	Nil	Nil	Cerebral palsy	Birth
16	Anisohypermetropia	N	Y	N	1.51	28/40	2	IVH	Nil	Age-appropriate	2 years
17	Myopia	N	Y	N	1.36	35/40	Nil	Nil	Nil	Age-appropriate	2 years
18	Constant accommodative esotropia	Y	Y	N	1.64	30/40	Nil	Nil	Nil	Age-appropriate	1 year
19	Congenital idiopathic nystagmus	N	Y	N	1.2	34/40	Nil	Nil	2 sibling with squint + glasses	Age-appropriate	1 month (astigmatism 2 years)

IVH, intraventricular haemorrhage; PVH, periventricular haemorrhage.

Haemangioma

One patient had an upper lid haemangioma and required occlusion therapy for stimulus deprivation amblyopia.

Re-referrals

Eight of the 59 infants who had been discharged at the 2 year review were re-referred in the following 2 year period (i.e. at 3–4 years of age). Three of these children had no abnormality when reassessed by the orthoptist. Five children were found to have an ocular defect: 2 were myopic, 1 hypermetropic, 1 had a constant esotropia, and 1 an intermittent exotropia.

Discussion

In accordance with previous studies, this retrospective case note review revealed a greater incidence of strabismus and related ocular defects in children previously screened for and found to have insignificant or no ROP compared with the normal population.[2–6] Most studies agree that although the incidence of strabismus is higher in those with a degree of ROP it is also higher than the normal population in those with no ROP.[4]

In this review 19 of the 78 infants (24%) screened who met the inclusion criteria were found to have some form of visual or binocular abnormality. Strabismus was found in 14%, amblyopia in 12% and refractive error in 9% of infants. Miscellaneous findings of CIN and an upper lid haemangioma were seen in 3 cases. Most recent large population studies indicate a prevalence of between 3% and 5% for strabismus and 1% and 4% for amblyopia in the normal population.[7,8] Figures for refractive error are more difficult to determine but one study conducted in The Netherlands found an incidence of 5% in the normal population of pre-school infants.[9]

Although many studies have addressed the association of strabismus with prematurity, very little has been documented on the types of strabismus found. O'Connor *et al.*[3] reported a 1:1 exotropia to esotropia ratio in a low-birth-weight cohort which included all stages of ROP. More specifically they found an especially high prevalence of intermittent near exotropia (10% of the strabismus group). Holmstrom *et al.*[5] reported esotropia to be the most predominant type of strabismus found in a group of 229 premature infants assessed which included those with all grades of ROP. Of the 31 children with strabismus, 24 had esotropia (77%) and 7 had some form of exotropia. In this review 8 children had constant esotropia, which represents 73% of those with strabismus. Four had esotropia with an accommodative element. All 3 cases of exotropia were intermittent distance exotropia.

The literature regarding other miscellaneous ophthalmological findings in infants with ROP is sparse. Holmstrom *et al.*[5] reported nystagmus in 11 of 229 premature children reviewed. Of these 11 cases, 10 children had severe ROP; only 1 child had no ROP.

Most studies concerned with the incidence of strabismus highlight the difficulties of studying a group of infants in which many variables exist. Many factors associated with premature birth are interrelated, such as

gestational age, ROP and abnormal ultrasonic brain scans. However, some studies have shown certain factors to be independently related to strabismus; these are severe ROP, birth weight, refractive error, family history, cerebral palsy and hand–eye co-ordination/ locomotor skills.[3,10] Regardless of these factors, prematurity alone appears to remain a risk factor for strabismus and related defects.

The follow-up programme used in this study was a minimum of two appointments: one at 6 months of age and one at 2 years of age. The rationale for the timing of the 6 month review was to assess early visual behaviour and ocular alignment at a time when this should be fairly well established. The 2 year review was chosen as this is when cooperation with testing improves and when most aspects of eventual strabismus have developed. Five patients who were discharged at the 2 year check were re-referred and confirmed to have an ocular defect. They had therefore been 'missed' by the follow-up programme. Ten children were uncooperative for full orthoptic testing and consequently the presence or absence of a defect was not confirmed during the 2 year follow-up period.

Whilst clear guidelines for ophthalmic screening of ROP exist there are no recommendations for the longer term follow-up of premature infants. Schalij-Delfos *et al.*[2] recommended that parents should be given 'uniform screening advice' and informed that their child is more at risk of developing an ophthalmic problem in time. They concluded that all infants born before 32 weeks gestation should be selected for long-term ophthalmic follow-up in order to detect strabismus, amblyopia and refractive error. They suggested 'screening' these infants at 1 year, in the third year of life (preferably at 30 months) and just before school age. Holmstrom *et al.*[5] suggested beneficial timings of follow-up of 12 months (if one examination was performed), at 12 and 24 months (if two were performed), and at 12, 24 and 42–48 months (if three were performed). They reported that increased ophthalmic morbidity is to be expected in all prematurely born children, and this included infants who had not suffered ROP. They recommended follow-up for preterm infants screened for ROP.

The data presented in this study support the need for orthoptic and ophthalmic follow-up for children previously screened for ROP to ensure early diagnosis and implementation of treatment for conditions such as strabismus, amblyopia and refractive error. The frequency and timing of the follow-up need to be determined. With this information the development of nationally defined guidelines for the specialised eye care of premature infants with no or mild ROP would aid the clinician.

Conclusions

This study confirmed a higher incidence of visual and binocular defects in children previously screened for and found to have no, or insignificant, ROP. Constant esotropia was more prevalent than exotropia, and all the cases of exotropia were intermittent.

The research and development co-ordinator at the Countess of Chester Hospital NHS Trust and the local research ethics committee representative have approved this work. The authors have no competing interests.

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