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Retinopathy of Prematurity: Results of a Two-Years Follow-Up

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Abstract

Objective: To determine the frequency of retinopathy of prematurity (ROP) and the clinical course of the disease in premature infants that were referred to our hospital and followed in our premature intensive care unit.

Material and Methods: The premature infants with a gestational age of ≤34 weeks and a birth weight of ≤2500 gr that were referred to our hospital and hospitalized in Samsun Maternity and Pediatrics Hospital, Neonatal Intensive Care Unit between January 2012 and December 2013 were studied in terms of ROP development. They were recorded as singletons, twins, or triplets with their gestational ages and birth weights.

Results: In the study, 319 premature infants were screened and ROP was found in 133 (41,6%) infants. The infants's gestational weeks were between 23-34 (mean:30,7±4,2) while their birth weights were between 540-2480 (mean:1517,60±318,2) g. Of the 133 infants who had ROP, 70 (52,6%) had stage 1 ROP, 22 (16,5%) had stage 2 ROP, 33 (24,8%) had stage 3 ROP and 8 (6%) had aggressive posterior ROP (APROP) while none of the infants had stage 4 or stage 5 ROP. Diode laser photocoagulation (LP) was performed on 31 cases with high risk of prethreshold ROP and on 5 cases with APROP. Retinal detachment developed in two eyes which LP was performed.

Conclusion: ROP associated blindness can be partly prevented with timely diagnosis and treatment of babies who are in risk group. It is important to raise awareness in physicians working in this field.

Key Words: Retinopathy of Prematurity; Prematurity; Laser Photocoagulation.

Prematürite Retinopatisi: İki Yıllık İzlem Sonuçlarımız

Özet

Amaç: Yenidoğan yoğun bakım ünitemizde takip ettiğimiz ve dış merkezlerden hastanemize refere edilen prematüre bebeklerde prematürite retinopatisi (PR) sıklığını saptamak ve hastalığın klinik gidişatını değerlendirmek.

Gereç ve Yöntemler: Ocak 2012-Aralık 2013 tarihleri arasında Samsun Kadın Doğum ve Çocuk Hastalıkları Hastanesi yenidoğan yoğun bakım ünitesinde takibi yapılan ve ayrıca dış merkezlerden hastanemize refere edilen 34 hafta ve altında doğum haftası olan bebekler ile doğum ağırlığı 2500 gr ve daha düşük doğum ağırlıklı olan prematüre bebekler PR gelişimi açısından tarandı. Bebeklerin doğum haftaları ile doğum kiloları ve tek, ikiz ya da üçüz eşi olup olmadıkları kaydedildi.

Bulgular: Tarama programına toplam 319 bebek alındı. Bebeklerin doğum haftaları 23-34 hafta (ortalama 30,7±4,2), doğum ağırlıkları ise 540-2480 (ortalama 1517,60±318,2) gr arasında değişmekte idi. Taramaya alınan bebeklerin 133'ünde (%41,6) PR saptandı. PR tespit edilen bebeklerden 70'inde (%52,6) evre 1, 22'sinde (%16,5) evre 2, 33'ünde (%24,8) evre 3 ve 8'inde (%6) agresif posterior prematürite retinopatisi (APPR) saptandı. Hiçbir bebekte evre 4 veya evre 5 PR görülmedi. Yüksek riskli eşik öncesi hastalığı olan 31 olguya ve APPR'si olan 5 olguya diod lazer fotokoagülasyon (LFK) uygulandı. LFK yapılan iki bebeğin birer gözünde retina dekolmanı gelişti.

Sonuç: Prematürite retinopatisine bağlı körlükler risk grubundaki bebeklerin zamanında tanı ve tedavisi ile kısmen önlenebilir. Bu konuda ilgili tüm hekimlerin farkındalıklarının artırılması büyük önem taşımaktadır.

Anahtar Kelimeler: Prematürite Retinopatisi; Prematürite; Lazer Fotokoagülasyon.

INTRODUCTION

Retinopathy of prematurity (ROP), which can lead to blindness in premature infants, is a complex and multifactorial disease of developing retinal vasculature (1, 2). As a serious cause of blindness, ROP first emerged in the 1940s and 1950s in industrialised countries following the increase in the survival rate of premature babies as a result of unmonitored use of supplemental oxygen (3).

Low birth weight, low gestational week and mechanical ventilation are among the most well-known risk factors for the development of the disease despite oxygen therapy, perinatal asphyxia, episodes of apnea, respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), sepsis, intraventricular hemorrhage, blood transfusion, surfactant therapy, acidosis, anaemia, vitamin E deficiency, and multiple pregnancies are responsible other risk factors (4,5). 90% of ROP cases begin to regress spontaneously before the 44th postmenstrual (PM) week whereas, in less than 10% of the cases, the disease progresses, and if untreated, leads to retinal detachment and blindness (2, 6). Because there are no overt signs and symptoms of ROP, having timely diagnosis and treatment for the infants at risk is of utmost importance (7).

In this study, we aim to investigate the ROP frequency and the clinical course of the disease in the premature infant that have been referred to our neonatal intensive care unit.

MATERIAL AND METHODS

Between January 2012 and December 2013, a total of 319 premature infants, who were referred to our hospital and hospitalized in Samsun Maternity and Child Health Hospital neonatal intensive care unit, were followed for the development of ROP.

Newborns who were born in the 34th postmenstrual (PM) week and earlier and those with a birth weight of 2500g or less were included in the screening program. The screening was terminated in cases when full retinal vascularization occurred; when infants passed the PM 45th week without took place prethreshold ROP or more severe ROP; and when ROP regressed.

To determine the incidence of retinopathy of prematurity, newborns were divided into three groups on a basis of PM age: newborns in the 28th PM week or below; those between 28th to 32nd weeks, and those who were born in the 32nd PM week and later (Table 1). The classification based on birth weight classified newborns into four groups: those 1000g and below, those between 1001g and 1500g, those between 1501g and 1999g, and those 2000g and above (Table 2). In addition, patients were also divided into groups of single and multiple pregnancies.

Table 1. The distribution of the cases according to gestational age.

Gestational age	Number of cases (%)
28th weeks and earlier	77 (24,1%)
28-32 weeks	79 (24,7%)
32nd week and later	163 (51%)
Total	319 (100%)

Table 2. The distribution of the cases according to birth weight.

Birth weight	Number of cases (%)
1000 gr and under	52 (16,3%)
1001-1500 gr	101 (31,6%)
1501-1999 gr	120 (37,6%)
2000 gr and higher	46 (14,4%)
Total	319 (100%)

The first eye examination of the infants included in the screening program was conducted in the neonatal intensive care unit after the 31st PM week. For those who were discharged or referred to our clinic in the postnatal 4th-8th weeks, the first eye examinations were carried out in the eye clinic. One hour before the eye examination, we applied a single dose of 0.5% cycloplegic eye drop (cyclopentolate) and two doses of mydfrin (2.5% phenylephrine) in 5-minute intervals to both eyes. Feeding was discontinued one hour prior to the examination. After the topical anaesthesia with Alcaine solution (0.5% proparacaine), we started the indirect ophthalmoscope examination by using an eyelid speculum for babies and the examination of the anterior and posterior segment of both eyes by using 20 and/or 28 D lens and a scleral depressor. Findings were recorded in accordance with international ROP classification (ICROP: International Classification of Retinopathy of Prematurity) (8). According to the severity of retinopathy of prematurity, examinations were repeated for 3 days to 4 weeks. Until they were excluded from the screening program, each patient was examined at least twice to up to a maximum of 7 times.

The patients without regular follow-ups were excluded from the study.

RESULTS

162 (50.7%) of 319 infants admitted to our clinic were males and 157 (49.2%) were females. The birth weeks were between 23rd and 34th weeks (mean 30.7±4.2), and the birth weights were between 540g and 2480g (mean 1517.60±318.2). We detected ROP at different stages in 133 (41.6%) of the newborns who attended the follow-ups. Table 3 shows the distribution of patients according to stages. As far as birth weight is concerned, the incidence of ROP was rather high in newborns under 1000g while it was rare in the babies with 2000g or above birth weight. The ROP incidence rates according to birth weight and birth week are given in Table 4 and Table 5, respectively.

Table 3. The distribution of the ROP cases according to stages.

Stage	Number of cases (%)
Stage 1	70 (52,6%)
Stage 2	22 (16,5%)
Stage 3	33 (24,8%)
Stages 4-5	0 (0%)
APROP	8 (6%)
Total	133 (100%)

Table 4. The distribution of the cases according to birth weight and the ROP incidence rates.

	Number of cases	(%)
1000 gr and under	52	47 (90,3%)
1001-1500 gr	101	52 (51,4%)
1501-1999 gr	120	28 (23,3%)
2000 gr and higher	46	6 (13%)
Total	319	133 (100%)

Table 5. The distribution of the cases according to birth week and the ROP incidence rates.

	Number of cases	(%)
28th weeks and earlier	77	64 (83,1%)
28-32 weeks	79	35 (44,3%)
32nd week and later	163	34 (20,8%)
Total	319	133 (100%)

In all the stage 1 and stage 2 ROP cases, retinopathy ceased without the need for treatment and the retinal vascularization was completed. None of the retinopathies in zone 1 regressed spontaneously

whereas all retinopathies in zone 3 ceased without any treatments. In a case with stage 3 ROP in zone 2 in 3-4 contiguous clock hours of both eyes effected, the retinopathy regressed without any intervention. Upon detecting aggressive posterior retinopathy of prematurity (APROP) in three of our patients, we suggested intravitreal antiVEGF due to insufficient vascularization. But because our laser device was malfunctioning at the time, we referred one of our patients with stage 3 ROP in zone 2 to another centre. We performed 810 nm diode laser photocoagulation (LP) to both eyes to 31 patients diagnosed with the high-risk prethreshold ROP and to 5 patients with APROP. Two patients with the high-risk prethreshold ROP and APROP had to undergo additional LP. Retinal detachment developed in one of the eyes of the two babies who underwent LP due to the high-risk prethreshold ROP and APROP. For vitreoretinal surgery, patients were referred to another center.

Each 56 of the 319 patients were one of twins, and 6 patients were one of triplets each. The distribution of the patients according to the presence of single and multiple pregnancies and the ROP incidence are shown in Table 6.

Table 6. The distribution of the cases according to single/multiple pregnancies and the ROP incidence rates.

	ROP+	ROP-	Total
Singletons	121 (47,0%)	136 (52,9%)	257 (100%)
Multiple pregnancies	12 (19,3%)	50 (80,6%)	62 (100%)
Total	133 (41,6%)	186 (58,3%)	319 (100%)

DISCUSSION

In retinopathy of prematurity (ROP), the most important risk factors are low birth weight and immaturity, which is determined by low birth week (4,5). Therefore, although the widely accepted screening criteria for ROP vary according to the limit values of different protocols, gestational age and birth weight form the basis for ROP criteria. However, these two criteria have low specificity despite the high sensitivity they provide. Meanwhile, a new algorithm with allegedly higher specificity has been proposed for ROP that includes weight gain and serum insulin-like growth factor 1 (IGF-1) levels in the early postpartum period in addition to gestational age and birth week (WINROP: Weight, Insulin-like growth factor 1, Neonatal, Retinopathy of Prematurity). Research on the effectiveness and usability of this algorithm is still underway (9,10).

According to the American Academy of Pediatrics criteria, it is recommended that all babies born under 1500g or before the 30th week, or those who are born between 1500g and 2000g with poor general condition need to be added to the screening programme (11). In Turkey, while Basmak et al. suggests that babies who are born ≤2500g and before ≤35th week should undergo screening (12), Akman et al.'s study recommends the same for babies who are born before the 34th week with poor clinical condition (13). The examinations should be conducted either between the PN 4th and 6th weeks or after the PM 31st week when the tunica vasculosa lentis declines and the optical media are transparent. In our clinic, we screened the newborns who were born in the 34th week or earlier with a birth weight of 2500g or below for ROP. In babies who were born with a birth weight of 2000g and above or in the PM 32nd week and later, we did not need to apply any treatment for ROP.

About the frequency and severity of retinopathy of prematurity, studies conducted in different countries report various results. In a multicenter study of 4099 babies with a birth weight of 1,251g and lower, the ROP incidence at any stage has been reported to be 65.8%. The same study has detected ROP in 81.6% of the neonates with less than 1000g of birth weight and in 47% of those who were born weighing 1000g to 1250g (14). Another multicenter clinical study on 6998 newborns weighing below 1251g at birth shows the ROP incidence rate to be 68%, a similar rate to that of the first study in terms of birth weight. However, zone 1 ROP frequency is reported to be higher in the latter compared to the results of the previous study (15).

In Turkey, studies conducted in different centres to detect ROP rates vary. Özbek et al.'s study on 179 premature infants who were born in the 37th week and below 2400g shows the ROP incidence at any stage as 36.3%. The same study reports the ROP incidence rate to be 21% in the newborns with a birth weight higher than 1500g and 86.6% in newborns with a birth weight below 1000g, respectively. The study reports the incidence rates according to the severity of desease as follows: 58.4%, 12.4%, 27.7%, and 1.5% for stages 1, 2, 3, and 5, respectively (4). Öner et al.'s study of 306 premature infants discloses an incidence rate of 20.9%. The ROP incidence in babies with a birth weight higher than 1500g was 5.8% while the same rate was 89.2% in infants under 1000g. The distribution according to the stage was 76.5%, 20.3%, and 3.2% for stages 1, 2, and 4-5, respectively (16). The ROP incidence rate was 17.6% in Kavuncuoğlu et al.'s study covering 170 premature newborns (17). In our study of 319 premature infants, the ROP incidence rate at any stage was found to be 41.6%. The ROP frequency was 90.3% in babies with a birth weight of 1000g and below; it was 36.3% for infants above 1500g. 52.6% of our patients had stage 1 ROP. We had 16.5% stage 2 and 24.8% stage 3 ROP infants. 6% had APROP while no cases had either stage 4 or stage 5 ROP. We believe that the reason why we did not detect any stage 4 or stage 5 ROP newborns was because the babies were examined in time, in other words, it is safe to claim that the doctors are now more sensitive to ROP. Besides, we also assume that the reason behind having a higher incidence rate of ROP at any stage in our study is because our clinic is a centre where we have referred patients only.

It is known that 90% of retinopathy of prematurity shows spontaneous regression (6). In a study, the spontaneous regression rates have been reported as 86.7%, 57.1%, and 5.9% for stage 1, 2, and 3, respectively. The same

study reveals that the changes in zone 3 and zone 2 have shown spectacular declines with a rate of 100% and 46.2%, respectively. However, it is also reported that there was no spontaneous regression in zone 1 and that retinal haemorrhage is a poor, independent indicator in the regression of ROP (2). In our study, in all stage 1 and stage 2 newborns along with a patient with stage 3 ROP in zone 2, we observed regression without any treatments. None of the newborns with retinopathy in zone 1 experienced spontaneous regression whereas all patients with ROP in zone 3 had spontaneous regression.

Although multiple pregnancy is defined as a risk factor for ROP, it is should be questioned whether it is a result of multiple pregnancy itself or the increased risk of prematurity and low birth weight, two expected outcomes of multiple pregnancy. A study reports that the main factors at work in ROP are low birth weight and low gestational age though single babies are more likely to develop stage 2 and stage 3 ROP compared to twins and triplets (18). In our study, too, ROP incidence was higher in single newborns than in twins and triplets.

Today, with the improvement of neonatal intensive care units, more newborns with low birth weight and birth weeks survive, which is an admirable development. Nonetheless, it also brings about the fact that we now face more problems with various challenges related to premature babies. To this end, recent publications report more ROP cases than they did in the past. Because ROP is a preventable cause of blindness, family physicians, paediatrics, and neonatal experts should refer the newborns at risk timely to the eye doctors to be included in screening programmes to ensure diagnosis and to prevent delays in treatment.

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