Observational study *Clin Ter 2023; 174 (1):48-52* *doi: 10.7417/CT.2023.2496*

Effectiveness of diagnosis and early treatment of ocular motility alterations in premature infants

A. M. Comberiati[1], M. Graziani[1], M. Malvasi[1], E. Trovato Battagliola[1], S. Compagno[1], V.M. Malvasi[2], R. Migliorini[1], M. Salducci[1]

[1]Department of Sense Organs, University Sapienza of Rome, Rome, Italy; [2]Department of Odontostomatological and Maxillo-Facial Sciences, University Sapienza of Rome

Abstract

Objective. Prematurity often results in important developmental sequelae of brain structures, particularly those involved in processing visual information, such as the optic nerve, primary visual cortex and visuomotor integration areas. The aim of this study is to analyse the functionality of the sensory and motor pathways of the visual system by means of an orthoptic-ophthalmological assessment.

Materials and methods. In this retrospective study, 151 records were examined, covering a period from 2000 to 2020, of preterm patients with gestational age < 32 weeks and birth weight ≤ 1,500 g up to an average age of about 8 years, referred to the Centre for Paediatric Ophthalmology and Strabology of the Ophthalmology Clinic of the Policlinico Umberto I, La Sapienza University of Rome, who underwent a complete ophthalmological and orthoptic assessment including the following tests measurement of ocular deviations according to the Hirschberg method, Lang I-II test, Titmus Stereotest, objective convergence assessment and ocular motility examination.

Results. From the charts reviewed, 24.5% (37/151) of patients had Retinopathy of the Premature (ROP); while 38% of the whole sample (57/151) had strabismic amblyopia, of the latter only 31.5% (18/57) had ROP. In 8% of patients (12/151) the stereoscopic sense was absent, in 45% (8/151) stereopsis was gross (> 60 seconds of arc). In addition, 20.52 % (31/151) had a manifest eye deviation. 7.28% (11/151) had hypermetropia in the right eye (RE); 7.95% (12/151) hypermetropia in the left eye (OS); 3.31% of the patients (5/151) had myopia in the RE; 2% (3/151), myopia in the left eye (LE). In addition, the study of ocular motility revealed varying degrees of alteration poorly correlated with prematurity status.

Conclusion. It was found that amblyopia, stereopsis and objective convergence are more affected by ROP than strabismus, refractive defects and ocular motility, indicating that premature children are particularly susceptible to ophthalmological and orthoptical alterations.
Clin Ter 2023; 174 (1):48-52 doi: 10.7417/CT.2023.2496

Key words: *refractive defects, premature children, ROP, stereopsis, ocular motility*

Introduction

"The World Health Organization" (WHO) defines preterm birth as any birth before 37 completed weeks of gestation, or fewer than 259 days since the first day of the woman's last menstrual period (LMP)" (1). A preterm birth occurs when labour contractions begin before the foetus has completed its normal development and the chances of survival depend essentially on its weight at the time of delivery (2,3). According to gestational age, preterm birth is further subdivided into 'late preterm' between 34 and 37 weeks, 'moderate preterm' is defined as between 32 and 34 weeks, 'very preterm' between 28 and 32 weeks and 'extremely preterm' before 28 weeks of gestation (4, 5). Despite the reduction in the mortality rate of preterm infants, thanks to scientific progress and improved neonatal supportive care, there is still a higher incidence of chronic systemic sequelae such as asthma and visual and neurodevelopmental abnormalities (such as cerebral palsies, reduced motor skills, cognitive and behavioural deficits) in preterm infants than in term-born children, leading to a progressive medical and scientific development of long-term care of ophthalmic and neurological problems (6, 7).

It is known that the ophthalmological impairment most commonly associated with preterm birth is retinopathy of prematurity, (ROP), which causes severe consequences on visual function. Other conditions of visual impairment in preterm infants include: increased incidence of refractive errors, amblyopia, reduced stereoscopic sense, and alterations in ocular motility, negatively impacting the development of brain structures, particularly those involved in processing visual information, such as the optic nerve, primary visual cortex, and visuomotor integration areas, and also affecting other aspects of development, including psychological and educational ones (8-10). The aim of this study is to assess which ocular and orthoptic changes are most frequent in patients with gestational age < 32 weeks and birth weight ≤ 1,500 g, subsequently treating them with the most appropriate care on a case-by-case basis. Early ophthalmological and orthoptic assessment of preterm infants can limit the functional and visual deficits of these young patients and facilitate their early recovery and insertion into the school and thus educational environment.

Correspondence: Mariaelena Malvasi. email: mariaelena.malvasi@uniroma1.it

ISSN 1972-6007

Materials and methods

In our retrospective study, 151 medical records of preterm infants with a mean age of about 8 years ± 4.62 standard deviation (SD), with a minimum age of 2 and a maximum age of 20 years referred to the Centre for Paediatric Ophthalmology and Strabology of the Ophthalmology Clinic of the Policlinico Umberto I, La Sapienza University of Rome, were considered. The gestational age of the preterm infants was < 32 weeks with birth weight ≤ 1500 g (according to the recent American guidelines "Screening Examination of Premature Infants for Retinopathy of Prematurity" - Pediatrics 2018-3810, patients with presence or absence of ROP) (4,5).All patients underwent a general (provided by parents) and specialist ophthalmological history (including assessment of visual acuity using Snellen Octotype Tables in cooperating subjects, anterior and posterior segment examination performed in mydriasis with cyclopentolate 1% instilled 3 times at 15 minutes intervals, ophthalmoscopy) and orthoptic assessment (including corneal reflex tests for near and far by means of the Hirschberg Test in the most co-operating patients, objective convergence assessment, ocular motility examination, stereoscopic sense assessed with Lang I-II and Titmus Stereotest in co-operating patients), always performed by the same operator. All the clinical data collected were analysed by means of the prevalence by which we assessed the incidence of amblyopia, objective convergence, ocular motility examination and finally the stereoscopic sense analysis only in cases where it was possible to detect the results. The corneal reflex test (near and far) as well as the assessment of visual acuity for the analysis of refractive defects used the mean and standard deviation (SD).

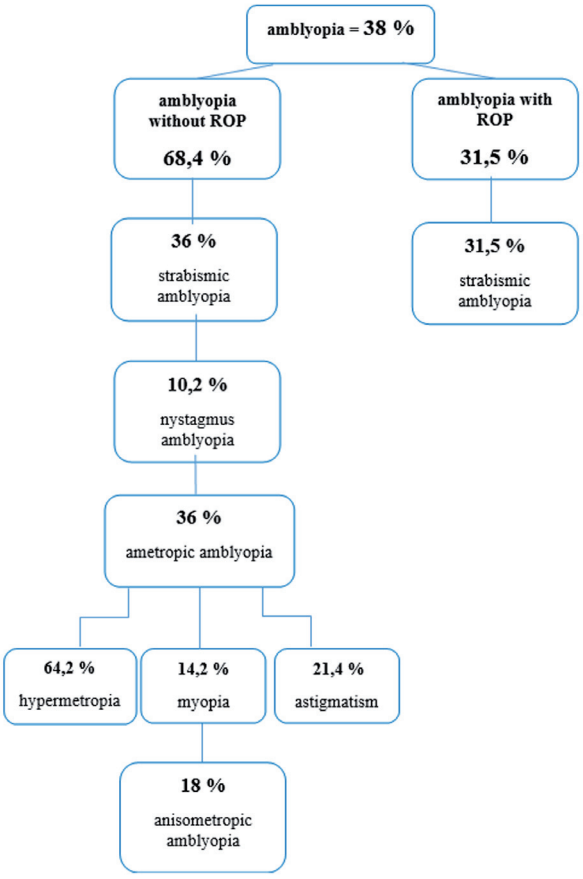

Fig. 1. Amblyopia analysis in patients without ROP and with ROP

Results

24.5 % of the patients (37/151) had ROP. 3.31% of the patients (5/151) had myopia in the right eye (OD) with mean 0.25 ± 0.25 SD; 2% (3/151), myopia in the left eye (OS) with mean 0.25 ± 0.25 SD; 7.28% of the patients (11/151) had hyperopia in OD with mean 0.25 ± 0.50 SD; 7.95% (12/151) had hyperopia in OS with mean 0.25 ± 0.25 SD; 7.28% of patients (11/151) had astigmatism in OD with mean 0.25 ± 0.25 SD; and 5.96% of patients (9/151) had astigmatism in OS with mean 0.25 ± 0.25 SD. Amblyopia was present in 38 % of the cases (57/151). 68.4 % of the amblyopic patients (39/57) did not exhibit ROP, particularly in 36 % of the latter (14/39) the amblyopia was ametropic strabismus, with hyperopia predominating in 64.2 % (9/14), myopia in 14.2 % (2/14) and astigmatism in 21.4 % (3/14). 15.3 % (6/39) had both refractive defects and strabismus. In 18 % of the cases (7/39) the amblyopia was anisometropic, while 10.2 % of the patients (4/39) had amblyopia from nystagmus. 31.5 % of the amblyopic patients (18/57) had strabismic amblyopia and also suffered from ROP (Fig. 1).

At the Corneal Reflexes test for near, performed at a distance of 33 cm 8% (12/151) had an esotropy with mean 2.15Δ ± 8.07 SD; 3% (5/151) an exotropy with mean 0.96Δ ± 6.34 SD; 5% (8/151) a microtropy with mean 0.22Δ ± 1.32 SD and 1% (2/151) a vertical deviation with mean 0.04Δ ± 0.49 SD. While at the Corneal Reflex Test from a distance (5 m), 5% of patients (8/151) had an esotropy with mean 1.34Δ ± 6.65 SD; 3% (5/151) an exotropy with mean 0.68Δ ± 4.09 SD; 5% of patients (8/151) a microtropy with mean 0.07Δ ± 0.59 SD and 1% (2/151) a vertical deviation with mean 0 ± 0 SD (Table 1).

Table 1. Evaluation of corneal reflexes for near (33 cm) and far (5 m)

R.C.			
N (33 cm)		F (5 m)	
ESOTROPY 2,15Δ ± 8,07 DS	8%	ESOTROPY 1,34Δ ± 6,65 DS	5%
EXOTROPY 0,96Δ ± 6,34 DS	3%	EXOTROPY 0,68Δ ± 4,09 DS	3%
MICROTROPY 0,22Δ ± 1,32 DS	5%	MICROTROPY 0,07Δ ± 0,59 DS	5%
VERTICAL DEVIATION 0,04Δ ± 0,49 DS	1%	VERTICAL DEVIATION 0 ± 0 DS	1%

Stereopsis assessed with the Lang I-II Test and the Titmus Stereotest (in cooperating patients) revealed that 47% of patients (71/151) had a complete stereoscopic sense, 45% (68/151) coarse (> 60 arc seconds), while stereopsis was absent in 8% of cases (12/151). Objective convergence was poor, with near point of convergence (PPC) > 6 cm in 15% of patients (23/151), fair (PPC = 6 cm) in 16% (24/151) and optimal in the remaining 69% (104/151).

While the ocular motility examination showed: hypofunction of the lateral rectus (LR) of the RE in 3% of the cases (4/151) in the right lateral gaze (right lateroversion) and hyperfunction in no case; while the medial rectus (MR) of the LE was hypofunctioning in 1% of the patients (2/151) and hyperfunctioning in 3% (4/151) of them. In 2% (3/151) in left lateral gaze (left lateroversion) the LR of the LE was hypofunctioning and in no case hyperfunctioning; the MR of the RE in no patient was hypofunctioning, while in 2% of them (3/151) it was hyperfunctioning. In the over right gaze (right overaction) there was hypofunction of the superior rectum (SR) of the RE in 12% of the patients (18/151) and hyperfunction in none of them. The inferior oblique (IO) muscle of the LE hypofunctioned in 1% (2/151) and hyperfunctioned in 15% of patients (23/151). In the upper left gaze (left overaction) the SR of the LE hypofunctioned in 11% of patients (17/151) and hyperfunctioned in 1% (2/151); while the IO of the RE hypofunctioned in 3% of patients (4/151) and hyperfunctioned in 15% (23/151). In the lower right gaze (right underaction) in 1% of cases (2/151) the inferior rectum (IR) of the RE was hypofunctioning and in 2% (3/151) hyperfunctioning. The superior oblique muscle of the LE was hypofunctioning in 3% of cases (4/151) and hyperfunctioning in 1% (2/151). Finally, in the lower left gaze (left underaction) the LE IR in 1 % of the patients hypofunctioned and in 1 % hyperfunctioned; whereas the SO muscle of the RE in 2 % of the cases (3/151) hypofunctioned and in 1 % of them (2/151) hyperfunctioned (Table 2).

Table 2. Evaluation of ocular motility in different positions of gaze

	Muscle	Hypofunction	Hyperfunction
Right lateroversion	LR RE	3%	0%
	MR LE	1%	3%
Left lateroversion	LR OS	2%	0%
	MR LE	0%	2%
Right overaction	SR OD	12%	0%
	IO LE	1%	15%
Left overaction	SR LE	11%	1%
	IO RE	3%	15%
Right underaction	IR RE	1%	2%
	SO LE	3%	1%
Left underaction	IR LE	1%	1%
	SO RE	2%	1%

Discussion

Vision-related problems represent one of the major sequelae of prematurity, which increase the lower the gestational age but especially the birth weight.

ROP was present in 24.5% of the patients, of which spontaneous regression occurred in 45.9%, while in 24.3 %, stabilisation of ROP resulted from photocoagulative laser retinal treatments.

Amblyopia was present in only 38% of the patients (57/151) and was accompanied by ROP in 31.5% of the cases (18/57) and was strabismic amblyopia.

Amblyopia patients without ROP were 68.4% (39/57). Strabismic amblyopia was present in 36% of the patients (14/39). In the same percentage of patients there was ametropic amblyopia, with hyperopia predominating in 64.2 per cent (9/14), myopia in 14.2 per cent (2/14), while 21.4 per cent of patients (3/14) had southern amblyopia from astigmatism. 15.3% of the amblyopic patients (6/39) had both refractive defects and strabismus. In 18% of the patients (7/39) anisometropic amblyopia and in 10.2% (4/39) amblyopia from nystagmus were found, all these different forms of amblyopia were adequately treated according to the guidelines and best treatment protocols (11,12).

Some studies report, regardless of the presence of ROP, persistent visual acuity deficits in preterm infants, even into adulthood, secondary to damage to the retinal cones to prolonged phototherapy for the treatment of jaundice (13-15), the same result was shown in 19.9% of the patients examined in our study with amblyopia (11/57) who had undergone the aforementioned treatment for more than one month (16,17).

At the Corneal Reflex Test we noted a higher percentage of patients with near deviations in 11.25% of cases (17/151), than for distance 9.27% (14/151), with a prevalence of esotropy (2, 15Δ ± 8.07 SD) in 8% of patients (12/151) for near and esotropy (1.34Δ ± 6.65 SD) in 5% of patients (7/151) and microtropy (0.07Δ ± 0.59 SD) in 5% of patients (7/151) for distance (7,8). In patients with ROP, 8.1% had esotropy for near and 2.7% for distance. The stereoscopic sense was coarse (> 60 seconds of arc) in 45 % of preterm births, many had stereopsis even greater than 200 seconds of arc and absent in 8 % of patients. In those with ROP the stereopsis was gross in 16.2 % of the cases, in none of them was stereopsis absent.

Following treatment of the amblyopia according to the guidelines and best treatment protocols resulted in the recovery of stereopsis (18-20).

Assessing objective convergence showed poor objective convergence (PPC > 6 cm) in 15 % of the patients, fair objective convergence (PPC = 6 cm) in 16% of them; of these latter 1.3% 2/151 had latent eye deviation (exofrtr). In the ROP patients, objective convergence was fair in 35.1 % of them, while in only one patient was poor. Those who had poor objective convergence showed reading difficulties. With regard to the ocular motility examination, it was found that 1% of the patients had hyperfunction of both the right and left IO muscle, while 12% of them had hypofunction of the right SR and 11% had hypofunction of the left SR. In patients with ROP, the same percentage of patients (5.4 %) had a hypofunction of the IO of the right eye and a hypofunction of the LR of both eyes (21).

The motor deficit was adequately treated with exercises according to the guidelines and best treatment protocols (22, 23).

Contrary to numerous studies in the literature, where there is a clear prevalence of myopia as a refractive defect, in our study we found the highest percentage of patients with hyperopia (15.23%), astigmatism accounted for 13.24 % and 5.3% of patients were myopic. Hyperopia also predominated among the refractive defects in ROP patients (5.4%) (9-11). The latter were also corrected with frontal lenses and/or LAC.

Conclusions

This study shows, in line with other studies in the literature, that prematurity has a decisive influence on the development of the visuomotor system, making it particularly susceptible to ophthalmological and orthoptical alterations (12).In fact, premature infants with ROP were found to have a higher percentage of amblyopia, altered stereopsis and objective convergence, while strabismus, refractive defects and ocular motility were also found in premature patients without ROP.

At present, premature babies manage to survive thanks to improvements in both early diagnosis and neonatal care, but it is necessary to provide the best possible quality of life. Therefore, in conclusion, we believe in agreement with the literature the importance of ophthalmological and orthoptical assessment of these children with a low gestational age and low birth weight, as early diagnosis and equally early treatment (13).

Ophthalmological and orthoptical changes can also guarantee a better quality of life and relationships, which if not diagnosed and treated in good time have negative consequences during the various stages of development, especially in the school age of learning (19, 21).

In view of the therapeutic successes achieved in the treatment of the pathologies highlighted in these young patients, from the treatment of ROP, amblyopia, strabismus to refractive defects, it follows that prevention and early diagnosis are two indispensable aspects, especially in the preverbal and pre-school age, to allow adequate recovery of visual function and inclusion in society with greater educational possibilities for the child (1,15). Otherwise, if not diagnosed and treated in good time, it could have negative repercussions during the various stages of development, especially in the school age of learning (1, 2, 22, 23).

References

1. Quinn JA, Munoz FM, Gonik B, et al. Brighton Collaboration Preterm Birth Working Group. Preterm birth: Case definition & guidelines for data collection, analysis, and presentation of immunisation safety data. Vaccine. 2016; 1;34(49):6047-6056
2. Di Renzo GC, Pacella E, Di Fabrizio L, et al. Preterm birth: Risk factors, identification and management in Management and Therapy of Late Pregnancy Complications: Third Trimester and Puerperium, 2017; 81–94
3. Malvasi A, Bochicchio M, Vaira L, et al.The fetal head evaluation during labor in the occiput posterior position: The ESA (evaluation by simulation algorithm) approach .Journal of Maternal-Fetal and Neonatal Medicine, 2014; 27(11): 1151–1157
4. Glass HC, Costarino AT, Stayer SA, et al. Outcomes for extremely premature infants. Anesth Analg. 2015 Jun; 120(6):1337-51
5. Barbera AF, et al. Intrapartum Ultrasonography for Labor Management, 2013; 61–72
6. O'Connor AR, Wilson CM, Fielder AR. Ophthalmological problems associated with preterm birth. Eye (Lond). 2007 Oct;21(10):1254-60. doi: 10.1038/sj.eye.6702838. PMID:17914427
7. Malvasi A, Tinelli A, Barbera A, et al. Occiput posterior position diagnosis: Vaginal examination or intrapartum sonography? A clinical review.Journal of Maternal-Fetal and Neonatal Medicine, 2014; 27(5):520–526
8. Leung MP, Thompson B, Black J, et al. The effects of preterm birth on visual development. Clin Exp Optom. 2018 Jan; 101(1):4-12. doi: 10.1111/cxo.12578. Epub 2017 Sep 3. PMID: 28868651
9. Fierson WM. American Academy of Pediatrics Section on Ophthalmology; American Academy of Ophthalmology; American Association for Pediatric Ophthalmology and Strabismus; American Association of Certified Orthoptists. Screening examination of premature infants for retinopathy of prematurity. Pediatrics. 2013 Jan;131(1):189-95
10. Fronius M. Okklusionstherapie bei Amblyopie. Altersabhängigkeit und Dosis-Wirkungs-Beziehung [Occlusion treatment for amblyopia. Age dependence and dose-response relationship]. Ophthalmologe. 2016 Apr; 113(4):296-303
11. Pacella E, Pacella F, Mazzeo F, et al. Effectiveness of vision rehabilitation treatment through MP-1 microperimeter in patients with visual loss due to macular disease. Clin. Ter. 2012; 163:e423–e428
12. Pacella F, Migliorini R, Marchegiani C, et al. Neurovisual training (TRIGRAM) in young patients with visualperceptive Dyslexia. Senses Sci 2017; (1):323-330 doi: 10.14616/sands-2017-1-323330
13. Hakeem AH, Mohamed GB, Othman MF. Retinopathy of prematurity: a study of prevalence and risk factors. Middle East Afr J Ophthalmol. 2012 Jul-Sep;19(3):289-94
14. Migliorini R, Comberiati AM, Pacella F, et al. Anisometropia and isoametropia associated with microstrabismus: effectiveness of late anti-amblyopia treatment. Clin Ter. 2019 Sep-Oct;170(5):e339-e344
15. Mazzeo L, Mazzeo G, Mazzeo F, et al. Surgical correction of congenital esotropia alternating and subsequent abnormal correspondence retinal: a case report. Senses Sci 2015; 2 (1):13-15
16. Migliorini R, Comberiati AM, Pacella F, et al. Utility of Ocular Motility Tests in Orbital Floor Fractures with Muscle Entrapment That is Not Detected on Computed Tomography. Clin Ophthalmol. 2021 Apr 23;15:1677-1683
17. Arrico L, Migliorini R, Bianchini D, et al. Ocular motility alterations in orbital fractures: Pre-post evaluation in maxillofacial surgical treatment, Giornale di Chirurgia 2018; 39 (6):363-367
18. Bilbao C, Piñero DP. Clinical Characterization of Oculomotricity in Children with and without Specific Learning Disorders. Brain Sci. 2020 Nov 11;10(11):836
19. Migliorini R, Malagola R, Comberiati AM, et al. Inferior oblique weakening and abnormal head position: Controlled myotomy versus recession. Journal of Ophthalmology, 2016; 1725484
20. Migliorini R, Comberiati AM, Galeoto G, et al. Eye motility alterations in retinitis pigmentosa. Journal of Ophthalmology 2015: 145468.

21. Cook A, White S, Batterbury M, et al. Ocular growth and refractive error development in premature infants without retinopathy of prematurity. Invest Ophthalmol Vis Sci. 2003 Mar;44(3):953-60. doi: 10.1167/iovs.02-0124. PMID: 12601014
22. Pacella E, Mipatrini D, Pacella F, et al. Suspensory Materials for Surgery of Blepharoptosis: A Systematic Review of Observational Studies PLoS One. 2016; 11(9):e0160827
23. Leat SJ. To prescribe or not to prescribe? Guidelines for spectacle prescribing in infants and children. Clin Exp Optom. 2011 Nov; 94(6):514-27