UDC: 617.735-002-053.32(497.7)"2010/2020"
Professional paper

SCREENING FOR RETINOPATHY OF PREMATURITY IN PREMATURE BABIES BORN IN NORTH MACEDONIA – 10 YEARS RESULTS (2010-2020)

Bekim TATESHI, Suzana KLENKOSKI

PHI University clinic for eye diseases, Skopje, North Macedonia
Faculty of Medical Sciences, Goce Delcev University, Stip, North Macedonia
**Corresponding author e-mail: bekim.tateshi@unite.edu.mk*

Abstract

Purpose: Retinopathy of prematurity (ROP) is a vasoproliferative disorder of the retina and a leading cause of visual impairment and childhood blindness worldwide. The purpose of this paper is to analyze the possibility of developing ROP and the need for treatment in premature babies, born in North Macedonia in period from 2010-2020.
Materials and methods: In this retrospective study was analyzed the data of premature babies which were followed in the period from 2010-2020. In Republic of North Macedonia for screening of ROP are used recommendations from the American Association for Pediatric Ophthalmology and Strabismus, with clearly defined inclusions for the screening program for ROP of all prematurus with a birth weight (BW) of 1500 g or less and / or born at 30 gestational weeks (GW) or earlier and selected infants with a birth weight between 1500 to 2000 g with unstable clinical course.
Results: According to the analysed data from a total of 15825 examinations carried out, according to the adopted criteria, screening was conducted in 4,518 (11,66%) premature babies. Screening in these prematures resulted in the detection of active premature retinopathy with an absolute indication of active treatment and treatment in 580(12.84%) prematures. In addition, 345 (59.48%) newborns were treated with laser photocoagulation, while 243 (41.9%) children with Anti-VEGF therapy.
Conclusion: The results concluded that premature infants born at 30 gestational weeks (GW) or earlier and/or birth weight (BW) 1500g or less and selected prematures with a birth weight between 1500 g and 2000 g but with unstable clinical course and neonatology high risk assessment, should mandatorily be screened for ROP.

Keywords: screening for ROP, retinopathy of prematurity (ROP), prematures, birth weight (BW), gestational age (GA), laser photocoagulation (LPC).

1. Introduction

Retinopathy of prematurity (ROP) is a proliferative retinal vascular disease affecting the premature infant with an incompletely vascularized retina. The spectrum of ophthalmological findings in ROP exists from minimal sequelae, which do not affect vision, to bilateral retinal detachment and total blindness (Casteels et al. 2012). The latest technological advances in neonatology have increased the survival rate of very small infants, leading to an increased incidence of ROP. On the other hand, this problem is a major challenge for all doctors involved in the treatment of premature babies and in the studying of pathogenesis, prevention, and methods of treating retinopathy of prematurity.

Numerous risk factors are responsible for the development of retinopathy of prematurity, which interfere with the normal development of the blood vessels of the retina, and among them the most significant are gestational age, low birth weight, hypoxia, the duration of administration of supplemental oxygen therapy, sepsis, intraventricular haemorrhage, blood transfusions and many others that are mutually combined and complement each other. The greater the immaturity at birth and the longer the duration of developmental arrest during exposure of the retina to damaging factors, together with the deficiency of normal intrauterine developmental factors, the more aggressive the later pathological response will be (Kinsey, Patz, and Stern 1978; Ober et al. 2006; Saugstad 2006; Tin 2002).

Figure 1. Survival pattern and its impact on ROP incidence(Jefferies and Canadian Paediatric Society, Fetus and Newborn Committee 2016).

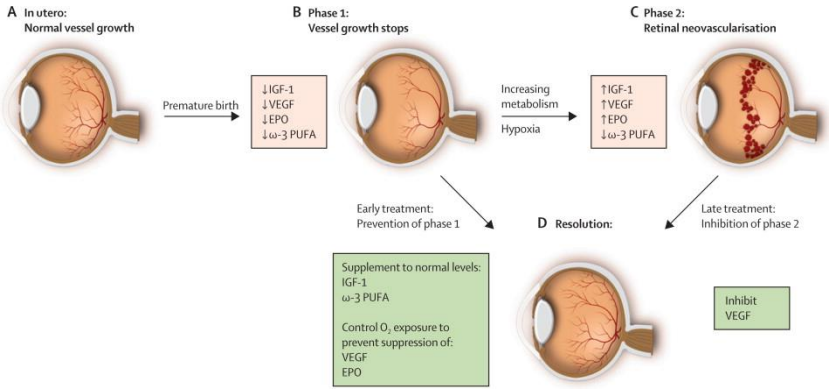

Figure 2. ROP is characterized by abnormal neovascularization. The disruption of angiogenesis in preterm infants with ROP typically occurs in two postnatal phases (Chen and Smith 2007). In phase 1 (from birth up to 30 weeks' postmenstrual age), hyperoxia inhibits vascular growth in the retina (Hellström, Smith, and Dammann 2013) As the retina becomes more metabolically active (from around 30 weeks' postmenstrual age), its incomplete vascularization causes it to become hypoxic, resulting in the secretion of various angiogenic factors including VEGF and subsequently to VEGF-driven neovascularization and intraocular fibrosis (Hellström et al. 2013). Ultimately this can result in retinal detachment and visual disability (Chen and Smith 2007; Hellström et al. 2013).

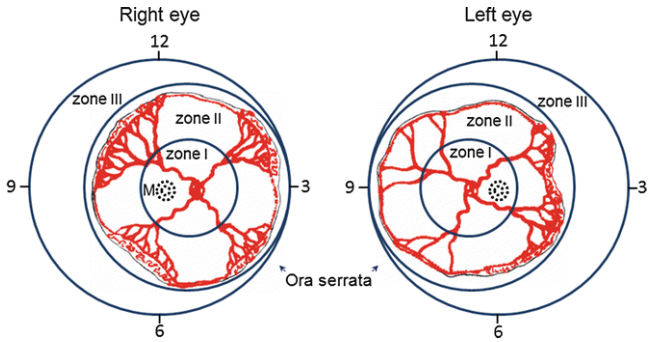

Figure 3. According to international classification of ROP terminology, ROP is categorized according to the zones of the retina in which disease is visible via dilated fundus examination and the severity (or stage) of the disease (International Committee for the Classification of Retinopathy of Prematurity 2005). Zone 1 includes the macula and optic nerve; it forms a circle, the radius of which is twice the distance from the optic nerve to the macula. ROP in Zone 1 is the most likely to progress and become severe. Zone 2 surrounds Zone 1 and extends to the ora serrata on the nasal side. ROP found here may progress quickly, although warning signs such as increasing vascular dilation and tortuosity usually predate the threshold by a week or 2. Zone 3 is a crescent area of temporal retina, which rarely shows aggressive disease (Molinari, Weaver, and Jalali 2017).

2. Materials and methods

In Republic of North Macedonia, for screening for ROP are used the recommendations of the American Academy of Pediatric section of Ophthalmology, American association for Pediatric Ophthalmology and Strabismus and American Academy of Ophthalmology from 2001, last revised in 2013 (Fierson et al. 2018): All prematures with a birth weight (BW) of 1500 g or less and / or born at 30 gestational weeks (GW) or earlier and selected infants with a birth weight between 1500 to 2000 g with unstable clinical course and neonatology assessment for high risk, should have at least 2 eye exams / fundus exams, performed in a wide dilated pupil with a binocular indirect ophthalmoscope for detection of ROP.
The need for a ROP screening program arises from the fact that: ROP is a blinding disease, Identification of all babies is essential who are at risk or likely to get severe ROP, its timely and early detection prevents undesirable sequelae and progression to advanced stages (RBSK 2017).
Despite all the efforts invested in the prevention and treatment of retinopathy of prematurity throughout the ten-year period (from 2010-2020) of work and cooperation between the Cabinet for Retinopathy of Premature at the University Clinic for Eye Diseases, the Department for Intensive Neonatal Care and Therapy at the University Clinic for Gynecology and Obstetrics, the Department of Intensive Care and Therapy and the Department of Neonatology at the University Clinic for Children's Diseases, this disease continues to be one of the leading cause of blindness among children in our area. This is the reason for this paper to shed light on the problem of retinopathy of prematurity in the Republic of North Macedonia and to scientifically process and present the results of the long-term follow-up of prematurely born children and the treatment of this disease.

3. Results

Premature babies from several health facilities are included in our research, namely: the Unit for Intensive Neonatal Care and Therapy at the University Clinic for Gynecology and Obstetrics, the Unit for Intensive Neonatal Care and Therapy and the Department of Neonatology at the University Clinic for Children's Diseases and the Cabinet for Premature Retinopathy at the University Clinic for Eye Diseases in Skopje in the period from 2010-2020.
According to the analysed data from a total of 15825 examinations carried out, according to the adopted criteria, screening was conducted in 4,518 (11,66%) premature babies. Screening in these prematures resulted in the detection of active premature retinopathy with an absolute indication of active treatment and treatment in 580 (12.84%) prematures. In addition, 345 (59.48%) newborns were treated with laser photocoagulation, while 243 (41.9%) children with Anti-VEGF therapy.

Table 1. Results of screening conducted in period from 2010-2020

Year	No. of examined babies	Total examinations	Laser photocoagulation	Anti-VEGF	Total treated
2010	397	1456	58		58
2011	321	1199	37		37
2012	315	1095	42		42
2013	410	1449	30	27	57
2014	399	1425	23	29	52
2015	468	1630	20	21	41
2016	445	1571	24	27	51

2017	533	1809	33	42	75
2018	501	1768	37	37	74
2019	341	1071	10	30	40
2020	388	1352	31	30	53
Total	4518	15825	345	243	580

According to the results, we conclude that retinopathy of prematurity is dependent on body weight and gestational age. After the diagnosis of an active form of ROP during the screening, the premature infant should be treated with LFC for 72 hours in order to deactivate the ischemia of the avascular peripheral zones of the retina. After the intervention with LFC, examinations of the eye fundus are required.
The fundus finding obtained during screening is classified according to the International Classification of Retinopathy of Prematurity (ICROP) (International Committee for the Classification of Retinopathy of Prematurity 2005).
By applying a unique anatomical classification, it is possible to equalize the criteria's of the status of the retina and the development of its vascularization. The classification allows the perception of prognosis, prevention and therapeutic possibilities and their results. Based on the analysis of the screening findings, the screening criteria can be shifted to lower values of birth weight and gestational age, without fear of the possibility of missing active forms of ROP.

4. Discussion

Retinopathy of prematurity is the most important cause of blindness in the child population, which in many cases can be prevented. The primary prevention of ROP is to prevent premature birth. Although antenatal obstetric care in Macedonia shows a trend of improvement, it still lags behind that of developed countries.
Realizing the complexity of the problem of the theory of genesis, development and progression of retinopathy of prematurity and the possibility of prevention, imposes a constant dynamism of questions that neonatologists, ophthalmologists and basic scientists encounter. In clinical work, prevention is highlighted, which is carried out within the framework of neonatal care of premature babies. The incidence of ROP increases with the degree of prematurity of the child, that is, the earlier the child is born, the more likely it is to develop more severe forms of ROP (Stoll et al. 2010).
Retinopathy of prematurity is a process manifested by developmental irregularities of the vascular network in prematurely born children. With premature birth, part of the vasculogenesis process continues in extrauterine conditions, which can be the reason for the development of retinopathy of prematurity.
Ophthalmological screening is a very important tool for detecting premature infants at risk of developing retinopathy of prematurity. The screening program is developed in close cooperation with a pediatrician-neonatologist and an ophthalmologist and should include the detection of all cases of retinopathy of prematurity and follow them up. The good selection of children with high risk for the occurrence of retinopathy of prematurity and the timely initiation of examinations enables proper implementation of prevention and treatment. The goal of an effective screening program must be the identification of the relatively small number of children with an absolute indication for treatment of ROP. Given the progressive nature of ROP and the proven benefit of laser therapy (Anon 1994; Hunter and Repka 1993; Iverson et al. 1991; McNamara et al. 1991), the standard of practice requires periodic careful retinal examination in at-risk children in neonatal intensive care units and therapy from on the part of an experienced ophthalmologist, with sufficient knowledge in the field of premature newborns and ROP, how could he identify the locations and subsequent possible retinal changes and mark them according to the international classification of ROP

(International Committee for the Classification of Retinopathy of Prematurity 2005). Screening protocols vary according to the characteristics of the preterm population and treatment protocols in the Intensive Care and Therapy Units (ICU). To identify all infants who would benefit from treatment, repeated dilated eye examinations are done until the retina is fully vascularised (Kleberg et al. 2008).

Prevention by reduction of risk factors that disrupt normal retinal vascularisation is likely to be more effective than late treatment of neovascularisation, not only with respect to vision, but also other comorbidities of premature birth. Careful control of oxygen saturation, normalisation of serum IGF-1 concentrations, provision of adequate nutrition, minimisation of hyperglycaemia and insulin use, normalisation of ω-3 polyunsaturated fatty acid concentrations, and curbing the negative effects of infection and inflammation could promote adequate postnatal growth and improve neural and vascular development of the retina. The coming decade will hopefully see the development of these and other new treatment approaches to prevent the disease and to reduce associated complications of preterm birth (Hellström et al. 2013).

5. Conclusions

Retinopathy of prematurity is one of the most common causes of avoidable blindness in children, causing irreversible visual impairment to many premature infants worldwide each year. An extremely important common problem faced by pediatricians and ophthalmologists in medical practice. The results suggest that in premature newborns born in the 30th gestational week or earlier and/or birth weight of 1500 grams or less, as in selected newborns over 30 gestational weeks and at birth weight between 1500–2000 grams, however with an unstable clinical course and a neonatal high-risk assessment, ROP screening should be required.

References

[1]. Anon. 1994. “Laser Therapy for Retinopathy of Prematurity. Laser ROP Study Group.” Archives of Ophthalmology (Chicago, Ill.: 1960) 112(2):154–56. doi: 10.1001/archopht.1994.01090140028007.

[2]. Casteels, Ingele, Catherine Cassiman, Joachim Van Calster, and Karel Allegaert. 2012. “Educational Paper: Retinopathy of Prematurity.” European Journal of Pediatrics 171(6):887–93. doi: 10.1007/s00431-011-1610-7.

[3]. Chen, Jing, and Lois E. H. Smith. 2007. “Retinopathy of Prematurity.” Angiogenesis 10(2):133–40. doi: 10.1007/s10456-007-9066-0.

[4]. Fierson, Walter M., AMERICAN ACADEMY OF PEDIATRICS Section on Ophthalmology, AMERICAN ACADEMY OF OPHTHALMOLOGY, AMERICAN ASSOCIATION FOR PEDIATRIC OPHTHALMOLOGY AND STRABISMUS, and AMERICAN ASSOCIATION OF CERTIFIED ORTHOPTISTS. 2018. “Screening Examination of Premature Infants for Retinopathy of Prematurity.” Pediatrics 142(6):e20183061. doi: 10.1542/peds.2018-3061.

[5]. Hellström, Ann, Lois E. H. Smith, and Olaf Dammann. 2013. “Retinopathy of Prematurity.” Lancet (London, England) 382(9902):1445–57. doi: 10.1016/S0140-6736(13)60178-6.

[6]. Hunter, D. G., and M. X. Repka. 1993. “Diode Laser Photocoagulation for Threshold Retinopathy of Prematurity. A Randomized Study.” Ophthalmology 100(2):238–44. doi: 10.1016/s0161-6420(93)31664-7.

[7]. International Committee for the Classification of Retinopathy of Prematurity. 2005. “The International Classification of Retinopathy of Prematurity Revisited.” Archives of Ophthalmology (Chicago, Ill.: 1960) 123(7):991–99. doi: 10.1001/archopht.123.7.991.

[8]. Iverson, D. A., M. T. Trese, I. K. Orgel, and G. A. Williams. 1991. “Laser Photocoagulation for Threshold Retinopathy of Prematurity.” Archives of Ophthalmology (Chicago, Ill.: 1960) 109(10):1342–43. doi: 10.1001/archopht.1991.01080100022007.

[9]. Jefferies, Ann L. and Canadian Paediatric Society, Fetus and Newborn Committee. 2016. “Retinopathy of Prematurity: An Update on Screening and Management.” Paediatrics & Child Health 21(2):101–8. doi: 10.1093/pch/21.2.101.

[10]. Kinsey, V. E., A. Patz, and L. Stern. 1978. “Oxygen and Retrolental Fibroplasia: In Defense of Data.” Pediatrics 62(3):439–40.

[11]. Kleberg, Agneta, Inga Warren, Elisabeth Norman, Evalotte Mörelius, Ann-Cathrine Berg, Ezam Mat-Ali, Kristina Holm, Alistair Fielder, Nina Nelson, and Lena Hellström-Westas. 2008. "Lower Stress Responses after Newborn Individualized Developmental Care and Assessment Program Care during Eye Screening Examinations for Retinopathy of Prematurity: A Randomized Study." Pediatrics 121(5):e1267-1278. doi: 10.1542/peds.2006-2510.
[12]. McNamara, J. A., W. Tasman, G. C. Brown, and J. L. Federman. 1991. "Laser Photocoagulation for Stage 3+ Retinopathy of Prematurity." Ophthalmology 98(5):576–80. doi: 10.1016/s0161-6420(91)32247-4.
[13]. Molinari, Andrea, Dan Weaver, and Subhadra Jalali. 2017. "Classifying Retinopathy of Prematurity." Community Eye Health 30(99):55–56.
[14]. Ober, Richard R., Earl A. Palmer, Arlene V. Drack, and Kenneth W. Wright. 2006. "Retinopathy of Prematurity." Pp. 284–349 in Handbook of Pediatric Retinal Disease, edited by K. W. Wright, P. H. Spiegel, and L. S. Thompson. New York, NY: Springer New York.
[15]. RBSK. 2017. "Guidelines for Universal Eye Screening in Newborns Including Retinopathy Of Prematurity (ROP)."
[16]. Saugstad, O. D. 2006. "Oxygen and Retinopathy of Prematurity." Journal of Perinatology: Official Journal of the California Perinatal Association 26 Suppl 1:S46-50; discussion S63-64. doi: 10.1038/sj.jp.7211475.
[17]. Stoll, Barbara J., Nellie I. Hansen, Edward F. Bell, Seetha Shankaran, Abbot R. Laptook, Michele C. Walsh, Ellen C. Hale, Nancy S. Newman, Kurt Schibler, Waldemar A. Carlo, Kathleen A. Kennedy, Brenda B. Poindexter, Neil N. Finer, Richard A. Ehrenkranz, Shahnaz Duara, Pablo J. Sánchez, T. Michael O'Shea, Ronald N. Goldberg, Krisa P. Van Meurs, Roger G. Faix, Dale L. Phelps, Ivan D. Frantz, Kristi L. Watterberg, Shampa Saha, Abhik Das, Rosemary D. Higgins, and Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. 2010. "Neonatal Outcomes of Extremely Preterm Infants from the NICHD Neonatal Research Network." Pediatrics 126(3):443–56. doi: 10.1542/peds.2009-2959.
[18]. Tin, Win. 2002. "Oxygen Therapy: 50 Years of Uncertainty." Pediatrics 110(3):615–16. doi: 10.1542/peds.110.3.615.