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Original scientific paper

Prevalence of Severe Retinopathy of Prematurity in a Geographically Defined Population in Croatia

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A B S T R A C T

The aim of this study was to evaluate the prevalence of stage III of retinopathy of prematurity (ROP) among newborns of birth weight <1500 g and gestational age (GA) ≤32 weeks, and to compare these prevalences during two time periods (1998–2002 and 2003–2007). The investigation was conducted at the Department of Gynecology and Obstetrics, University Hospital in Rijeka, Croatia. The screening for ROP was performed by an ophthalmologist using a binocular indirect ophthalmoscope. Over a period of 10 years, there were 28,627 liveborn newborns, with 136 (0.48%) premature newborns with a birth weights <1500 g and 226 (0.79%) newborns with GA at birth ≤32 weeks. The proportions of survivors among newborns with birth weights <1500 g (51.1% vs.70.5%) and among newborns with GA at birth ≤32 weeks (67.9% vs. 77.0%) were significantly higher in the later period. During the period 2003–2007, the proportion examined for ROP was higher among newborns with birth weight <1500 g (52.9% vs. 97.1%) and among newborns with GA at birth ≤32 weeks (46.5% vs. 96.9%). The prevalence of stage III ROP was significantly lower in 2003–2007 compared to that in 1998–2002 among newborns with birth weight <1500 g (30.6% vs. 14.0%) and newborns with GA at birth ≤ 32 weeks (22.4% vs. 8.8%). The prevalence of total ROP among newborns was significantly lower in 2003–2007 compared with 1998–2002. This decrease in prevalence may be explained by advances in neonatal intensive care unit, increased survival of very low birth weight infants and carefully timed retinal examinations.

Key words: *preterm infants, prevalence, retinopathy of prematurity, Croatia*

Introduction

In the last 60 years, the survival of premature babies has increased, and this has led to increases in the number of infants with immature retinal vasculature and in the incidence of severe retinopathy of prematurity (ROP)[1,2]. The risk of ROP increases with decreasing gestational age and birth weight. Premature babies have less vascularized retinas at birth, and the retinal blood vessels are very sensitive to the variations from hypoxia to hyperoxia[1]. Threshold ROP occurs most frequently in infants with a birth weight of less than 1250 g, and despite treatment, it can progress to tractional retinal detachment[3]. Approximately 10% to 15% of these children will become blind[4].

In the last twenty years in Croatia, ROP has been the cause of blindness among 3.6% of blind young persons[5]. The screening and treatment of ROP is still insufficient and not routine in many intensive care units in Croatia[6].

The aim of this study was to present the results of early screening and the prevalence of stage III ROP among preterm newborns over a 10-year period in a geographically defined population in Croatia.

Patients and Methods

This study was conducted at the Department of Gynecology and Obstetrics, University Hospital in Rijeka, Croatia, from 1998–2007. We divided the ten-year period into two periods: Period l (1998–2002) and Period ll (2003–2007). In this study, we included newborns with a birth weights <1500 g and gestations ≤32 weeks.

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We evaluated the following outcomes in the two time periods: the proportion of babies with a birth weight of <1500 g and a gestation of ≤32 weeks, the survival (past six months) of these babies, the proportions examined by an ophthalmologist, and the prevalence of severe ROP in surviving babies with a birth weight of <1500 g and a gestation of ≤32 weeks.

The first examination was performed 4 to 6 weeks after birth, and the follow-up examinations were carried out approximately 2 weeks after every examination or more frequently depending on the severity of disease.

The examination was performed by an ophthalmologist, using a binocular indirect ophthalmoscope, after dilatation of the pupils with tropicamid drops (»Mydriaticum stulln« a 5.0 mg, Pharma Stulln), one drop every 15 minutes, 3 times before examination**.**

Retinopathy of prematurity staging was defined according to the International ROP classification[7].

Results

There were 28,627 liveborn newborns over 10 years (14,186 in Period I and 14,441 in Period II). The number of liveborn babies with birth weight <1500 g, the number that survived, and the number examined by an ophthalmologist are presented for the total period, and separately by Period l and Period ll in Table 1.

TABLE 1
NUMBER OF LIVEBORNS WITH BIRTH WEIGHTS <1500 G, NUMBER THAT SURVIVED, AND NUMBER EXAMINED OVER THE PERIOD AND IN TWO REVIEWED PERIODS SEPARATELY

	Period l (1998–2002)	Period ll (2003–2007)	Total (1998–2007)
Liveborn with birth weight <1500 g	133 (0.94%)*	146 (1.01%)*	279 (0.97%)*
Survived	68 (51.1%)**	103[a] (70.5%)**	171 (61.3%)**
Examined	36 (52.9%)***	100[a] (97.1%)***	136 (79.5%)***

[a] p≤0.001
* Among total liveborns in reviewed period
** Among all liveborns with birth weight <1500 g in reviewed period
*** Among all surviving newborns with birth weight <1500 g in reviewed period

There were significantly more survivals among newborns birth weight <1500 g (χ^2=10.26; p=0.001) and more examinations in Period II than in Period I (χ^2= 46.16; p=0.0001).

The number of liveborn babies with ≤32 weeks' gestation, the number that survived and the number examined by an ophthalmologist are presented for the total period, and separately by Period l and Period ll in Table 2.

There were significantly more survivals among newborns 32 weeks' gestation (χ^2=3.94; p=0.047) and more examinations in Period II than in Period I (χ^2=77.34; p=0.0001).

TABLE 2
NUMBER OF LIVEBORNS WITH ≤32 WEEKS' GESTATION, NUMBER THAT SURVIVED, AND NUMBER EXAMINED OVER THE PERIOD AND IN TWO REVIEWED PERIODS SEPARATELY

	Period l (1998–2002)	Period ll (2003–2007)	Total (1998–2007)
Liveborn with ≤32 weeks' gestation	212 (1.49%)*	213 (1.47%)*	425 (1.49%)*
Survived	144 (67.9%)**	164[a] (77%)**	308 (72.5%)**
Examined	67 (46.5%)***	159[a] (96.9%)***	226 (73.4%)***

[a] p<0.05
* Among total liveborns in reviewed period
** Among all liveborns with ≤32 weeks' gestation in reviewed period
*** Among all surviving newborns with ≤32 weeks' gestation in reviewed period

The prevalences of total ROP and severe ROP among examined newborns with birth weighs <1500 g are presented in Table 3.

TABLE 3
NUMBER OF ROP III AND TOTAL ROP IN EXAMINED NEWBORNS WITH BIRTH WEIGHT <1500 G IN THE TOTAL PERIOD, AND SEPARATELY IN PERIOD l AND PERIOD ll

	Period l (1998–2002)	Period ll (2003–2007)	Total (1998–2007)
ROP lll	11 [36] (30.6%)	14 [100][a] (14.0%)	25 [136] (18.4%)
Total ROP	21 [36] (58.3%)	31 [100][a] (31.0%)	52 [136] (38.2%)

[a] p<0.02
[ ] – in brackets: number of examined newborns birth weight <1500 g in reviewed period
() – in brackets: percentage of examined newborns birth weight <1500 g in reviewed period

There were statistically significantly lower rates of ROP lll (χ^2=4.80, p=0.028) and total ROP (χ^2=8.37, p=0.003) among examined newborns with birth weights <1500 g in Period II than in Period I.

The prevalence of total ROP and severe ROP among examined newborns with ≤32 weeks' gestation were presented in Table 4.

There was a statistically significantly lower prevalence of ROP lll among examined newborns with ≤32 weeks' gestation in Period ll (χ^2=6.61; p=0.010) than in Period I.

There was statistically significantly lower prevalence of total ROP among examined newborns with ≤32 weeks' gestation in Period ll (χ^2=12.20; p=0.0004) (Table 5).

TABLE 4
NUMBER OF ROP lll AND TOTAL ROP IN EXAMINED NEWBORNS WITH ≤ 32 WEEKS' GESTATION IN THE TOTAL PERIOD, AND SEPARATELY IN PERIOD I AND PERIOD II

	Period l (1998–2002)	Period ll (2003–2007)	Total (1998–2007)
ROP lll	15 [67] (22.4%)	14 [159][a] (8.8%)	29 [226] (12.8%)
Total ROP	32 [67] (47.8%)	37 [159][a] (23.3%)	69 [226] (30.5%)

a p<0.01
[ ] – in brackets: number of examined newborns with ≤32 weeks' gestation in reviewed period
() – in brackets: percentage of examined newborns with ≤32 weeks' gestation in reviewed period

Discussion

Our results revealed that in the reviewed period from 1998 to 2007, the prevalence of total ROP among examined newborns with birth weights <1500 g was 38.2%, and that among examined newborns with ≤32 weeks' gestation was 30.5%.

Retinopathy of prematurity (ROP) is a major cause of childhood blindness or visual disabilities[8]. In the last twenty years in Croatia, ROP has been the cause of blindness in 3.6% of blind young persons. The prevalence of retinopathy of prematurity in newborns with birth weights <1500 g was 56.5%, and in newborns with gestational ages ≤32 weeks, it was 28.9%[5,6]. In another investigation from Croatia, the incidence of ROP in newborns with birth weights ≤2000 g was 12.8%[9].

Larsson et al reported a prevalence of ROP of 25% in Stokholm, Sweden, and Nodgar et al reported a prevalence of ROP of 19.2% in Denmark[10,11]. In the United Kingdom, the prevalence of ROP was 19.3%[12]. In Mexico, the prevalence of ROP of any stage was 22% in high-risk premature infants. The highest prevalence, 48%, was in the birthweight 500–1000 g group[13]. In Brazil, the prevalence of ROP was 27.2%. ROP was confirmed in 50% of infants with weights below 1000 g and 71.5% of newborns born at gestational ages of less than 28 weeks[14]. ROP is a leading cause of childhood blindness and visual disability in the United States. It affects more than 80% of babies born with birth weights less than 1000 g. The prevalence of ROP was 20% in newborns with birth weights ≤1500 g and 33% in newborns with birth weights ≤1000 g[8,15].

All of these results should be interpreted with caution due to the studies' different methodologies, inclusion or exclusion criteria and relative subjectivity in ROP staging. Wallace et al reported a pilot study using a special fully-automated computer program that identified and measured dilation and tortuosity of retinal blood vessels (»ROPtool«). It can reduce the subjectivity and improve the accuracy in assessing the presence of disease[16].

According to the Recommendations for Screening examination of premature infants for ROP, infants with a birth weight of less than 1500 g or a gestational age of 32 weeks or less should have a first retinal screening examination 4 to 6 weeks after birth by an ophthalmologist using a binocular indirect ophthalmoscope[3,17].

In our investigation over the 10-year period from 1998–2007, the prevalence of ROP lll among examined newborns with birth weights <1500 g was 18.4%, and the prevalence among examined newborns with ≤32 weeks' gestation was 12.8%; the differences in the prevalences were not statistically significant. Therefore, we suggest that examinations for ROP should be performed in all infants with birth weights less than 1500 g, regardless of their gestational age. There were significantly lower rates of ROP of stage lll among examined newborns with birth weights <1500 g (14% vs. 30.6%) and among examined newborns with ≤32 weeks' gestation (8.8% vs. 22.4%) in Period ll than in Period I.

These results were consistent with those from a study from the United States, where the prevalence of ROP with threshold disease was 9.5%[8,15]. In Canada, the incidence of severe ROP was 48 per 1000 among infants with mean gestational age of 26 weeks and the mean birth weight of 750 g[18]. Various reports revealed that in the last two decades of the 20th century, the incidence of severe ROP increased because of the improved survival of extremely low birth weight infants associated with advances in neonatal intensive care[2,19,20].

TABLE 5
NUMBER OF LIVEBORN WITH BIRTH WEIGHTS <1500 G OR ≤32 WEEKS' GESTATION, NUMBER THAT SURVIVED, NUMBER EXAMINED AND NUMBER OF ROP III NEWBORNS IN THE ENTIRE REVIEWED PERIOD

1998–2007	Liveborn	Survived	Examined	ROP lll
Birth weight <1500 g	279 (0.97%)*	171 (61.3%)**	136 (79.5%)***	25[a] (18.4%)****
≤32 weeks' gestation	425 (1.49%)*	308 (72.5%)**	226 (73.4%)***	29[a] (12.8%)****

[a] p=0.199
* Among all liveborns in reviewed period
** Among all liveborns with birth weights <1500 g/≤32 weeks' gestation in the reviewed period
*** Among all surviving newborns with birth weights <1500 g/≤32 weeks' gestation in the reviewed period
**** Among all examined newborns with birth weights <1500 g/≤32 weeks' gestation with ROP lll in the reviewed period

In our investigation, significantly more infants with birth weights <1500 g or ≤32 weeks' gestation survived, and significantly more surviving infants were examined in the years 2003–2007 (Period ll) than in 1998–2002 (Period I). However, there was a statistically lower prevalence of total ROP among examined newborns with birth weights <1500 g and among examined newborns with ≤32 weeks' gestation (47.8% vs. 23.3%) in the years 2002–2007 than in the years 1998–2002. This could be explained by the use of surfactants, continuous pulse oximetry, improvements in nutritional support, the use of antenatal steroids, and improvements in overall care in the neonatal intensive care unit at our Department. Our results support the findings of Bullard et al., who also found that the incidence of all levels of ROP across all birth weights decreased in the last decades of the 20th century[21].

In the future, the genetic testing of premature newborns for genotypes predictive of a higher risk for ROP could eventually alert neonatologists to at-risk cases. Until then, moderate exposure to supplemental oxygen, the avoidance of repeated variations in hypoxia-hyperoxia in premature newborns, and the timely detection and treatment of serious ROP will help the rate of blindness from ROP to drop even further[8,22–25].

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PREVALENCIJA RETINOPATIJE U PRIJEVREMENO POĐENE DJECE U GEOGRAFSKI DEFINIRANOJ POPULACIJI HRVATSKE

SAŽETAK

Cilja rada bio je istražiti prevalneciju retinopatije prematuriteta (ROP) III stupnja u skupini novorođenčadi rođene sa <1550 g porodne težine i gestacijske dobi (GD) ≤32 tjedna te usporediti prevalenciju u dva vremenski razlčiita razdoblja (1998.–2002. god. i 2003.–2007. god.). Istraživanje je sprovedeno u Klinici za ginekologiju i porodništvo Kliničkog bolničkog centra Rijeka, Hrvatska. Probir na ROP provodio je oftalmolog koristeći binokularni indirektni oftalmoskop. Tijekom 10 godišnjeg razdoblja bilo je 28,627 živorođene novorođenčadi od toga 136 (0,48%) prematurusa sa porodnom težinom <1500 g i 226 (0,79%) novorođenčadi sa GD ≤32 tjedna. Omjer preživaljavanja u novorođenčadi sa porodnom težinom <1500 g (51,1% vs.70,5%) i između novorođenčadi sa GD ≤32 tjedna bila je značajno viša u drugom razdoblju (2003.–2007. god.). Veći broj novorođenačdi sa porodnom težinom <1500 g (52,9% vs. 97,1%) i novorođenčadi sa GD ≤32 tjedna (46,5% vs. 96,9%) podvrgnuto je probiru na ROP u razdoblju od 2003.–2007. god. Prevalencja III stupnja ROP-a značajno je bila niža u razdoblju od 2003.–2007. god. u usporedbi sa razdobljem 1998.–2002. god. u novorođenačdi sa porodnom težinom <1500 g (30,6% vs. 14,0%) i u novorođenčadi sa GD ≤32 tjedna (22,4% vs. 8,8%). Ukupna prevalencija ROPa-u skupini novorođenčadi značajno je bila niža u razdoblju 2003.–2007. god. u usporodbi sa razdobljem od 1988.–2002. god. Snižavanje prevalencije ROP-a može se objasniti napretkom u intezivnom novorođenačkom liječenju, povećanju preživaljavanja novorođenčadi vrlo niske poroden težine i sustavnom, vremenski definiranom provođenju probira na ROP.