Retinopathy of Prematurity among 1000-2000 gram Birth Weight Newborn Infants

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Abstract

Objective: The goal of this study was to identify the risk factors of retinopathy of prematurity (ROP) in neonatal intensive care unit in preterm infants born with birth weight 1000-2000g or at gestational age less than 34 weeks.

Material & Methods: From August 2000 to December 2001, 50 preterm newborn infants with birth weights less than 2000 g or gestational age less than 34 weeks admitted to the NICU were studied. Newborn infants with birth weight between 1200-2000g who received more than 6 hours oxygen and newborn infants with birth weight 1000-1200 g regardless of oxygen therapy, who survived until 4 weeks postnatal, were enrolled and followed. Patients underwent indirect ophthalmologic examination by two ophthalmologists between 4-8 weeks post partum. The newborn infants who had ROP were assigned to case group and those without ROP to control group, both groups were reexamined every 2-4 weeks or according to international classification of retinopathy of prematurity (ICROP) advice.

Findings: Fifty newborn infants, 36 (72%) in control group, 14 (28%) in case group, were studied. Gestational age and birth weight of the patients with ROP were significantly lower than those of control group. Duration of oxygen therapy, hyperoxia, acidosis, hypercarbia, hypocarbia and phototherapy are suggested as risk factors contributing to ROP.

Conclusion: The results of this study demonstrate that the ROP frequency remains elevated among premature and very low birth weight infants. Infants at risk for ROP should have screening eye examinations and proper treatment.

Key Words: Retinopathy; Prematurity; Low birth weight; Retrolental fibroplasia

Introduction

Retinopathy of prematurity (ROP) is a vasoproliferative disorder of the eye that primarily affects premature infants weighting 1250g or less that are born before 31 weeks of gestation. This disorder, which usually develops in both eyes, is one of the most
common causes of visual loss in childhood and can lead to lifelong vision impairment and blindness. ROP afflicts over 300,000 infants worldwide\[1,2\]. International incidence is unknown, but the incidence is inversely proportional to the birth weight (16-60%)\[3,4\]. The significant time in history of ROP was 1941-1953; ROP was first described in the medical literature in 1942 by Terry\[2,5\]. In 1952, Campbell theorized that the condition was caused by the use of Oxygen therapy to treat the immature lungs in premature infants\[1,2,6-8\]. ROP is a leading cause of childhood blindness, its impact in developing countries is not well documented and the decision which babies to screen is somewhat controversial. The aim of this study was to identify the risk factors in preterm infants, who were born with birth weight 1000-2000g or at gestational age less than 34 weeks, in order to provide a frame work reducing the incidence of ROP.

**Material & Methods**

This is a prospective, analytic, cross-sectional, case-control study, from August 2000 to December 2001. This study includes 60 preterm newborns with birth weights less than 2000 g, and gestational age less than 34 weeks admitted to the NICU. Newborn infants with a birth weight between 1200 -2000g who received more than 6 hours oxygen and newborn infants with birth weights 1000-1200 g who survived until 4 weeks postnatal, regardless of oxygen therapy, were enrolled and followed in Ghaem Medical Center, Mashad University of Medical Sciences (in Iran). Patients, who died, transferred or did not complete the allocation procedure and for disagreement between ophthalmologists diagnoses are excluded (10 patients). Owing to limited resources, very low birth weight infants (less than 1000g and less than 28 weeks gestational age) also were not included; therefore the study population consisted of large preterm infants at commencement of the study. For all patients we had informed consent from a parent or guardian and the ethics committee on research affairs of the university. All infants were singletons. The records provided information on sex, birth weight, gestational age, mechanical ventilation, oxygen therapy, atrial blood gases (ABG), serum level of bilirubin, phototherapy, apnea, blood exchange transfusion, blood transfusion, sepsis, duration of NPO, and length of hospitalization up to the end of the study.

All patients had an initial ABG and blood culture obtained after admission in the NICU. ABG was obtained q3-6 h during acute phase of disease according to the patient’s condition or until oxygen therapy was discontinued, while simultaneously monitored by pulse oximeter. Blood culture was repeated whenever there was clinical suspicion of sepsis. Serum bilirubin was measured routinely in jaundiced infants. This study defined sepsis as positive bacterial blood culture, hypercarbia as pCO2>50 mmHg, hypocarbia as pCO2<25mmHg, hyperoxia as paO2>80 mm Hg, and acidosis as pH<7.25. Gestational age was assessed according to new Ballard scoring. We did not prescribe recombinant erythropoietin for patients. Indirect ophthalmoscopy was performed by two ophthalmologists separately and retinopathy was confirmed by both. First eye examination was performed between 4-8 weeks post partum, rechecked after 2-4 weeks, and followed according to international classification of retinopathy of prematurity (ICROP) advice. Ophthalmologic evaluation was performed in the office. Two drops containing 2.5% of phenylephrine and 0.5% tropicamide were applied, and then a lid speculum was inserted between the lids. If retinal lesions were detected by both ophthalmologists the newborn was considered a case, patients without ROP were allocated in control group.

Data was analyzed by SPSS software and using student’s t-test and chi-square test.and P-value less than 0.05 was considered statistically significant.
Findings

From 50 newborn infants, ROP was confirmed in 14 (28%) of newborns, and was not present in 36 (72%) patients. The mean gestational age was 33.5 weeks and 31.2 weeks in control and case group respectively. ROP was seen in 4 newborns with gestational age less than 30 weeks, in 8 newborns with gestational age of 30-32 weeks, and in 2 newborns with 32-34 weeks gestational age.

There are significant differences between gestational age, birth weight, episodes of hyperoxia, acidosis and ROP ($P < 0.001$). There is also a significant difference between the mean episodes of hypocarbia and hypercarbia, duration of oxygen therapy and duration of exposure to phototherapy light in two groups. (Tables 1 and 2).

There are not significant differences between sex, serum bilirubin level, sepsis, episodes of apnea, blood exchange transfusion, blood transfusion, and the duration of NPO, duration of hospitalization and use of mechanical ventilation.

Discussion

The present study suggests that the risk factors of ROP in premature infants with birth weight 1000-2000 g are: duration of oxygen therapy, hyperoxia, acidosis, hypercarbia, hypocarbia, and phototherapy.

Retinopathy of prematurity, previously known as Retrolental Fibroplasia (RLF) is a disease of the eye that affects prematurely born babies. International classification of retinopathy of prematurity uses a number of parameters to describe the disease. ROP is categorized on the basis of the severity (stage) and on the basis of the anatomical location of the retina (zone) of disease[1-3]. The circumferential extension of the disease is based on the clock hours. The severity of the disease is classified to stage 1 to 5 and the presence or absence of "Plus Disease" that is the hallmark of rapidly progressive ROP[9,10]. Many babies who develop ROP have stage I or II, which improve with no treatment. Ophthalmoscopic findings in our study were concordant with zone 1 (13 patients), zone 2

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>Case group (N=14)</th>
<th>Control group (N=36)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)</td>
<td>0.7/1</td>
<td>1/1</td>
<td>0.2</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>1000-1700 (mean 1375)</td>
<td>1250-1950 (mean 1668)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gestational age (week)</td>
<td>29-33 (mean 31.2)</td>
<td>31-34 (mean 33.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of NPO(h)</td>
<td>24-120 (mean 52)</td>
<td>12-168 (mean 49)</td>
<td>0.8</td>
</tr>
<tr>
<td>Episodes of apnea</td>
<td>0-10 (mean 3.5)</td>
<td>0-10 (mean 2.05)</td>
<td>0.2</td>
</tr>
<tr>
<td>Duration of phototherapy (h)</td>
<td>72-168 (mean 130)</td>
<td>10-192 (mean 102)</td>
<td>0.04</td>
</tr>
<tr>
<td>Duration of hospitalization(day)</td>
<td>9-33 (mean 19)</td>
<td>7-60 (mean 16)</td>
<td>0.3</td>
</tr>
<tr>
<td>Volume of blood Transfusion (ml)</td>
<td>0-45 (mean 12)</td>
<td>0-60 (mean 5.8)</td>
<td>0.2</td>
</tr>
<tr>
<td>Frequency of transfusion</td>
<td>0-3 (mean 0.8)</td>
<td>0-3 (mean 0.3)</td>
<td>0.1</td>
</tr>
<tr>
<td>number of blood exchange transfusions</td>
<td>4</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Duration of oxygen Therapy (h)</td>
<td>36-120 (mean 66)</td>
<td>6-216 (mean 43)</td>
<td>0.02</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>4</td>
<td>7</td>
<td>0.8</td>
</tr>
</tbody>
</table>
Table 2 - Laboratory characteristics in case and control groups

<table>
<thead>
<tr>
<th>Findings</th>
<th>Case group (N=14)</th>
<th>Control group (N=36)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive blood culture</td>
<td>5</td>
<td>7</td>
<td>0.4</td>
</tr>
<tr>
<td>Serum bilirubin (mg/d)</td>
<td>8-17 (Mean 11.28)</td>
<td>4-21 (Mean 11.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>Hypercarbia (mmHg) (episodes/patient)</td>
<td>2.1</td>
<td>0.9</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypocarbia (mmHg) (mean episodes/patient)</td>
<td>2.2</td>
<td>1.1</td>
<td>0.008</td>
</tr>
<tr>
<td>Acidosis (mean episodes/patient)</td>
<td>3.2</td>
<td>1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pao2&gt;100mmHg (mean episodes/patient)</td>
<td>1</td>
<td>0.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Pao2&gt;80mmHg (mean episodes/patient)</td>
<td>3.2</td>
<td>1.5</td>
<td>0.001</td>
</tr>
</tbody>
</table>

(1 patient) and stage I (11 patients), stage II (2 patients), stage III (1 patient) of ROP.

Many causative factors have been proposed for ROP, only low birth weight, low gestational age and supplemental oxygen therapy following delivery have been consistently associated with disease[11-14]. A multi center study of infants born in 1986-87 reported that of those infants weighing less than 1000g, 81.6% developed ROP, while 46.9% of newborns with birth weights of 1000-1250g developed the disorder. Other investigators reported in babies weighing less than 1700g at birth over 50% will develop ROP[1,5,13,15]. Severe disease is seen especially in babies under 26 weeks' gestation[16]. Including larger preterm infants who are at lower risk for ROP limited accuracy of this study.

ROP may develop in premature infants who have received little or no supplemental Oxygen. The studies were performed within zygosity data for premature twins, concluded that in addition to prematurity and environmental factors, there is a strong genetic predisposition to ROP[1,6,17]. Some other risk factors suggested as contributors to ROP include: race, sex, infants conceived through fertility programs, multiple birth, shock, pneumothorax, bronchopulmonary dysplasia, hyperglycemia, frequent blood transfusions, parenteral nutrition, hypo/hypercarbia, early intubation, hypotention, patent ductus arteriosus, necrotizing enterocolitis, administration of recombinant human erythropoietine to baby, administration of β blockers to mother before delivery, intraventricular hemorrhage, poor postnatal weight gain and Candida sepsis[1,5,11,18,19]. Evidence is provided that light reduction does not decrease incidence of ROP[2,20,21]. No relation exists between ROP and maternal smoking or maternal alcohol intake[1,8,13,21]. Recently Bilirubin is considered as an anti oxidant agent which protects Oxygen damage[22].

In this study we found also significant relation between ROP and the episodes of acidosis, hyperoxia, hypo/hypercarbia, duration of oxygentherapy and phototherapy, but we could not detect significant correlation between ROP and sex, blood transfusion, blood exchange transfusion, sepsis, apnea episodes, serum bilirubin level, the duration of NPO, use of mechanical ventilation and duration of hospitalization.

Enrollments of larger preterm infants who are at lower risk for ROP were a limited capacity of this study.
Conclusion

The results of this study demonstrated that the ROP frequency remained elevated among premature and very low birth weight infants, so prevention of prematurity is essential. Infants at risk for ROP should have screening eye examinations and proper treatment. Meticulous oxygen therapy and control of blood gas in preterm infants are important.

Acknowledgement

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References


